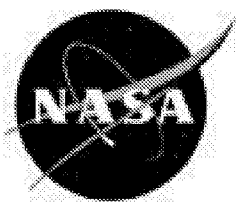
NASA/SP—2000-7011/SUPPL507
December 2000

AEROSPACE MEDICINE AND BIOLOGY

A CONTINUING BIBLIOGRAPHY WITH INDEXES



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Typical Report Citation and Abstract

❶ 19970001126 NASA Langley Research Center, Hampton, VA USA
❷ **Water Tunnel Flow Visualization Study Through Poststall of 12 Novel Planform Shapes**
❸ Gatlin, Gregory M., NASA Langley Research Center, USA Neuhart, Dan H., Lockheed Engineering and Sciences Co., USA;
❹ Mar. 1996; 130p; In English
❺ Contract(s)/Grant(s): RTOP 505-68-70-04
❻ Report No(s): NASA-TM-4663; NAS 1.15:4663; L-17418; No Copyright; Avail: CASI; A07, Hardcopy; A02, Microfiche
❼ To determine the flow field characteristics of 12 planform geometries, a flow visualization investigation was conducted in the Langley 16- by 24-Inch Water Tunnel. Concepts studied included flat plate representations of diamond wings, twin bodies, double wings, cutout wing configurations, and serrated forebodies. The off-surface flow patterns were identified by injecting colored dyes from the model surface into the free-stream flow. These dyes generally were injected so that the localized vortical flow patterns were visualized. Photographs were obtained for angles of attack ranging from 10' to 50', and all investigations were conducted at a test section speed of 0.25 ft per sec. Results from the investigation indicate that the formation of strong vortices on highly swept forebodies can improve poststall lift characteristics; however, the asymmetric bursting of these vortices could produce substantial control problems. A wing cutout was found to significantly alter the position of the forebody vortex on the wing by shifting the vortex inboard. Serrated forebodies were found to effectively generate multiple vortices over the configuration. Vortices from 65' swept forebody serrations tended to roll together, while vortices from 40' swept serrations were more effective in generating additional lift caused by their more independent nature.
❽ Author
❾ *Water Tunnel Tests; Flow Visualization; Flow Distribution; Free Flow; Planforms; Wing Profiles; Aerodynamic Configurations*

Key

1. Document ID Number; Corporate Source
2. Title
3. Author(s) and Affiliation(s)
4. Publication Date
5. Contract/Grant Number(s)
6. Report Number(s); Availability and Price Codes
7. Abstract
8. Abstract Author
9. Subject Terms

AEROSPACE MEDICINE AND BIOLOGY

A Continuing Bibliography (Suppl. 507)

DECEMBER 2000

51
LIFE SCIENCES (GENERAL)

Includes general research topics related to plant and animal biology (non–human); ecology; microbiology; and also the origin, development, structure, and maintenance, of animals and plants in space and related environmental conditions. For specific topics in life sciences see categories 52 through 55.

20000116166 National Bioethics Advisory Commission, Rockville, MD USA

Research Involving Human Biological Materials: Ethical Issues and Policy Guidance, Executive Summary

August 1999; 14p; In English

Report No.(s): PB2000-103305; No Copyright; Avail: National Technical Information Service (NTIS)

Biomedical researchers have long studied human biological materials--such as cells collected in research projects, biopsy specimens obtained for diagnostic purposes, and organs and tissues removed during surgery--to increase knowledge about human diseases and to develop better means of preventing, diagnosing, and treating these diseases. Today, new technologies and advances in biology provide even more effective tools for using such resources to improve medicine's diagnostic and therapeutic potential. Yet, the very power of these technologies raises a number of important ethical issues. In this report, National Bioethics Advisory Commission (NBAC) offers a series of recommendations that have been developed to address perceived difficulties in the interpretation of federal regulations and in the language of position statements of some professional organizations; ensure that research involving human biological materials will continue to benefit from appropriate oversight and review, the additional burdens of which are kept to a minimum; provide investigators and Institutional Review Boards (IRBs) with clear guidance regarding the use of human biological materials in research, particularly with regard to informed consent; provide a coherent public policy for research in this area that will endure for many years and be responsive to new developments in science, and provide the public with increased confidence in research that makes use of human biological materials. In particular, this report provides interpretation to several important concepts and terms in the Common Rule and recommends ways both to strengthen and clarify the regulations and to make the implementation more consistent.

Derived from text

Diseases; Organizations; Policies; Regulations; Ethics; Research; Bioassay

20000116331 NASA Johnson Space Center, Houston, TX USA

Lymphocyte Functions in Microgravity

Pellis, Neal R., NASA Johnson Space Center, USA; Risin, Diane, Wyle Labs., Inc., USA; Sundaresan, A., Wyle Labs., Inc., USA; Cooper, D., La Jolla Inst., USA; [1999]; 1p; In English; 15th, 10-13 Nov. 1999, Seattle, WA, USA; Sponsored by American Society for Gravitational and Space Biology, USA

Contract(s)/Grant(s): NRA-OLMSA-02/NSCORT; No Copyright; Avail: Issuing Activity; Abstract Only

To understand the mechanism of immunity impairment in space it is important to analyze the direct effects of space-related conditions on different lymphocytes functions. Since 1992, we are investigating the effect of modeled and true microgravity (MG) on numerous lymphocyte functions. We had shown that modeled (MMG) and true microgravity inhibit lymphocyte locomotion through type I collagen. Modeled microgravity also suppresses polyclonal and antigen-specific lymphocyte activation. Polyclonal activation of lymphocytes prior to exposure to MMG abrogates the MG-induced inhibition of lymphocyte locomotion. The relationship between activation deficits and the loss of locomotion in MG was investigated using PKC activation by phorbol ester (PMA) and calcium ionophore (ionomycin). Direct activation of PKC by PMA substantially restored the MMG-inhibited lymphocyte locomotion and PHA-induced lymphocyte activation lonomycin by itself did not restore either locomotion or activation of the lymphocytes, indicating that these changes are not related to the impairment in the calcium flux in MMG. Treatment of lymphocytes with PMA before exposure to MMG prevented the loss of locomotion. It was observed that DNA

synthesis is not necessary for restoration of locomotion since mitomicin C treated and untreated cells recovered their locomotion to the same level after PKC activation. Our recent data indicate that microgravity may selectively effect the expression of novel Ca2+ independent isoforms of PKC, in particularly PKC sigma and delta. This provides a new insight in understanding of the mechanisms of MG-sensitive cellular functions.
Author
Lymphocytes; Microgravity; Immune Systems; Gravitational Physiology; Aerospace Medicine

20000116332 NASA Johnson Space Center, Houston, TX USA
Novel Approaches to Cellular Transplantation from the US Space Program
Pellis, Neal R., NASA Johnson Space Center, USA; Diabetes Technology and Therapeutics; 1999; Volume 1, No. 1, pp. 73-75; In English; Copyright; Avail: Issuing Activity; Abstract Only

Research in the treatment of type I diabetes is entering a new era that takes advantage of our knowledge in an ever increasing variety of scientific disciplines. Some may originate from very diverse sources, one of which is the Space Program at National Aeronautics and Space Administration (NASA). The Space Program contributes to diabetes-related research in several treatment modalities. As an ongoing effort for medical monitoring of personnel involved in space exploration activities NASA and the extramural scientific community investigate strategies for noninvasive estimation of blood glucose levels. Part of the effort in the space protein crystal growth program is high-resolution structural analysis insulin as a means to better understand the interaction with its receptor and with host immune components and as a basis for rational design of a "better" insulin molecule. The Space Program is also developing laser technology for potential early cataract detection as well as a noninvasive analyses for addressing preclinical diabetic retinopathy. Finally, NASA developed an exciting cell culture system that affords some unique advantages in the propagation and maintenance of mammalian cells in vitro. The cell culture system was originally designed to maintain cell suspensions with a minimum of hydrodynamic and mechanical sheer while awaiting launch into microgravity. Currently the commercially available NASA bioreactor (Synthecon, Inc., Houston, TX) is used as a research tool in basic and applied cell biology. In recent years there is continued strong interest in cellular transplantation as treatment for type I diabetes. The advantages are the potential for successful long-term amelioration and a minimum risk for morbidity in the event of rejection of the transplanted cells. The pathway to successful application of this strategy is accompanied by several substantial hurdles: (1) isolation and propagation of a suitable uniform donor cell population; (2) management of host immune rejection; (3) protection from the autoimmune component of the disease; and (4) anatomic placement of the engrafted cells that permits timely response to blood sugar levels as well as effective release and deployment of insulin. Bioreactor technology may provide some critical advances for surmounting some of these scientific hurdles. The NASA bioreactor is a horizontally rotating cylinder that is completely filled with culture medium. Gaseous exchange is maintained by a concentric cylinder of permeable silicon. In slow rotation (15-25 rpm) particles of small mass such as cells and tissue aggregates remain suspended in the rotating body of fluid. This novel approach suspends cells without stirring thus, allowing objects of different size mass to colocate and interact in a very low shear environment. In fact, analysis of the forces acting on individual cells in the rotating bioreactor reveals that the cells are continuously falling through the fluid medium. The conditions in the bioreactor permit assembly of cells into aggregates. three-dimensional tissue growth, synthesis of intercellular matrix,10 differentiation, and some sinusoid formations that may serve as a surrogate vasculature for larger tissue segments.
Derived from text
Bioreactors; Culture Techniques; Insulin; Metabolic Diseases; Diabetes Mellitus

20000116339 Notre Dame Univ., Dept. of Biological Sciences, IN USA
Structure/Function Studies of Insect Antifreeze Proteins *Final Report, 1 Jan. 1995 - 31 Dec. 1997*
Duman, John G.; Dec. 31, 1997; 11p; In English
Contract(s)/Grant(s): F49620-1-95-0188
Report No.(s): AD-A380908; AFRL-SR-BL-TR-00-0369; No Copyright; Avail: Defense Technical Information Center (DTIC)

Antifreeze proteins (AEPs) from overwintering larvae of the beetle Dendroides canadensis are the most active AFPs known. Thirteen similar AFPs were purified and characterized. These consist of varying numbers of 12 and 13 mer repeating units with the consensus sequence Cys-Thr-X3-Ser-x5-x6-Cys-X8-X9-Ala-X11-Th-X13 where X3 and X1 tend toward charged residues, X5 toward threonine or serine, X9 toward asparagine or aspartate, X6 toward asparagine or lysine, and X13 toward alanine. All of the cysteine residues are disulfide bridged, usually to the other cysteine within the repeat unit. This provides an extremely stable protein structure and probably positions the hydroxyl group of the highly conserved serine and threonine residues so they can hydrogen bond to ice, a requisite for the antifreeze activity. The secondary structure of these AFPs is 46% 6-sleet, 39% turn, 2% helix and 13% random. Several low molecular mass salutes, mostly organic, were shown to enchance the activity of the AFPs several fold. The most active of these is citrate which enchances activity as much as sixfold. Succinate, malate, aspartate,

glutamate, ammonium sulfate, glycerol, sorbitol, alanine and ammonium bicarbonate were also very effective. The mechanism of the enhancement is unknown.
DTIC
Antifreezes; Insects; Larvae; Proteins; Glutamic Acid; Hydroxyl Radicals; Ammonium Sulfates

20000116346 Agency for Toxic Substances and Disease Registry, Atlanta, GA USA
Report of the Expert Panel Workshop on the Psychological Responses to Hazardous Substances.
Tucker, P.; 2000; 94p; In English; Original contains color illustrations
Report No.(s): PB2001-100288; No Copyright; Avail: CASI; A05, Hardcopy; A01, Microfiche

This purpose of this workshop was to thoroughly explore and examine all that is known about how communities and individuals respond socially and psychologically to hazardous substances and the possible effects of those responses on their health.
NTIS
Physiological Effects; Psychological Effects; Psychophysiology; Stress (Psychology)

20000116497 Ibadan Univ., Nigeria
Background radiation and man-made and sources of radiation
Babalola, I. A.; Dec. 31, 1997; 13p; In English; National workshop on radiation protection and waste management
Report No.(s): DE99-626787; INIS-NG-0010; No Copyright; Avail: Department of Energy Information Bridge, Microfiche

This paper describes the development of the use of the atom and its present applications in food and agriculture, industry medicine and health care, energy- environment and research. These applications have inevitably led to concerns about nuclear safety and radioactive waste management and the need for the adoption of procedures for control, safe use and disposal of radioactive sources.
NTIS
Atoms; Food; Background Radiation; Safety Management; Energy Technology

20000116518 Czech Technical Univ., Faculty of Nuclear Sciences and Physical Engineering, Prague, Czechoslovakia
Proceedings of the IRPA regional symposium on radiation protection in neighbouring countries of Central Europe
Dec. 31, 1998; 24p; In English; IRPA regional symposium on radiation protection in neighboring countries of Central Europe
Report No.(s): DE99-626783; INIS-CZ-0021; No Copyright; Avail: Department of Energy Information Bridge

At the Symposium, a total of 169 papers were presented at six sessions: 1. General aspects of radiation protection; 2. Natural radiation exposure; 3. Radiation protection at workplace; 4. Environmental aspects of radiation protection; 5. Instrumentation of methods; 6. Non-ionizing radiation protection. Of the papers, 162 were input to INIS.
NTIS
Radiation Dosage; Conferences; Radiation Protection

20000116593 Old Dominion Univ., Research Foundation, Norfolk, VA USA
Multi-Dimensional Data Assimilation for Physical-Biological Models *Final Report, Jun. 1998 - Jun. 2000*
Hofmann, Eileen E., Old Dominion Univ., USA; [2000]; 3p; In English
Contract(s)/Grant(s): N00014-98-1-0100
Report No.(s): AD-A380222; No Copyright; Avail: Defense Technical Information Center (DTIC)

This study focused on the development of Empirical Orthogonal Function (EOF) techniques that can be used to determine data needs for marine ecosystem models. The EOF structures allow determination of the primary interconnections of the ecosystem, which in turn, allow insight into the processes that need to be well represented in the forward model developed for a particular ecosystem. The method was tested with a model developed to simulate time development of lower trophic levels observed in an enclosed microcosm. For this system, the EOF model improved data reproducibility even when a reduced number of eigenstructures was used. The results imply that the model and data were inconsistent. The EOF approach used in this study potentially provides a powerful method for evaluating data%model consistency, and for determining data needs for marine ecosystem models, which are important factors in combining data and forward models in a data assimilative mode.
DTIC
Bionics; Ecosystems; Marine Environments; Marine Biology; Environment Models

20000117675 Wisconsin Univ., Madison, WI USA
Investigating the Role of Cooperative Interactions Between the Neu Protooncogene and the Other erbB Family Members in Rat Mammary Carcinogenesis *Annual Report, 1 Jul. 1998 - 30 Jun. 1999*
Gould, Michael N., Wisconsin Univ., USA; Watson, Philip, Wisconsin Univ., USA; July 1999; 19p; In English
Contract(s)/Grant(s): DAMD17-96-1-6263
Report No.(s): AD-A381235; No Copyright; Avail: Defense Technical Information Center (DTIC)

The phenotype of two additional MMTV-neu N transgenic rats has been determined. Females of both of these lines do not display an abnormal phenotype. In contrast, males of the line 6500 develop mammary carcinomas with an average latency of 387 days. This phenotype is highly penetrant, with 77.8 percent and 100 percent of the transgenic males carcinoma positive at 14 months and 18 months of age, respectively. Among those rats with carcinomas, the average number of carcinomas per rat was 9.6 and 11.7 for 14 months and 18 months of age, respectively. Nuclease protection assays have shown that 6500 transgenic females overexpress neu within the mammary gland by approximately tenfold. This demonstrates that the lack of mammary carcinomas in the 6500 females is not due ot lack of neu overexpression in the mammary gland. Experiments are in progress to investigate the mechanisms underlying the male-specific mammary carcinogenesis in line 6500. In additional experiments, retrovival vectors were used to direct expression of EGFR, erbB3, or erbB4 in the mammary gland of the 6500 transgenic and non-transgenic females. None of these retrovival constructs resulted in mammary carinomas for transgenic or non-transgenic females.
Author
Cancer; Carcinogens; Females; Males; Mammary Glands

20000117705 Gordon Research Conferences, Inc., Kingston, RI USA
Molecular Membrane Biology Gordon Research Conference *Final Report, 1 May 1999 - 30 Apr. 2000*
Rapoport, Tom, Gordon Research Conferences, Inc., USA; Storm, Carlyle B., Gordon Research Conferences, Inc., USA; July 2000; 7p; In English; Molecular Membrane Biology, 4-9 Jul. 1999, Andover, NH, USA
Contract(s)/Grant(s): DAMD17-99-1-9470
Report No.(s): AD-A380876; No Copyright; Avail: Defense Technical Information Center (DTIC)

The Molecular Membrane Biology Gordon Research Conference schedule is presented.
DTIC
Conferences; Membranes; Molecular Biology; Proteins; Metabolism; Cells (Biology)

20000119104 Pennsylvania State Univ., Office of Sponsored Programs, University Park, PA USA
Life in Extreme Environments Research #2 *Final Report, 1 Aug. 1999 - 31 Jul. 2000*
Fisher, Charles R., Pennsylvania State Univ., USA; [2000]; 2p; In English
Contract(s)/Grant(s): NCC2-5341; No Copyright; Avail: Issuing Activity; Abstract Only

The goal of this project was to collect suspended particles and microbes for spectral analysis from deep water around hydrothermal vent study sites on the Juan de Fuca Ridge. to accomplish this, the McLane WTS 6-24-47 Sampler (McLane Research Laboratories, Falmouth, MA) was used. The WTS sampler is a programmable unit which is able to collect individual samples across twenty-four 47mm diameter filters at predetermined intervals and duration. Although only one successful deployment was needed, a maximum of three 3 deployments were possible (deployment opportunities were limited by the number of battery packs available). The initial behavior of the WTS and the ship's schedule both indicated that three deployments would be possible. However, it was revealed upon recovery after the first deployment that the WTS failed as it was preparing to collect its first sample.
Derived from text
Spectrum Analysis; Deep Water; Hydrothermal Systems; Vents

20000121132 NASA Ames Research Center, Moffett Field, CA USA
Resting Energy Expenditure of Rats Acclimated to Hyper-Gravity
Wade, Charles E., NASA Ames Research Center, USA; Moran, Megan M., Lockheed Martin Engineering and Science Services, USA; Oyama, Jiro, NASA Ames Research Center, USA; Schwenke, David, NASA Ames Research Center, USA; [2000]; 1p; In English; 21st; Gravitational Psysiology, USA; No Copyright; Avail: Issuing Activity; Abstract Only

To determine the influence of body mass and age on resting energy expenditure (EE) following acclimation to hyper-gravity, oxygen consumption (VO2) and carbon dioxide production (VCO2) were measured to calculate resting energy expenditure (EE), in male rats, ages 40 to 400 days, acclimated to 1.23 or 4.1 G for a minimum of two weeks. Animals were maintained on a centrifuge to produce the hyper-gravity environment. Measurements were made over three hours in hyper-gravity during the

period when the lights were on, the inactive period of rats. In rats matched for body mass (approximately 400 g) hyper-gravity increased VO2 by 18% and VCO2 by 27% compared to controls, resulting in an increase in RER, 0.80 to 0.87. There were increases in resting EE with an increase in gravity. This increase was greater when the mass of the rat was larger. Rating EE for 400g animals were increased from 47 +/- 1 kcal/kg/day at 1 G, to 57 +/- 1.5 and 5.8 +/- 2.2 kcal/kg/day at 2,3 and 4.1 G, respectively. There was no difference between the two hyper-gravity environments. When differences in age of the animals were accounted for, the increase in resting EE adjusted for body mass was increased by over 36% in older animals due to exposure to hyper-gravity. Acclimation to hyper-gravity increases the resting EE of rats, dependent upon body mass and age, and appears to alter substrate metabolism. Increasing the level of hyper-gravity, from 2.3 to 4.1 G, produced no further changes raising questions as to a dose effect of gravity level on resting metabolism.
Author
Gravitational Effects; Acclimatization; Experimentation

20000121145 Texas Univ. Health Science Center, Dept. of Radiology, San Antonio, TX USA
Hybridization Oven for Research Exploring Molecular Changes in Cells Exposed to Microwave Radiation *Final Report, 25 Aug. - 24 Dec. 1999*
Meltz, Martin, Texas Univ. Health Science Center, USA; December 1999; 1p; In English
Contract(s)/Grant(s): F49620-99-1-0315
Report No.(s): AD-A382171; AFRL-SR-BL-TR-00-0034; No Copyright; Avail: CASI; A01, Microfiche; A01, Hardcopy
Normal human monocytes exposed to pulsed wave 2.45 GHz RFR for a continuous period of 90 minutes were analyzed for genes that are involved in double strand break-repair and mis-match repair. The hybridization chamber was used to successfully carry out the RNase protection assay. In addition, MM-6 cells exposed to the pulsed wave 2.45GHz RFR for a continuous period of 90 minutes was used to characterize the subunit composition of nuclear factor-kB. The hybridization chamber was used to successfully perform the Immunobloting and Enhanced Chemiluminescence detection of expressed proteins.
DTIC
Assaying; Microwaves; Radiation Effects; Detection; Molecules; Cells (Biology); Ovens

20000121165 Universal Energy Systems, Inc., Dayton, OH USA
Evaluation of Life Sciences Research Program *Final Report, 1 Mar. 1999 - 29 Feb. 2000*
Flory, Judith M., Universal Energy Systems, Inc., USA; Jun. 23, 2000; 182p; In English
Contract(s)/Grant(s): F49620-95-C-0026
Report No.(s): AD-A379772; AFRL-SR-BL-TR-00-0297; No Copyright; Avail: CASI; A02, Microfiche; A09, Hardcopy
During the performance of this contract UES, Inc. provided research evaluations services for the Chemistry and Life Sciences Directorate, Air Force Office of Scientific Research in the areas of Polymer Chemistry, Surface Science, Theoretical Chemistry, Molecular Dynamics, Chronobiology and Neural Adaptation, Perception and Cognition, Sensory Systems and Toxic Biological Interactions. Evaluations were secured for 506 AFOSR Grant Proposals. UES provided administrative tasks for following meeting functions: Twenty-one program reviews - 1 in the area of Chronobiology and Neural Adaptation; 9 in the area of Surface Science; 5 in the areas of Molecular Dynamics and Theoretical Chemistry; 3 in area of Polymer Chemistry; 3 in the area of Toxic Biological Interactions. Twelve workshops were held; 3 in the area of Chronobiology and Neural Adaptation; 3 in the area of Polymer Chemistry. Thirteen panel meetings were held; 8 in Molecular Dynamics and Theoretical Chemistry; 4 in Polymer Chemistry and 1 in the area of Chronobiology and Neural Adaptation.
DTIC
Life Sciences; Research

20000121170 Sverdrup Technology, Inc., Moffett Field, CA USA
Evaluation of Fieldbus and OPC for Advanced Life Support
Boulanger, Richard P., Sverdrup Technology, Inc., USA; Cardinale, Paul, Sverdrup Technology, Inc., USA; Bradley, Matthew, NASA Ames Research Center, USA; [2000]; 1p; In English; 4th; Life Support and Biosphere Science, 6-9 Aug. 2000, Baltimore, MD, USA
Contract(s)/Grant(s): RTOP 131-20-10; No Copyright; Avail: Issuing Activity; Abstract Only
FOUNDATION(Tm) Fieldbus and OP(TM) (OLE(TM)for Process Control) technologies were integrated into an existing control system for a crop growth chamber at NASA Ames Research Center. FOUNDATION(TM) Fieldbus is a digital, bi-directional, multi-drop, serial communications network which functions essentially as a LAN for sensors. FOUNDATION(TM) Fieldbus is heterarchical, with publishers and subscribers of data performing complex control functions at low levels without centralized control and its associated overhead. OPC(TM) is a set of interfaces which replace proprietary

drivers with a transparent means of exchanging data between the fieldbus and applications. The objectives were: (1) to integrate FOUNDATION(TM) Fieldbus into existing ALS hardware and determine its overall effectiveness and reliability and, (2) to quantify any savings produced by using fieldbus and OPC technologies. We encountered several problems with the FOUNDATION(TM) Fieldbus hardware chosen. Our hardware exposed 100 data for each channel of the fieldbus. The fieldbus configurator software used to program the fieldbus was simply not adequate. The fieldbus was also not inherently reliable. It lost its settings twice during our tests for unknown reasons. OPC also had issues. It did not function at all as supplied, requiring substitution of some of its components with those from other vendors. It would stop working after a fixed period of time. Certain database calls eventually lock the machine. Overall, we would not recommend FOUNDATION(TM) Fieldbus: it was too difficult to implement with little overall added value. It also seems unlikely that FOUNDATION(TM) Fieldbus will gain sufficient penetration into the laboratory instrument market to ever be cost effective for the ALS community. OPC had good reliability and performance once a stable installation was achieved. It allowed a rapid change to an alternative software strategy when our first strategy failed. It is a cost effective solution to distributed control systems development.
Author
Active Control; Life Support Systems; Reliability; Stability; Systems Engineering; Electronic Control

20000121326 NASA Ames Research Center, Moffett Field, CA USA
The Evolution of Sulfide Tolerance in the Cyanobacteria
Miller, Scott R., NASA Ames Research Center, USA; Bebout, Brad M., NASA Ames Research Center, USA; [2000]; 1p; In English; Astrobiology Workshop, 3-5 Apr. 2000, Moffett Field,, USA
Contract(s)/Grant(s): RTOP 344-50-92-02; No Copyright; Avail: Issuing Activity; Abstract Only

Understanding how the function of extant microorganisms has recorded both their evolutionary histories and their past interactions with the environment is a stated goal of astrobiology. We are taking a multidisciplinary approach to investigate the diversification of sulfide tolerance mechanisms in the cyanobacteria, which vary both in their degree of exposure to sulfide and in their capacity to tolerate this inhibitor of photosynthetic electron transport. Since conditions were very reducing during the first part of Earth's history and detrital sulfides have been found in Archean sediments, mechanisms conferring sulfide tolerance may have been important for the evolutionary success of the ancestors of extant cyanobacteria. Two tolerance mechanisms have been identified in this group: (1) resistance of photosystem II, the principal target of sulfide toxicity; and (2) maintenance of the ability to fix carbon despite photosystem II inhibition by utilizing sulfide as an electron donor in photosystem I - dependent, anoxygenic photosynthesis. We are presently collecting comparative data on aspects of sulfide physiology for laboratory clones isolated from a variety of habitats. These data will be analyzed within a phylogenetic framework inferred from molecular sequence data collected for these clones to test how frequently different mechanisms of tolerance have evolved and which tolerance mechanism evolved first. In addition, by analyzing these physiological data together with environmental sulfide data collected from our research sites using microelectrodes, we can also test whether the breadth of an organism's sulfide tolerance can be predicted from the magnitude of variation in environmental sulfide concentration it has experienced in its recent evolutionary past and whether greater average sulfide concentration and/or temporal variability in sulfide favors the evolution of a particular mechanism of sulfide tolerance.
Author
Bacteria; Sulfides; Tolerances (Physiology)

20000121333 Missouri Univ., Columbia, MO USA
Estrogen Effects on Breast Tumor Growth in Estrogen Receptor-Minus Mice *Final Report, 15 Aug. 1996 - 15 Aug. 1998*
Lubahn, Dennis B., Missouri Univ., USA; September 1998; 33p; In English
Contract(s)/Grant(s): DAMD17-96-1-6055
Report No.(s): AD-A382532; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

Although nearly half of human breast cancers at diagnosis are estrogen-responsive and respond to antiestrogen therapy at least for a time, more than half are estrogen receptor negative (ER-) and are predicted to be estrogen-nonresponsive tumors. However, some tumors which are ER- appear to respond to antiestrogen therapy in patients, which is beneficial because antihormonal therapy is less toxic than the alternative chemotherapy. The SCID mouse model has been recently used to study the hormonal dependence of growth of human breast cancer cells as tumors. Recent work has identified a potential model system where ER- breast cancer cells are estrogen- independent in cell culture, and yet intriguingly show estrogen-stimulated growth as tumors in SCID mice. This model system will extend understanding of the host contribution to tumor growth by isolating the host portion of estrogen-stimulated breast tumor growth. The potential to control tumor growth by modulating the host animal mechanism would be of particular value in the treatment of estrogen- nonresponsive tumors which recur alter "breakthrough" of tamoxifen therapy, as well as tumors that are ER- and assumed to be estrogen-nonresponsive at diagnosis. Understanding how estrogens can

lead to the increased growth of estrogens-nonresponsive breast tumors may lead to new mechanisms to better control the growth of estrogens-independent breast cancer.
DTIC
Hormones; Diagnosis; Cells (Biology); Chemotherapy; Estrogens; Mammary Glands; Cancer

20000121342 University of Southern California, Los Angeles, CA USA
Characterization of the BRCA1 Protein Product *Annual Report, 1 Aug. 1998 - 31 Jul. 1999*
Park, John J., University of Southern California, USA; Press, Michael, University of Southern California, USA; August 1999; 13p; In English
Contract(s)/Grant(s): DAMD17-97-1-7161
Report No.(s): AD-A382528; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

Breast cancer is the second leading cause of cancer-related death among women in the USA. Approximately 5-10% of breast cancer cases are associated with inheritable genetic factors. Two familial breast cancer susceptibility genes, BRCA1 and BRCA2, have been isolated to date, with a third gene, BRCA3, still being actively sought. Mutations in BR CA1 are associated with both ovarian and breast cancer, while mutations in BRCA2 are associated with breast cancer in both women and men. It is not known why this difference occurs, but these findings may have important implications for the development of future surveillance, diagnosis, and treatment strategies of familial breast cancer. In keeping with the design of our original proposal, we have successfully generated a panel of monoclonal antibodies directed against various regions of the BRCA2 protein as a result of three independent fusions. In addition, we have cloned the full-length BRCA2 coding sequence into various mammalian expression vectors to study BRCA2 function in either transient or stable-inducible expression systems. We are now in the process of characterizing our antibodies and beginning experiments studying aspects of BRCA2's putative functions in both DNA-repair and transcriptional activation.
DTIC
Mammals; Proteins; Genes; Mammary Glands; Cancer; Diagnosis

20000121344 California Univ., San Francisco, CA USA
Effects of c-Myc and TGF-Alpha on Polarized Membrane Traffic *Annual Report, 30 Sep. 1998 - 29 Sep. 1999*
Altschuler, Y., California Univ., USA; Mostov, Keith E., California Univ., USA; October 1999; 15p; In English
Contract(s)/Grant(s): DAMD17-97-1-7326
Report No.(s): AD-A382519; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

In polarized epithelial cells, components of the membrane fusion machinery, the t-SNAREs syntaxin 2, 3, 4 and SNAP-23 are differentially localized at the apical and/or basolateral plasma membrane domains. Surprisingly, all of these t-SNAREs redistribute to intracellular locations when cells lose their cellular polarity during mammary carcinogenesis. Apical SNAREs re-localize to the previously characterized vacuolar apical compartment (VAC) while basolateral SNAREs redistribute to a novel organelle that appears to be the basolateral equivalent of the VAC. Both intracellular plasma membrane compartments' are associated with the actin cytoskeleton and receive membrane traffic from cognate apical or basolateral pathways, respectively. These findings demonstrate a fundamental shift in plasma membrane traffic towards intracellular compartments while protein sorting is preserved when epithelial cells lose their cell polarity.
DTIC
Membranes; Mammary Glands; Cancer; Polarization

20000121348 Boston Univ., Boston, MA USA
Role of TGF-B1-Mediated Down Regulation of NF-kB/Rel Activity During Growth Arrest of Breast Cancer Cells *Annual Report, 1 May 1998 - 30 Apr. 1999*
Kim, Dong, Boston Univ., USA; Sonenshein, Boston Univ., USA; May 1999; 16p; In English
Contract(s)/Grant(s): DAMD17-98-1-8034
Report No.(s): AD-A381151; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

The NF-kappaB/Rel family of dimeric transcription factors has been shown to promote cell survival, and increasing evidence suggests involvement in carcinogenesis. Recently, NF-kappaB/Rel was found to be constitutively active in the nuclei of human breast cancer cell lines, as well as in 7,12-dimethylbenz(a) anthracene (DMBA)-induced mammary tumors from Sprague-Dawley rats (S-D). Malignantly transformed human mammary epithelial cells (HMEC), derived by carcinogen treatment of non-tumorigenic parental MCF- 1 OF cells displayed increased constitutive NF-KappaB activation. In premalignant HMECs immortalized by carcinogen treatment in vitro, NF-kappaB activity was dysregulated in quiescence. Six founder lines of transgenic mice with targeted ectopic expression of the c-Rel subunit in the mammary gland were established, and studies are in

progress to directly test the role of NF-kappaB/Rel in the mammary gland. AhR and RelA synergized to transactivate the c-myc promoter in the MCF- 1 OF HMECs, as well as in the Hs578T breast cancer cells. These results suggest that the activation of NF-kappaB/Rel and AhR may be critically involved in proliferation and/or malignant transformation of the mammary gland and its functional target may be the c-myc proto-oncogene. Overall, these studies provide evidence for involvement of the AhR, NF-%B/Rel, and c-Myc proteins in a common pathway towards malignant progression of mammary epithelial cells.
DTIC
Mammary Glands; Cancer; Proteins; Epithelium; Cells (Biology); In Vitro Methods and Tests

20000121353 Minnesota Univ., Minneapolis, MN USA
Development of a New Mouse Model to Study the Interactions of Obesity on the Development of Breast Cancer *Annual Report, 1 Sep. 1998 - 31 Aug. 1999*
Cleary, Margot, Minnesota Univ., USA; September 1999; 20p; In English
Contract(s)/Grant(s): DAMD17-97-1-7055
Report No.(s): AD-A381223; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy
Hybrid transgenic/genetically obese mice have been bred to evaluate the effects of obesity and weight gain on mammary tumor development.
DTIC
Models; Mammary Glands; Cancer; Mice; Obesity

52
AEROSPACE MEDICINE

Includes the biological and physiological effects of atmospheric and space flight (weightlessness, space radiation, acceleration, and altitude stress) on the human being; and the prevention of adverse effects on those environments. For psychological and behavioral effects of aerospace environments see 53 Behavioral Science. For the effects of space on animals and plants see 51 Life Sciences.

20000115486 Air Force Academy, Dean of Faculty, CO USA
Near Infrared, High Energy, Ultrashort Pulse Laser-Light Exposure Genetically Induces p53, a Gene in the DNA Repair and Cell Suicide Pathways in Cultured Human Cells
Obringer, John W., Air Force Academy, USA; Phipps, Steve, Air Force Academy, USA; Johnson, Martin D., Air Force Academy, USA; Nov. 1999; 13p; In English; Prepared in collaboration with B&J Enterprises, Inc., Colorado Springs, Colorado.
Report No.(s): AD-A381797; USAFA-TR-2000-01; No Copyright; Avail: CASI; A03, Hardcopy; A01, Microfiche
The use of laser light for targeting devices and weapons has sharply increased the likelihood that aircrew and support personnel will be exposed to laser light during operations. The increased potential for exposure of humans highlights the need for scientifically-based safety standards for laser exposure at the ultrashort pulse lengths. Current safety standards are largely extrapolations of exposure limits at longer pulse lengths using a minimal visible lesion endpoint in the Rhesus monkey retinal model. A non-animal model for assessing laser-light damage to tissue, particularly human, is quite desirous for obvious scientific, political, and fiduciary reasons. We assessed the sublethal insult to human cells using a tissue culture system for specific genes that have been shown to be important in several biological processes that could lead to cancer or cell death. Using the CAT-Tox (L) (Xenometrix, Inc.) assay, it appears that 1064 nm, nanosecond pulses of laser light is sensed and induces several stress response genes, including p53, a gene in the DNA repair and apoptosis (cell suicide) regulatory pathways in a dose dependent fashion. This approach provides insight into a more global methodology for characterizing environmental stressors via genetic profiling.
DTIC
Exposure; Laser Beams; Cells (Biology); Culture Techniques; Assaying; Cancer; Genes; High Power Lasers; Tissues (Biology); Deoxyribonucleic Acid

20000116072 Naval Health Research Center, San Diego, CA USA
Review of the Naval Health Research Center's Development of Medical Information Systems for Far-Forward Echelons of Care: 1983-1997 *Final Report, Jan. 1983-Dec. 1997*
Tropeano, Anne M.; Pugh, William M.; Dec. 1997; 32p; In English
Contract(s)/Grant(s): Proj-M2332
Report No.(s): AD-A381330; NHRC-00-07; No Copyright; Avail: CASI; A03, Hardcopy; A01, Microfiche
It is imperative that medical treatment information be gathered quickly and accurately to ensure continuity of care at far-forward echelons. Each echelon employs a manual method of recording the medical information required for that particular

level of care. The methods in use prior to and during the Vietnam War revealed the need for considerable improvements in medical information documentation, patient registration, patient tracking, facility status reporting, and effective transference of data throughout each of the first three echelons of care. The US military targeted these inadequacies for development; automation was determined as the direction in which documentation techniques could most significantly be enhanced. The Naval Health Research Center (NHRC) has been an integral part of the development of automation for the far-forward echelons of care. The prototypes designed by NHRC for Echelons I and II can successfully raise the standard of treatment while simultaneously reducing the number of individuals needed for administrative duties, and increasing the number of medical staff available for patient care. An overview of NHRC's work in automation from 1983 to 1997 is presented.
DTIC
Information Systems; Medical Services; Automation; Health

20000116214 Pacific Northwest National Lab., Richland, WA USA
Using Mode of Action of Assess Health Risks From Mixtures of Chemical/Physical Agents *Annual Report*
December 1998; 17p; In English
Report No.(s): AD-A379649; No Copyright; Avail: Defense Technical Information Center (DTIC)

Mixtures of carcinogenic chemicals are a major problem in ground water and soils on DoD and DOE facilities. While there is frequently data available for interactions between chemicals to judge risks from short term exposures, data that describe how interactions influence the development of cancer are very rare. This is largely because of the high cost associated with conducting complex interaction studies over the lifetime of experimental animals. Therefore, it is important that the limited resources that are available for studying interactions be directed towards the development of general principles that can be applied to wide variety of circumstances. The co- occurrence of chlorinated solvents at DoD and DOE facilities such as trichloroethylene (TCE), tetrachloroethylene (PERC) and carbon tetrachloride (CT) is a case in point.
DTIC
Health; Toxicity; Carcinogens; Chlorination; Cancer; Chemical Compounds; Solvents

20000116215 Army Medical Center, Aurora, CO USA
Prevention and Control of Plague
September 1995; 105p; In English
Report No.(s): AD-A379617; USACHPPM-TG-103; No Copyright; Avail: Defense Technical Information Center (DTIC)

Plague can infect a wide variety of wild and domestic animals, although some species are much more susceptible than others. Plague is believed to circulate in small rodent populations such as mice, rats, and chipmunks, causing little mortality. Known, probable, and susceptible primary maintenance hosts of plague include rodent species that exhibit: (1) Moderately high resistance to plague. (2) Broad heterogeneity to challenge with Yersinia pestis within a population. (3) Long multiestrous breeding season with successive multiple litters and high reproductive potential. (4) Short natural life expectancy and a high replacement rate of individuals in a population. Occasionally, populations of more susceptible mammals (e.g., prairie dogs, rock squirrels and California ground squirrels) are infected with plague. These rodents live, for the most part, in colonies covering large areas of land. When a plague outbreak within these colonial rodent populations occurs, the potential for human exposure to infected mammals and fleas increases greatly. Plague-susceptible rodents are called "amplifying hosts" because they are highly infective and enable the disease to spread rapidly.
DTIC
Breeding (Reproduction); Reproduction (Biology); Mammals; Mortality; Diseases; Exposure

20000116216 Burnham Inst., La Jolla, CA USA
Training in Support of Research Project Entitled "Tumor Cell De-adhesion by Aberrant, Single Skubmit Integrins" *Annual Report, 1 Jul. 1998 - 30 Jun. 1999*
Zhang, Yan, Burnham Inst., USA; July 1999; 6p; In English
Contract(s)/Grant(s): DAMD17-96-1-6212
Report No.(s): AD-A379615; No Copyright; Avail: Defense Technical Information Center (DTIC)

My purpose is try to identify a plasma membrane protein fingerprint which can be used to distinguish invasive breast cancer cell lines from non- invasive breast cancer lines. The methods included those for purification of plasma membrane proteins , extraction of proteins using urea/thiourea mixture, a standard procedure for 2D PAGE, excision of polypeptide "spots" from gels, trypsin digestion, MALDI TOF mass spectrometry and database searching for protein identity are well-established for this project. Three breast cancer cell lines (MDA-MB435, MDA-MB23 1 and MCF7) with different metastatic potential have been grown and 2-D maps of plasma membrane proteins have been generated in the laboratory. Computer- assisted analysis of the 2D polypeptide

pattern showed that 56% of the polypeptide spots were the same between MCF7 and MDA-MB23 1 (two non-metastatic Breast Cancer cell lines), only 42% of the polypeptide spots were the same between MCF7 and MDA-MB435 (metastatic vs non-metastatic Breast Cancer cell lines). This differential expression of proteins is being characterized in order to determine which proteins are important to the metastatic condition. A number of proteins from the 2D gels has been identified by MALDI TOF mass spectrometry. Recently, antibody library phage display, has been expanded for further identifying the plasma membrane proteins.
DTIC
Plasmas (Physics); Cells (Biology); Mammary Glands; Cancer; Proteins; Adhesion; Antibodies

20000116223 Baylor Coll. of Medicine, Houston, TX USA
The Role of Cyclin Dependent Kinase Inhibitor, CIP1, in Breast Cancer *Final Report, 15 Sep. 1994 - 14 Sep. 1999*
Harper, J. W.; Oct. 1999; 27p; In English
Contract(s)/Grant(s): DAMD17-94-J-4399
Report No.(s): AD-A381538; No Copyright; Avail: Defense Technical Information Center (DTIC)

The final report for my award, DAMDl7-94-J-4399 was prematurely submitted in the Fall of 1998 and approved in 1999. This report was changed from a final to an annual by the Office of the Deputy Chief of Staff for Information Management due to the fact that we had asked for and was granted a one year no cost extension. This extension allowed us to finish up our work on the p2l knockout mouse, as summarized below, and led to an additional publication. The attached material is submitted as an appendices to our report submitted in the Fall of 1998. The Fall 1998 report should be reclassified as a final and this award closed. All pertinent information relating to a final report can be found in the Fall 1998 report.
DTIC
Mammary Glands; Cancer; Information Systems; Inhibitors

20000116307 Pennsylvania Univ., Medical Image Processing Group, Philadelphia, PA USA
A Novel Fuzzy Topological Approach to the Detection of Mammographic Lesions and Qualifications of Parenchymal Density *Annual Report, 1 Aug. 1998-31 Jul. 1999*
Udupa, Jayaram K.; Aug. 1999; 33p; In English
Contract(s)/Grant(s): DAMD17-97-1-7271
Report No.(s): AD-A382475; No Copyright; Avail: CASI; A03, Hardcopy; A01, Microfiche

This research focuses on mammographic image processing for the purpose of density quantification, lesion detection and classification. The approaches proposed are different from those taken in the literature in two respects: (1) They emphasize on identifying the dense regions and analyzing their parenchymal architecture. (2) They use a novel fuzzy connectedness method of object definition and image segmentation. During this report period, the following have been accomplished. The development of a novel method of defining the "hanging togetherness" of dense regions via scale-based affinity and connectedness. An interactive method of lesion segmentation using live wire. An automatic, validated method of mammographic density quantification and the development of a host of intensity-based parameters that are more accurate than the measure of the area of dense regions. A novel method of detecting architectural distortions without explicitly delineating lesions (the method being tested for its effectiveness in predicting the on- set of lesions).
DTIC
Computer Techniques; Diagnosis; Image Processing; Fuzzy Systems; Connective Tissue; Identifying; Imaging Techniques

20000116308 Michigan Univ., Ann Arbor, MI USA
An Examination of Ultrasound Measured Tissue Perfusion on Breast Cancer *Final Report, 1 Jun. 1994-30 Nov. 1998*
Fowlkes, Jeffrey B.; Dec. 1998; 37p; In English
Contract(s)/Grant(s): DAMD17-94-J-4144
Report No.(s): AD-A382522; No Copyright; Avail: CASI; A03, Hardcopy; A01, Microfiche

Mammography has proven reliable as a screening tool for breast cancer. However, its specificity may be as low as 10% as evidenced by the number of biopsies recommended compared to the number of cancers. This research was designed to develop measurement techniques for tissue perfusion including ultrasound contrast agent interruption and decorrelation techniques. Contrast interruption allows control of contrast agent flow in selected vessels and is used in conjunction with common ultrasound imaging methods that measure contrast agent signal levels dynamically or statically. The technique provides temporally sharp boluses not achievable by Iv administration and durations similar to arterial administration without catheterization. These are important attributes for tissue perfusion measurements by indicator-dilution techniques. The technique can also be used to eliminate the flow of contrast agents in selected vessels to demonstrate the vascular supply for specific tissues. Contrast

decorrelation measures motion of contrast through the ultrasound beam by examining the gradual loss of speckle coherence. The technique directly estimates a mean transit time, and at least in preliminary studies, appears to be quite angle independent. With certain modifications, the technique may directly yield perfusion in a real-time imaging application of flow in ultrasound accessible tissues.
DTIC
Cancer; Mammary Glands; Real Time Operation; Imaging Techniques; Ultrasonics; Tissues (Biology)

20000116310 Scripps Research Inst., La Jolla, CA USA
Chronic Stress and Neuronal Pathology: Neurochemical, Molecular and Genetic Factors *Annual Report, 15 Jun. 1999-14 Jun. 2000*
Koob, George F.; Jul. 2000; 18p; In English
Contract(s)/Grant(s): DAMD17-99-1-9501
Report No.(s): AD-A382530; No Copyright; Avail: CASI; A03, Hardcopy; A01, Microfiche

The purpose of this proposal is to test the hypothesis that chronic stress produces lasting changes in brain dopamine function leading to permanent neuronal damage through oxidative mechanisms. Certain subject populations may be uniquely susceptible to this pathological cascade through hyperresponsiveness of the corticotropin releasing factor stress response system. to test this hypothesis, two specific aims are currently in progress: 1) to examine the effects of chronic stress on behavioral, neurochemical and molecular measures of neuronal pathology to the brain dopamine system; 2) to develop a phenotype of hyperresponsiveness of the CRF hypothalamic pituitary adrenal axis by selective breeding. The results show evidence of CRF induced hypoactivity in the brain dopamine system as measured by an increase in catalepsy and a decrease in amphetamine-induced stereotyped behavior that last up to four months. In addition, the first phase of selective breeding of rats hyperresponsive to stress has been accomplished. The initial separation in HPA axis activity showed a two- to four-fold difference between low and high responders. These results should ultimately provide not only key information about neuronal dysfunction produced by chronic stress but critical knowledge of the genetic/molecular factors that contribute to individual vulnerability to stress and its pathological consequences.
DTIC
Nervous System; Pathology; Genetics; Neurophysiology; Brain; Stress (Biology)

20000116333 NASA Johnson Space Center, Houston, TX USA
Suppression of Antigen-Specific Lymphocyte Activation in Simulated Microgravity
Pellis, Neal R., NASA Johnson Space Center, USA; Cooper, D., La Jolla Inst. for Allergy and Immunology, USA; Pride, M., Weyth-Lederle, USA; Brown, E., Texas A&M Univ., USA; Risin, D., Wyle Labs., Inc., USA; [1999]; 1p; In English; No Copyright; Avail: Issuing Activity; Abstract Only

Various parameters of immune suppression are observed in astronauts during and after spaceflight, and in isolated immune cells in true and simulated microgravity. Specifically, polyclonal activation of T cells is severely suppressed in true and simulated microgravity. These recent findings with various polyclonal activators suggests a suppression of oligoclonal lymphocyte activation in microgravity. We utilized rotating wall vessel (RWV) bioreactors that simulate aspects of microgravity for cell cultures to analyze three models of antigen-specific activation. A mixed-lymphocyte reaction (MLR), as a model for a primary immune response; a tetanus toxoid (TT) response and a B. burgdorferi (Bb) response, as models of a secondary immune response, were all suppressed in the RWV bioreactor. Our findings confirm that the suppression of activation observed with polyclonal models also encompasses oligoclonal antigen-specific activation.
Author
Gravitational Physiology; Immunology; Microgravity; Physiological Responses; Immune Systems; Aerospace Medicine; Bioastronautics

20000116366 Johns Hopkins Univ., School of Medicine, Baltimore, MD USA
Clinical Evaluation of Digital Mammography *Annual Report, 1 Feb. 1999-31 Jan. 2000*
Feb. 2000; 163p; In English
Contract(s)/Grant(s): DAMD17-99-1-9001
Report No.(s): AD-A382368; No Copyright; Avail: CASI; A08, Hardcopy; A02, Microfiche

Our study entails two aspects of translational research related to the clinical application of digital mammography: technology optimization (Phase 1) and a clinical evaluation (Phase 2). The technology/system optimization work is near completion and has focused on optimizing the operational parameters most likely to impact mammographic image quality for radiodense breasts, including x-ray tube target material, filter composition, tube voltage, and x-ray exposure level/radiation dose. We have evaluated

digital mammography systems from 3 different manufacturers - comprising the systems to be used in the Phase 2 portion of this research. Expert physicists collaborating in this work have developed optimization parameters for each system to enable the best image quality within reasonable x-ray dose ranges. In addition, quality control standards have also been established to maintain optimized system performance and control the above cited parameters during the Phase 2 clinical study. The second phase of this project is a multicenter clinical evaluation comparing optimized digital mammography to SFM in women with moderate or marked breast density who present for problem-solving mammography. Eligible women consenting to participate will undergo a 4-view screen-film and digital mammogram. Total accrual will be 1075 women with moderately or markedly dense breasts. The clinical trial is scheduled to open July 1,2000. Our Phase 1 results demonstrate that successful system optimization and quality control of digital mammography systems can be efficiently achieved in a manner similar to conventional screen-film mammography. The clinical research to be carried out during Phase 2 will determine whether digital mammography has the same or better diagnostic accuracy as conventional mammography in the population of women who have radiodense breast tissue.
DTIC

Clinical Medicine; Mammary Glands; Digital Systems; Cancer; X Rays; Diagnosis

20000116367 Thomas Jefferson Univ., Philadelphia, PA USA

Contrast Enhanced 3D Color Amplitude Imaging of the Breasts *Annual Report, 15 Sep. 1998-14 Sep. 1999*

Forsberg, Flemming; Oct. 1999; 33p; In English

Contract(s)/Grant(s): DAMD17-97-1-7116

Report No.(s): AD-A382383; No Copyright; Avail: CASI; A03, Hardcopy; A01, Microfiche

In total, 22 patients with 6 cancers and 16 benign lesions have been enrolled in the Levovist arm of the study. These numbers were less than anticipated, and an initial data analysis indicated that Levovist was not as efficacious as expected. to increase recruitment and improve results the ultrasound contrast agent was changed to Optison. to date 13 patients with 3 cancers and 10 benign lesions have been enrolled in this part of the study. Moreover, 3D parameter extraction algorithms for the LIS 6000A system has been designed and tested, but no data analysis has yet been carried out due to the limited data set available for Optison. The histomorphometry system has been used to analyze vessel distribution and vessel density maps from 10 patients. Contrast enhanced color flow imaging was found to provide some quantitative parameters, which correlated with direct pathologic vascularity assessments such as the iMVD. Specifically, the microvessel area and count for vessels 30 to 39 microns in diameter were most significant. These results indicate that ultrasound imaging with contrast may produce a quantitative measure of the neovascularity within breast tumors. However, the current patient population in the sub-study is very small and further cases are currently being analyzed.
DTIC

Image Processing; Diagnosis; Mammary Glands; Cancer; Histology; Morphology; Lesions; Imaging Techniques; Computer Techniques

20000116591 Cornell Univ., Ithaca, NY USA

The Role of Dipeptidyl Peptidase 4 in Lung Metastasis of Breast Cancer Cells *Annual Report, 1 May 1998 - 30 Apr. 2000*

Cheng, Hung–Chi, Cornell Univ., USA; May 1999; 35p; In English

Contract(s)/Grant(s): DAMD17-98-1-8056

Report No.(s): AD-A381154; No Copyright; Avail: Defense Technical Information Center (DTIC)

Our studies focused on (1) cloning and sequencing of wild-type endothelial DPP IV (wtDPP IV) and preparation of truncated DPP IV (tDPP IV); (2) identification of surface-associated fibronectin polymers (polyFN) as DPP IV ligand; (3) use of DPP IV Fischer 344/CRJ rats as protein-knock-outs in metastasis; and (4) identification of the DPP IV/FN binding domains. A lull- length clone of endothelial wtDPP IV was isolated from a rat lung cDNA library that was identical to hepatic DPP IV. Acid extraction of rat lung yielded a tDPP IV, which was an effective inhibitor of breast cancer cell adhesion to wtDPP IV and lung metastasis. The DPP IV ligand, polyFN, provides multiple binding sites for DPP IV, thereby allowing lung vascular arrest of cancer cells under hemodynamic conditions. Fischer 344/CRJ rats are unsuitable as DPP IV protein knock-out model, because lung endothelia leak expression of DPP IV and are able to support breast cancer cell arrest. The DPP IV binding domains of FN was localized to an N- terminal 30-kDa region and FN type III repeats 13 to 14. Three approximately equal size fragments of the extracellular domain of DPP IV were expressed as GST fusion proteins and are currently studied for FN binding.
DTIC

Lungs; Cloning (Biology); Genetic Engineering; Cells (Biology); Blood Circulation; Mammary Glands; Proteins; Cancer; Rats

20000116605 Army Research Inst. of Environmental Medicine, Natick, MA USA

Amino Acid and Protein Requirements: Cognitive Performance, Stress, and Brain Function, Chapter 14

Lieberman, Harris R., Army Research Inst. of Environmental Medicine, USA; Protein and Amino Acids; 1999, pp. 289-307; In English

Report No.(s): AD-A380146; No Copyright; Avail: Defense Technical Information Center (DTIC)

This chapter will focus on amino acid and protein requirements and brain function. A particular focus will be the possibility that central demands for amino acids may modify nutritional requirements when individuals are exposed to extreme environments and other stresses associated with combat and high intensity military or civilian occupations.

DTIC

Brain; Mental Performance; Nutritional Requirements; Amino Acids; Cognition

20000116629 Army Medical Dept. Center and School, Dept. of Academic Support, Fort Sam Houston, TX USA

US Army Medical Department Journal, April-June 2000 *Quarterly Report, Apr. - Jun. 2000*

Nelson, Bruce, Editor, Army Medical Dept. Center and School, USA; April - June 2000; ISSN 1524-0436; 35p; In English

Report No.(s): AD-A381186; No Copyright; Avail: Defense Technical Information Center (DTIC)

Clinical and nonclinical professional information designed to keep U.S. Army Medical Department personnel informed of healthcare, research, and combat and doctrine development information. The Army Medical Department Journal is prepared quarterly for the Surgeon General by the U.S. Army Medical Department Center and School.

DTIC

Armed Forces; Medical Personnel; Medical Services; Research

20000116630 Pacific Northwest Cancer Foundation, Seattle, WA USA

The Assessment of Prostate Cells in Semen Using Flow Cytometry, For the Early Detection and Staging of Prostate Cancer (Prostate) *Annual Report, 1 Sep. 1998 - 31 Aug. 1999*

Murphy, Gerald, Pacific Northwest Cancer Foundation, USA; September 1999; 11p; In English

Contract(s)/Grant(s): DAMD17-98-1-8541

Report No.(s): AD-A381183; No Copyright; Avail: Defense Technical Information Center (DTIC)

This study involves the detection of prostatic epithelial cells in the seminal fluid. Relatively normal cells are identified by Cytokeratin 8/18. Up-regulated, or cancerous cells, are identified by means of PSMA staining. Increased prostate specific membrane antigen is associated with a poor prognosis. Data is being collected to differentiate the seminal fluid values in a ratio between the cytokeratin cells and the PSMA positive cells. At the present time, these clearly distinguish between BPH patients and prostate cancer patients, with prostatitis patients being intermediate. As more and additional patients are followed for repeat studies, and additional patients are seen from our control vasectomy clinic, we will define this test to its ultimate possibilities. The obtaining of fresh samples and the elimination of viable sperm have been two of our key progress notes at this particular time.

DTIC

Prostate Gland; Prognosis; Cancer; Cytometry; Epithelium; Sampling; Detection

20000116631 New York Univ. Medical Center, New York, NY USA

The Role of RPTP-Alpha-Like Protein Tyrosine Phosphatases in Mammary Tumorigenesis *Annual Report, 1 May 1998 - 30 Apr. 1999*

Sap, Jan M., New York Univ. Medical Center, USA; May 1999; 46p; In English

Contract(s)/Grant(s): DAMD17-98-1-8136; NIH-R29-CA-68365; NIH-5R21-CA-66229-04

Report No.(s): AD-A381182; No Copyright; Avail: Defense Technical Information Center (DTIC)

RPTPa is a protein tyrosine phosphatase implicated in the activation of SRc family kinases, and in the regulation of integrin signaling, cell adhesion, and growth factor responsiveness, to explore its potential contribution to human neoplasia, we surveyed RPTPa protein levels in 51 primary breast cancer samples. We found RPTPa expression to vary widely among individual tumors, with significant overexpression occurring in approx. 27% of cases. RPTPa overexpression reflected reduced tumor aggressiveness, being strongly negatively correlated with tumor grade. In cell culture, expression of RPTPa in MCF-7 breast carcinoma cells led to growth inhibition, associated with increased accumulation in the G1 phase of the cell cycle. RPTPa expression also resulted in delayed tumor growth and metastasis in nude mice tumorigenicity as says. We propose that RPTPa overexpression in breast cancer constitutes a secondary response by which the cell attempts to maintain homeostasis perturbed

during neoplastic transformation. to our knowledge, this is the first example of a study correlating expression level of a bonafide protein tyrosine phosphatase with neoplastic disease in humans.
DTIC
Cancer; Cell Division; Mammary Glands; Proteins; Tumors; Tyrosine; Physiological Responses

20000116632 Wistar Inst. of Anatomy and Biology, Philadelphia, PA USA
Characterization of Two Proteins Which Interact With the BRCA1 Gene *Annual Report, 1 Jun. 1998 - 31 May 1999*
Rauscher, Frank J., Wistar Inst. of Anatomy and Biology, USA; June 1999; 34p; In English
Contract(s)/Grant(s): DAMD17-96-1-6141
Report No.(s): AD-A381176; No Copyright; Avail: Defense Technical Information Center (DTIC)

We have made extensive progress in the past year to support our analysis of the BAP1 - BRCA1 interaction. We have published the co-localization and cell-cycle patterns of internuclear distribution for the two proteins. In addition, we have shown that BAP-1 is a bonafide tumor suppressor gene which is able to inhibit the malignant growth characteristics of cell lines when transfected back into the BAP1 null cells. This activity is dependent upon enzymatic function of the ubiquitin hydrolysis domain. In exciting preliminary studies we have shown that BAP1, like BRCA1, has a direct role in transcription-coupled DNA repair. The work accomplished conforms to the original SOW and has shed new light on the role of BRCA1 as a tumor suppressor in early onset familial breast-ovarian cancer families.
DTIC
Genes; Hydrolysis; Cancer; Growth; Enzymes; Proteins; Cell Division; Deoxyribonucleic Acid

20000116633 Alabama Univ., Birmingham, AL USA
Gene Therapy of Disseminated Breast Cancer Using Adenoviral Vectors Targeted Through Immunological Methods *Annual Report, 1 Aug. 1998 - 30 Jul. 1999*
Rogers, Buck E., Alabama Univ., USA; August 1999; 21p; In English
Contract(s)/Grant(s): DAMD17-97-1-7244
Report No.(s): AD-A381175; No Copyright; Avail: Defense Technical Information Center (DTIC)

Targeting of adenovirus vectors, encoding for therapeutic genes, to tumor-specific receptors on breast cancer cells should result in specific killing of these cells. Targeting is necessary to prevent gene transfer in normal tissues resulting from the infection of normal cells by adenovirus. We have previously reported the use of an anti-knob antibody fragment (Fab), which prevents Ad infection, conjugated to folate to target adenovirus to folate receptor positive cells. In this report, the Fab has been conjugated on a large scale to an anti-EGFR antibody (425) and an anti-erbB-2R antibody (Herceptin) to yield Fab-425 and Fab-Herceptin conjugates, respectively. These conjugates were used to target adenovirus specifically to E()F and erbB-2 receptors on BT-474, MDA-MB-468, MDA-MB-134, MDA-MB-231, MDA-MBA-453, and SK-BR-3 breast cancer cells. In addition, the conjugates could specifically target adenovirus to the receptors in a heterogeneous cell population. Preliminary in vivo studies were conducted which will be valuable for future evaluation of the conjugates. Also, studies using an adenovirus encoding for a therapeutic gene were evaluated. These results are significant in that they demonstrate that adenovirus vectors can be specifically delivered to breast cancer cells in a heterogeneous cell population. This will be significant for treating disseminated breast cancer with adenovirus vectors.
DTIC
Genes; Immunology; Cells (Biology); Mammary Glands; Cancer; Infectious Diseases; Antibodies

20000116636 California Univ., Lawrence Berkeley Lab., Berkeley, CA USA
Mechanisms of Abnormal Cell-Extracellular Matrix Interactions in Human Breast Cancer *Final Report, 1 Jul. 1994 - 30 Sep. 1999*
Chen, Huei–Mei, California Univ., Lawrence Berkeley Lab., USA; September 1999; 40p; In English; Sponsored in part by Danish Cancer Society, Thayssen Foundation and NOVO Foundation
Contract(s)/Grant(s): MIPR-94MM4558; DE-AC03-76SF-00098; CRADA-BG98-053(00); NIH-CA-64786-02
Report No.(s): AD-A381192; No Copyright; Avail: Defense Technical Information Center (DTIC)

To identify genes misregulated in the final stages of breast carcinogenesis, we performed differential display to compare the gene expression patterns of the human tumorigenic mammary epithelial cells, HMT-3522-T4-2, with that of their immediate pre-malignant progenitors, HMT-3522-S2. We identified a novel gene, called AZU-1, that was abundantly expressed in non- and pre-malignant cells and tissues but was appreciably reduced in breast tumor cell types and in primary tumors. The AZU-1 gene

encodes an acidic 571 amino acid protein containing at least two structurally distinct domains with potential protein- binding functions: an N-terminal serine and proline-rich domain with a predicted Ig-like fold and a C-terminal coiled-coil domain.
DTIC
Cancer; Mammary Glands; Genes; Proteins; Tumors; Amino Acids

20000116637 Georgetown Univ., Washington, DC USA
Molecular Diagnosis for Breast Malignancy *Final Report, 1 Jul. 1994 - 30 Jun. 1998*
Chen, Wen–Tien, Georgetown Univ., USA; July 1998; 75p; In English
Contract(s)/Grant(s): DAMD17-94-J-4033
Report No.(s): AD-A381191; No Copyright; Avail: Defense Technical Information Center (DTIC)

The overall project goal is to identify and evaluate new prognostic markers that can be used to indicate the metastatic potential of node-negative breast cancer. Cell surface antigens in the invading front; invadopodia, of cancer cells are considered as promising diagnostic indicators of metastatic potential. Five invasion-associated proteins are being examined in this project: seprase, dipeptidyl peptidase IV (DPPIV), membrane type matrix metalloprotease (MT-MMP), fibronectin, and extracellular matrix metalloprotease inducer (EMMPRIN).
DTIC
Mammary Glands; Cancer; Enzymes; Proteins; Deoxyribonucleic Acid; Diagnosis

20000116638 Sloan-Kettering Inst. for Cancer Research, New York, NY USA
Synthesis of Clustered ST-Antigens for the Development of Novel Breast Cancer Vaccines *Annual Report, 16 Mar. 1998 - 15 Mar. 2000*
Carson, Matthew W., Sloan-Kettering Inst. for Cancer Research, USA; Danishefsky, Samuel J., Sloan-Kettering Inst. for Cancer Research, USA; April 2000; 14p; In English
Contract(s)/Grant(s): DAMD17-98-1-8154
Report No.(s): AD-A381188; No Copyright; Avail: Defense Technical Information Center (DTIC)

The development of efficient routes for the preparation of complex oligosacoharide or carbohydrate conjugates has been a goal in the Danishefsky group for some time. Synthetic investigations in this area can help to provide a detailed knowledge of the structural and chemical behavior of carbohydrates and their conjugates. Moreover, it has been known for some time now that specific types of glycolipids or glycoproteins, which are chemically detectable in normal cells, are more highly expressed in tumors. It should be noted that abnormally high levels of expression on tumor cells cause an antibody response, consequently rendering the cell- surface glycoconjugate a tumor-associated antigen. The idea of such glycoconjugates as tumor-associated antigens is the basis for using carbohydrates in the development of antitumor vaccines. Since tumor antigens and vaccine constructs are usually inaccessible from natural sources, it falls to the organic chemist to supply necessary quantities of carbohydrates, in the form of both glycolipids and glycopeptides.
DTIC
Neoplasms; Organic Chemistry; Mammary Glands; Cancer; Tumors; Proteins

20000117655 Loyola Univ. Chicago, Maywood, IL USA
Prostate Cancer Immunotherapy Development in Prostate Specific Antigen Transgenic Mice
Kast, W. Martin, Loyola Univ. Chicago, USA; September 1999; 16p; In English
Contract(s)/Grant(s): DAMD17-98-1-8480
Report No.(s): AD-A380895; No Copyright; Avail: Defense Technical Information Center (DTIC)

Our research is focused towards the development of an immunotherapy for prostate cancer that specifically targets the expressed prostate specific antigen (PSA) of prostate tumor cells. With over forty thousand deaths a year and the near lack of curative treatments, an effective therapy would greatly benefit society. Our research to date has suggested that PSA can serve as a tumor rejection marker in our PSA transgenic mice whose prostates express human PSA. Vaccination with a tumor cell that expresses PSA elicited a specific anti- PSA response that prevented the outgrowth of a tumor challenge of PSA expressing cells. After indicating the pertinence of PSA as a target of an immunotherapy, we attempted to identify PSA derived peptides that are immunogenic in the HLA- A*020l haplotype. of nine PSA peptides selected for our study based on binding studies, two have proven to be immunogenic in the HLA- A*0201/Dd transgenic mouse model after vaccination of peptide pulsed dendritic cells. These results indicate that not only can we use PSA as a plausible rejection marker but we can also elicit a CTL response directed

against the human PSA peptides in a HLA- A*020l/Dd transgenic mouse. These results allow us to experiment with our vaccination strategies for the development of an efficacious anti-prostate cancer immunotherapy.
DTIC
Antigens; Cancer; Prostate Gland; Therapy; Peptides

20000117656 Georgetown Univ., Washington, DC USA
A Modulator of FGF's in Breast Cancer *Annual Report, 1 Aug. 1998 - 31 Jul. 1999*
Harris, Violaine K., Georgetown Univ., USA; Kagan, Benjamin L., Georgetown Univ., USA; August 1999; 64p; In English
Contract(s)/Grant(s): DAMD17-97-1-7109
Report No.(s): AD-A381144; No Copyright; Avail: Defense Technical Information Center (DTIC)

Fibroblast growth factors (FGF) are highly potent angiogenic factors. However, their role in cancer is not clear since they are frequently expressed by then stored in a non-secreted form. Recently a binding protein for FGF has been described, FGF-BP, which can activate dormant FGF during tumorigenesis. FGF-BP is aberrantly expressed in tumors and causes the development of tumors in vivo. In this grant the role of FGF-BP in breast cancer is examined. In order to understand the regulation of FGF-BP more clearly the principal investigator has cloned the gene promoter for FGF-BP and analyzed the transcription factors necessary for its activation in cancer cell lines. In addition the FGF-BP gene was found to be highly inducible by phorbol esters and by epidermal growth factor (EGF) in breast and other cancer cell lines. This induction occurs selectively through MEK2/ERK2 and p38 kinase pathways and suggests that pharmacological inhibition of these pathways could be useful for cancer therapy. During the analysis of the FGF-BP promoter a novel repressor site was found which controls the level of EGF and TPA regulation of this gene. Future studies will determine the role of this factor in breast tumorigenesis.
Author
Cancer; Mammary Glands; Proteins; Therapy; Tumors; Modulators

20000117657 Minnesota Univ., Minneapolis, MN USA
Biotherapy of Breast Cancer With EGF-Genistein *Annual Report, 16 Sep. 1998 - 15 Sep. 1999*
Gunther, Roland, Minnesota Univ., USA; October 1999; 96p; In English
Contract(s)/Grant(s): DAMD17-96-C-6064
Report No.(s): AD-A380880; No Copyright; Avail: Defense Technical Information Center (DTIC)

Our proposed research plan involves laboratory studies using a SCID mouse model of human metastatic breast cancer, as well as in vitro MTT(3- 4,5- DIMETHYLTHIAZOL-2-YL -2,5-diphenyl tetrazolium bromide) and colony assays, using established breast cancer cell lines, to examine the potency and toxicity of various EGE-Genistein conjugates. In an effort to generate more effective conjugates, we have employed a variety of crosslinking agents and photolysis conditions. Furthermore, we have established HPLC(high performance liquid chromatography) procedures to characterize and isolate the EGF components of the reaction mixture. We have also conjugated EGF to other small molecules which by themselves have been shown to possess anti-cancer activity. The knowledge gained from these studies is expected to lead to more effective biotherapy and combined biochemotherapy regimens for the treatment of breast cancer patients.
DTIC
Mammary Glands; Cancer; Photolysis; Therapy; Clinical Medicine

20000117661 Johns Hopkins Univ., Baltimore, MD USA
Recombinant Vaccine Strategies for Breast Cancer Prevention *Annual Report, 1 Oct. 1998 - 30 Sep. 1999*
Jaffee, Elizabeth M., Johns Hopkins Univ., USA; September 1999; 74p; In English
Contract(s)/Grant(s): DAMD17-96-1-6138
Report No.(s): AD-A381767; No Copyright; Avail: Defense Technical Information Center (DTIC)

Exciting new findings in autoimmune disease and cancer have led to the realization that a large set of antigenic determinants of the self have not induced self-tolerance. The peptide determinants could provide targets for antimmune attack as well as antitumor immune responses. We hypothesized that vaccine strategies can be devised that specifically generate an immune response against breast ductal epithelial cells. Since the overwhelming majority of breast tumors arise in these cells, destroying these cells prior to the development of neoplasia will effectively prevent cancer. We are attempting to augment the immune response to the breast-specific antigen, HER-2/neu, which is expressed by mammary tissue in HER-2/neu transgenic mice prior to mammary tumor development, by enhancing the T cell response using selected vectors that may alter antigen procession and T cell activation, thereby influencing antigen-specific immunity. We have evaluated vaccinia constructs that express antigen alone or together in co-simulatory molecules, to determine if immunity can be further enhanced. In our preliminary studies, we have found that this vaccinia approach is superior to vaccination with plasmid DNA. We are currently exploring additional methods

of enhancing this potency of this vaccine approach, including test a fusion protein that enhances the induction of helper T cell responses, and testing the vaccine in combination with other recently identified T cell activating signals, such as CD40, OX40, and anti-CTLA-4. This study will provide a paradigm for novel vaccine approaches to breast cancer prevention.
Author
Vaccines; Cancer; Prevention; Antigens; Mammary Glands; Physiological Responses; Tumors; Health

20000117663 Meharry Medical Coll., Nashville, TN USA
Breast Cancer and Risk Factors Among African-American Women Aged 20-54: A Case-Control Study According to Estrogen Receptor Status *Final Report, 1 Sep. 1996 - 28 Feb. 1999*
Zhu, Kangmin, Meharry Medical Coll., USA; March 1999; 41p; In English
Contract(s)/Grant(s): DAMD17-96-1-6270
Report No.(s): AD-A381706; No Copyright; Avail: Defense Technical Information Center (DTIC)

This is the final report of our exploratory case-control study on breast cancer. This study aimed to examine whether risk factor profiles differ according to estrogen receptor (ER) status among African-American women. During the period of the project, we established collaborations with the Tennessee Cancer Reporting System, hospitals in the study areas, and basic science researchers; we formulated a series of data collection and quality-control procedures; we identified and interviewed a number of cases and controls that is nearly equivalent to that expected in the study design; we collected breast cancer tissue specimens and measured ER status for most cases; and we conducted some preliminary analysis with results that are presented in this report. We also have published a hypothesis article based on the molecular biological progress on the topic. At the time of data analysis for this report, we were still waiting for responses from some cases and their doctors. We still need to collect tumor tissues and measure ER status for some cases and recruit some controls because these procedures lag the interviews with cases. These can be done soon and more deliberated analyses will be conducted.
Author
Cancer; Data Acquisition; Estrogens; Females; Mammary Glands; Risk; Public Health

20000117664 Texas Univ., Medical Branch, Galveston, TX USA
Mammography Use by Older Mexican American Women *Final Report, 1 Jul. 1996 - 31 Jul. 1999*
Freeman, Jean L., Texas Univ., USA; August 1999; 142p; In English
Contract(s)/Grant(s): DAMD17-96-1-6215
Report No.(s): AD-A381714; No Copyright; Avail: Defense Technical Information Center (DTIC)

This study examined the correlates of mammographic screening in older Mexican-American women, with a focus on the influence of strong family relationships on promoting screening behavior. A random sample of 549 Mexican-American women age 50-74 years in southeast Texas was identified through a one stage cluster sample. Data were collected on 452 subjects through in-home interviews on factors related to ever having a mammogram in the past two years. Mammography use increases with years of education, household income, having some private insurance, having a usual source of care, and perceived susceptibility to breast cancer. Use is significantly associated with age, marital status, and attitudes towards perceived care. Use increases with acculturation, with language use and proficiency having the strongest association. There is strong potential for family to play an important role in promoting screening behavior, particularly having young female family members encourage their older relatives to have mammograms. Self reports of mammography for 192 women were validated with medical chart reviews. The positive prediction value was 74 percent and the overall agreement was 77 percent.
Author
Cancer; Females; Mammary Glands; Random Sampling; Texas; Public Health

20000117665 Michigan Univ., Ann Arbor, MI USA
The Effect of Radiotherapy Upon Primary Human Mammary Epithelial Cells Which Harbor a Breast Cancer Susceptibility Gene *Final Report, 1 Sep. 1996 - 31 Aug. 1999*
Pierce, Lori, Michigan Univ., USA; September 1999; 15p; In English
Contract(s)/Grant(s): DAMD17-96-1-6194
Report No.(s): AD-A381716; No Copyright; Avail: Defense Technical Information Center (DTIC)

The purpose of this work is to determine whether genomic instability following radiotherapy is increase in breast cells that harbor either a BRCA-1 mutation relative to cells which carry two normal copies of the gene. Therefore mammary epithelial cells from women at high risk for carrying either BRCA-1 or BRCA-2 germline mutation were tested and two cell lines were found to harbor a germline mutation. These cells will be compared with mammary cells from women not at risk for carrying a mutation following radiation using the following assays: (1) growth factor independence, (2) growth in soft agar, and (3) tumor igenicity

in vivo. Radiation experiments using immortalization, growth factor independence, and soft agar growth as endpoints have not identified any differences in genomic stability in the presence of a mutated gene. The final phase of this research, i.e. injecting immuno deficient mice with irradiated breast cells, has also not shown differences relative to irradiated wild-type cells.
Author
Cancer; Females; Irradiation; Mammary Glands; Mutations; Radiation Therapy; Risk; Public Health

20000117666 Howard Univ., Washington, DC USA
Selectivity of Very High Dose Methotrexate in MCF-7 and Normal Cells Using a Priming and Non-Toxic 5-Fluorouracil Dose *Annual Report, 16 Sep. 1998 - 15 Sep. 1999*
Bowen, Donnell, Howard Univ., USA; October 1999; 17p; In English
Contract(s)/Grant(s): DAMD17-96-1-6291
Report No.(s): AD-A381717; No Copyright; Avail: Defense Technical Information Center (DTIC)

The growth inhibitory effects of high-dose methotrexate (MTX) and trimetrexate (TMQ) are maintained in MCF-7 breast cancer but is decreased in Hs824.T human bone marrow by a priming- and nontoxic 5-fluorouracil (5-FU) dose. Incubation of MCF-7 breast cells with a ten micro-M MTX, ten micro-M TMQ alone or in combination with ten micro-M 5-FU (MTX or TMQ two hours prior to 5-FU [MTX/5-FU or TMQ/5-FU] or 5-FU two hours prior to MTX or TMQ [5-FU/MTX or 5-FU/TMQ]) resulted in similar inhibitory patterns but dissimilar effects occurred in bone marrow cells. These studies suggest that a) MTX or TMQ and 5-FU combinations on the growth of breast cancer cells are independent of sequence of administration and are best related to MTX or TMQ rather than 5-FU (since 5-FU had no effect which differed from control and sequential MTX or TMQ plus 5-FU had no effect which differed from MTX or TMQ alone), b) a priming- and nontoxic dose of 5-FU will protect bone marrow against MTX and TMQ cytotoxicity while not affecting the maximum inhibitory effects of MTX or TMQ in breast cancer cells, and c) the results from the rise of nonclassical and nonpolyglutamyl antifolate TMQ suggest that polyglutamation is not a critical determinant of MTX cytoxicity in bone marrow.
Author
Bone Marrow; Cancer; Dosage; Mammary Glands; Public Health; Medical Science

20000117667 RAND Health, Santa Monica, CA USA
Managed Care and the Evaluation and Adoption of Emerging Medical Technologies
Garber, Steven, RAND Health, USA; Ridgely, M. Susan, RAND Health, USA; Taylor, Roger S., RAND Health, USA; Meili, Robin, RAND Health, USA; [2000]; 83p; In English; Sponsored by Health Industry Manufacturers Association and California Goldstrike Partnership
Report No.(s): AD-A381755; No Copyright; Avail: Defense Technical Information Center (DTIC)

New medical technologies--pharmaceuticals, medical devices, and procedures--often allow great improvements of medical care, but they are also widely believed to be a major cause of increasing costs. Selective adoption of new technologies, the taking on of only those technologies for which the medical benefits exceed the costs to society of developing and using them, is a crucial element in the quest to control healthcare costs while preserving or enhancing the quality of care. This report focuses on adoption of innovative medical technologies by managed care organizations (MCOs). We gathered empirical information from in-depth, semi-structured interviews with eight manufacturers of innovative devices and nine MCOs. We also collected information from representatives of manufacturers, MCOs, and the sponsors of this study. We had four primary audiences in mind when conducting this research and reporting our findings: (1) medical device developers and manufacturers, (2) MCOs, (3) public policy makers, and (4) researchers and analysts. Members of all four audiences will find something of interest here.
Derived from text
Public Health; Clinical Medicine; Policies; Operations Research; Cost Reduction; Decision Making; Regulations

20000117668 Washington Univ., Seattle, WA USA
Mutations in ATM, Radiation Exposure and Breast Cancer Risk Among Black and White Women *Final Report, 1 Aug. 1996 - 31 Jul. 1999*
Schubert, Elizabeth, Washington Univ., USA; August 1999; 18p; In English
Contract(s)/Grant(s): DAMD17-96-1-6248
Report No.(s): AD-A381762; No Copyright; Avail: Defense Technical Information Center (DTIC)

In some families, Predisposition to breast cancer is inherited as a genetic trait. Thus far, a few highly penetrant genes responsible for inherited breast cancer have been identified. An important and unresolved question of breast cancer etiology is whether there are other genes which have a more moderate effect on breast cancer risk, possibly involving more women than do other inherited mutations, It has been suggested that mutations in the Ataxia-Telangiectasia gene (ATM) and cellular damage such

as radiation exposure could be involved with breast cancer in this manner. In order to address this question, we screened a population-based series of African-American and Caucasian breast cancer patients and controls as well as a series of patients with particular phenotypes for mutations in the ATM gene which confer breast cancer risk.
Author
Cancer; Females; Genetics; Mammary Glands; Mutations

20000117670 Civil Aeromedical Inst., Oklahoma City, OK USA
Galactic Cosmic Radiation Exposure of Pregnant Aircrew Members, 2 *Final Report*
Nicholas, Joyce S., Medical Univ. of South Carolina, USA; Copeland, Kyle, Civil Aeromedical Inst., USA; Duke, Frances E., Civil Aeromedical Inst., USA; Friedberg, Wallace, Civil Aeromedical Inst., USA; OBrien, Keran, III, University of Northern Arizona, USA; October 2000; 10p; In English
Contract(s)/Grant(s): AM-PHY305
Report No.(s): DOT/FAA/AM-00/33; No Copyright; Avail: CASI; A02, Hardcopy; A01, Microfiche

This report is an updated version of a previously published Technical Note in the Journal Aviation, Space, and Environmental Medicine. The main change is that improved computer programs were used to estimate galactic cosmic radiation. The calculations also cover a greater range of altitudes. Small differences in the calculated doses were obtained, but the conclusions are the same. The International Commission on Radiological Protection (ICRP) and the Federal Aviation Administration (FAA) consider aircrews to be occupationally exposed to ionizing radiation. Although the USA has no regulations limiting aircrew exposure to cosmic radiation, the FAA has recommended limits. For pregnant crewmembers, starting when the pregnancy is reported to management, the FAA recommends: (1) a limit of one millisievert to the conceptus for the remainder of the pregnancy, in accordance with the ICRP policy/recommendation, and (2) a monthly limit of 0.5 millisievert to the conceptus, as recommended by the National Council on Radiation Protection and Measurements (NCRP). Here we address, principally, the ICRP policy. The stated ICRP policy is that a standard of radiation protection for any conceptus be broadly comparable with that provided for members of the general public, i.e. a yearly limit of one millisievert. In their 1990 recommendations, the ICRP indicated that this standard could be met by limiting the equivalent dose to the surface of pregnant women's abdomen to two millisieverts for the remainder of the pregnancy, once declared. They apparently assumed that the equivalent does to the conceptus would be about half the dose to the surface of the abdomen. We tested this assumption with respect to galactic cosmic radiation, the principal ionizing radiation to which aircrews are exposed.
Author
Cosmic Rays; Flight Crews; Ionizing Radiation; Pregnancy; Radiation Dosage; Radiation Protection

20000117671 Seattle Biomedical Research Inst., Seattle, WA USA
Mechanism of Integrim-Mediated Growth Control in Normal, Transformed and Neoplastic Breast Cells *Final Report, 30 Sep. 1994 - 29 Sep. 1999*
Wayner, Elizabeth, Seattle Biomedical Research Inst., USA; Tamura, Richard, Seattle Biomedical Research Inst., USA; October 1999; 21p; In English
Contract(s)/Grant(s): DAMD17-94-J-4303
Report No.(s): AD-A381108; No Copyright; Avail: Defense Technical Information Center (DTIC)

Anchorage-dependent cell growth by normal cells and the loss of this dependence during tumorigenesis is a phenomenon that has been recognized for many years. The primary cell adhesion receptors that mediate binding to extracellular matrix proteins are integrins. Our data suggest that (alpha)3(beta)1 and (alpha6(beta)4are the primary integrins responsible for mediating the GI/S transitiion in normal mammary epithelial cells and that these mechanisms may be defective in metastatic cancer cells. Other integrins also appears to influence components of the cell cycle regulatory machinery. For example,binding of GRDGS peptides to integrins((alpha)v(beta)5, (alpha)v(beta3), (alpha)5(beta)1) on both normal and cancer cells appears to regulate the activities of cdc2 kinase and cyclinA-associated kinases. Cancer cells appear to have numerous defects in both cell adhesion components ((alpha)6(beta)4, E-cadherin, laminin-5) and cell cycle regulatory components (cyclin D2, p21)which my contribute to the adhesion-independent phenotype. A difference in expression of the alternatively-spliced forms of the integrin ((alpha)6, (alpha)6A and (alpha)6B, suggests that this marker may have diagnostic or prognostic value. Further study of the significance of these defects may lead to the development of novel therapeutics for the treatment or cure of breast cancer.
Author
Peptides; Mammary Glands; Defects; Cell Division; Cancer

20000117672 Arkansas Univ. for Medical Sciences, Little Rock, AR USA

Inhibiting Tumorigeneis by Growth Factor Receptor Down Regulation Using a Sorting Nexin *Annual Report, 15 Apr. 1998 - 14 Apr. 1999*

Kurten, Richard C., Arkansas Univ. for Medical Sciences, USA; May 1999; 14p; In English

Contract(s)/Grant(s): DAMD17-98-1-8175

Report No.(s): AD-A381344; No Copyright; Avail: Defense Technical Information Center (DTIC)

Excessive activation of growth factor receptors can lead to the unrestrained cellular proliferation characteristic of tumors. Our objective is to determine if SNX1, a protein involved in intracellular membrane trafficking, can be used to downregulate EGF receptors in mammary gland. Our approach is to characterize the gene for SNX1 and to generate transgenic animals overexpressing SNX1 in mammary glands. We have characterized a genomic clone for SNX1 and had planned to use this clone for transgenic vector construction. However the size of the first intron in SNX1 is too large for this approach to be used successfully. The revised plan is to construct a WAP-SNX1 cDNA vector for transgenic mouse production. A Career Development Award was a second component of the application. Career development activities include: presentation of the inaugural seminar for the Arkansas Cancer Research Center Forum, participation as reviewer on the American Cancer Society Cell Structure and Metastasis study section, and participation on a search committee charged with identifying a Director for Breast Cancer Research at UAMS. In addition, the State of Arkansas Breast Cancer Research Program awarded me a one-year pilot research grant to examine the relationship between HER-2lneu and EGF receptors in mammary gland cell proliferation.

DTIC

Mammary Glands; Cells (Biology); Regeneration (Physiology); Mice; Cancer; Proteins; Deoxyribonucleic Acid

20000117674 Vermont Univ., Burlington, VT USA

Effect of Folate on the Efficacy and Toxicity of Cancer Chemotherapy

Branda, Richard F., Vermont Univ., USA; McCormack, John, Vermont Univ., USA; September 1999; 45p; In English

Contract(s)/Grant(s): DAMD17-98-1-8345

Report No.(s): AD-A381230; No Copyright; Avail: Defense Technical Information Center (DTIC)

The purpose of this research project is to understand better the effect of dietary folate levels on the cellular pharmacology and toxicology of chemotherapeutic agents. The scope of the research involves in vitro studies with cell lines and in vivo assessments in rats of folate-chemotherapeutic drug interactions. Studies at a molecular level led to a new model to explain the synergy between nutritional folate deficiency and alkylating agents. Our studies at a cellular level suggest that folate metabolism can modulate gluathione levels. This observation may explain at least in part why dietary folate levels influence the efficacy and toxicity of alkylating agents. Studies in rats confirm that dietary folate levels affect the toxicity of cyclophosphamide, but there may be an optimal amount of dietary folate to reduce that toxicity. These in vivo studies also indicate that other aspects of diet are important in determining sensitivity to chemotherapy. Rats maintained on a cereal based diet were much more resistant to the toxic effects of cyclophosphamide than rats eating a Purified Diet. Taken together, our studies suggest that dietary changes can have a profound and largely unappreciated effect on the outcome of cancer chemotherapy.

Author

Cancer; Chemotherapy; Diets; Toxicity; Toxicology; Pharmacology

20000117696 Texas Univ., M. D. Anderson Cancer Center, Houston, TX USA

Structural and Signaling Requirements for C-erbB2 Antiapoptosis in Breast Cancer *Annual Report, 1 Jun. 1998 - 31 May 1999*

Jing, Tong, Texas Univ., USA; June 1999; 19p; In English

Contract(s)/Grant(s): DAMD17-98-1-8313

Report No.(s): AD-A381239; No Copyright; Avail: Defense Technical Information Center (DTIC)

The c-erbB2 (or HER-2,neu) gene encodes a 185-kDa transmembrane glycoprotein (p815), which is a growth factor receptor of the epidermal growth factor receptor (EGF-r) family. Our previous studies demonstrated that c-erbB2 overexpression can enhance metastatic potential and infer increased chemoresistance to breast cancer cells, thereby leading to poor clinical outcome in breast cancer patients. Our recent study demonstrated that overexposure of c-erbB2 gene can protect human breast cancer cells from apoptosis induced by the chemotherapeutic agent Taxol, by gamma-radiation, or by serum starvation. These new findings provided an explanation on c-erbB2-mediated chemoresistance of breast cancer cells and poor prognosis of the patients. Therefore, it is very important to understand the mechanism of antiapoptosis by c-erbB2 overexposure in breast cancer cells. Since the p185(sup c-erbB2) is a receptor tyrosine kinase (RTK), we hypothesize that c-erbB2 overexposure may enhance the RTK signaling capacity that activates downstream effectors for antiapoptitic signaling. In this application, I will study: (1) Identify

structural requirements for c-erbB2 receptor antiapoptosis signaling. (2) Investigate the involvement of c-erbB2 immediate-downstream signaling (Shc-Grb2-Ras or PI2K) in antiapoptosis.
Author
Cancer; Chemotherapy; Mammary Glands; Patients; Prognosis; Public Health

20000117697 State Univ. of New York, Buffalo, NY USA
Risk Factors for Osteoporosis and Oral Bone Loss in Postmenopausal Women *Annual Report, 16 Sep. 1998 - 15 Sep. 1999*
Wactawski, Jean, State Univ. of New York, USA; October 1999; 24p; In English
Contract(s)/Grant(s): DAMD17-96-1-6319
Report No.(s): AD-A381140; No Copyright; Avail: Defense Technical Information Center (DTIC)

The overall purpose of this study is to determine the relationship between skeletal and oral bone density, identify factors influencing bone loss, and determining the relationship between osteoporosis and oral bone loss, periodontal disease and tooth loss. We hypothesize that reduction in bone density leading to osteoporosis plays a significant role in increasing susceptibility to destructive periodontis and tooth loss. Sensitive and accurate measurements of skeletal and oral bone mineral density, periodontal disease and tooth loss will be used. A wide variety of other risk factors for both osteopenia and periodontal disease will be assessed. A total of 1300 subjects are being recruited from an ongoing NIH funded study cohort, the Women's Health Initiative (WHI). Preliminary research findings from our pilot study determined that bone loss in the hip or spine is strongly associated with bone loss in the jaw. Also that bone loss in the hip was associated with tooth loss even with such controlling factors such as age, menopause, estrogen use, body mass, and smoking. We have just completed year three of a four year study. Data collection will continue into year-four, and as such, findings are not yet available to report.
Author
Bone Demineralization; Bones; Data Acquisition; Estrogens; Females; Health; Musculoskeletal System; Osteoporosis; Risk; Diseases

20000117698 Meharry Medical Coll., Nashville, TN USA
Obstacles to the Primary and Secondary Prevention of Breast Cancer In African-American Women *Final Report, 1 Sep. 1996 - 30 Aug. 1999*
Hargreaves, Margaret K., Meharry Medical Coll., USA; August 1999; 134p; In English
Contract(s)/Grant(s): DAMD17-96-1-6272
Report No.(s): AD-A381138; No Copyright; Avail: Defense Technical Information Center (DTIC)

Study objectives were to describe the barriers to primary and secondary prevention of breast cancer in African-American women, to develop tools to measure these barrier, and to describe prevalence in a community sample. This final report describes all four phases of our research. After a comprehensive review of the literature, we developed a structured interview, interviewed 155 African-American women, and developed a systematic and detailed coding system to successfully describe the barriers to reducing fat intake, increasing consumption of fruits and vegetables, doing breast self-examination, and getting a mammogram. These results were used to develop four questionnaires that were demonstrated to be reliable and valid in a sample of 117 African-American women. The questionnaires were then used to survey the occurrence of the barriers to behavioral change in a community sample of older white and black women in Nashville, TN. While many women in the community described themselves as already compliant with cancer prevention guidelines, a substantial subgroup reported varying degrees of difficulty with both psychological and environmental barriers to behavioral changes. Few differences were found between African-American and Caucasian women with members of each ethnic group falling into the five stages of change.
Author
Cancer; Ethnic Factors; Females; Mammary Glands; Prevention; Surveys; Public Health

20000117699 Whitehead Inst. for Biomedical Research, Cambridge, MA USA
Regulation of TGF-Beta Signal Transduction Pathways in Breast Cancer *Annual Report, 4 May 1998 - 3 May 1999*
Liu, Xue–Dong, Whitehead Inst. for Biomedical Research, USA; June 1999; 181p; In English
Contract(s)/Grant(s): DAMD17-98-1-8267
Report No.(s): AD-A381137; No Copyright; Avail: Defense Technical Information Center (DTIC)

The goal of my studies under the BCRP fellowship is to understand the role of the Smad proteins and the TGF-beta signal transduction pathways in breast cancer cell proliferetion, tumor progression, and prognosis. In the past nine months, I have focused on identifying intracellular molecules and trsnscription factors that might be involved in the TGF-beta signal transduction pathways. Using both genetic and biochemical approaches, I have successfully isolated a few key molecules that are either mediator of the TGF-beta-induced transcriptional response or suppressors of the TGF-beta signal pathways. Future studies will

be focused on understanding the detail mechanism of how the molecules interplay in mediating TGF-beta signaling and the significance of these interactions in tumor cell proliferation, progression, and prognosis.
Author
Tumors; Mammary Glands; Cells (Biology); Cancer; Regeneration (Physiology)

20000117700 Illinois Univ., Chicago, IL USA
Breast Carcinoma Cell Targeted Therapy by Novel Vitamin D Analog *Annual Report, 1 Sep. 1998 - 31 Aug. 1999*
Mehta, Rajeshwari, Illinois Univ., USA; September 1999; 17p; In English
Contract(s)/Grant(s): DAMD17-97-1-7263
Report No.(s): AD-A381134; No Copyright; Avail: Defense Technical Information Center (DTIC)

Vitamin D and its analogs have growth-suppressing and cell-defferentiating effect on various carcinoma cell types. We have synthesized a vitamin D analog (1(alpha)(OH)D(sub 5)) that is nontoxic and has both growth-inhibitory and cell-differentiating actions in various established breast cancer cell line. Our original goal was to covalently link this vitamin D analog to antibody against Her-2/neu protein and thus deliver 1(alpha)(OH)D(sub 5) specifically to highly aggressive human breast cancer cells. Using the xenograft model, we previously confirmed that 1(alpha)(OH)D(sub 5) supplemented in the diet inhibits growth of human breast carcinoma cells transplanted into athymic mice. As a second phase of the study, we covalently linked 1(alpha)(OH)D(sub 5) to Her-2/neu antibody using sulfo-SANPAH linker. The 1(alpha)(OH)D(sub 5)-Her-2 conjugate specifically binds for Her-2 receptor binding sites on the cancer cells. Our preliminary results show that the conjugate, when injected into Her-2+ tumor-bearing athymic mice, shows significantly higher accumulation in tumor than in other visceral organs. Experiments are in progress to further characterize the properties of 1(alpha)(OH)D(sub 5)-Her-2-antibody immunoconjugate and its effect on in vivo growth of human breast carcinoma cells.
Author
Calciferol; Cancer; Conjugates; Mammary Glands; Tumors

20000117701 Miami Univ., FL USA
Enhancing the Anti-Tumor Activity of Breast Cancer-Specific Cytotoxic T Lymphocytes *Annual Report, 1 Jul. 1998 - 30 Jun. 1999*
Malek, Thomas R., Miami Univ., USA; July 1999; 24p; In English
Contract(s)/Grant(s): DAMD17-98-1-8208
Report No.(s): AD-A381119; No Copyright; Avail: Defense Technical Information Center (DTIC)

Directing the immune system to attack tumors represents a potential powerful non-toxic approach for the treatment of breast cancer.Our goal is to ultimately engineer the interleukin-2 receptor (IL-2R) in cytotoxic T cells (CTL) to control signal transduction through this receptor and to improve the in vivo efficacy upon adoptive transfer to a tumor-bearing host. to this aim we have prepared a series of chimeric IL-2R constructs and show that signaling of one such pair appears to be induced by a small molecular weight dimerizing drug, We also established a sensitive in vivo animal tumor model system to be used to characterize such "engineering" CTL. The initial studies in this model indicate that unprimed tumor-specific T cell are essentially ignorant of growing tumor in vivo. by contrast, tumor growth is initially inhibited when adoptively transferred to tumor-bearing mice.
Author
Animals; Cancer; Dimerization; Drugs; Genetics; Lymphocytes; Toxins and Antitoxins; Tumors

20000117702 Nebraska Univ., Omaha, NE USA
Inhibition of Stem Cell Mobilization in Breast Cancer Patients by a Circulating Factor
Sharp, John G., Nebraska Univ., USA; September 1999; 30p; In English
Contract(s)/Grant(s): DAMD17-97-1-7238
Report No.(s): AD-A381106; No Copyright; Avail: Defense Technical Information Center (DTIC)

Some breast cancer patient are candidates for high dose therapy requiring collection of a cytokine-mobilized blood stem cell harvest for subsequent reinfusion to restore hematopoiesis and immune function. A proportion of patients respond poorly to mobilizing cytokines making collection of an adequate harvest inconvenient, prolonged and costly. The hypothesis of this project was that such patients had a circulating inhibitor of stem cell mobilization. Plasma from poorly versus vigorously mobilizing individuals was assayed in a mouse model for its ability to inhibit cytokine mobilization of stem and progenitor cells. THere was a significant positive correlation between the number of CD34+ stem cell per collection and inhibition or stimulation of CD45CD34+cell, GM-CFC progenitor cells and spleen weight of mice receiving plasma injections prior to cytokine injection. The majority of individuals who mobilized poorly (less than 10(exp 6) CD34+cells/coollection) showed inhibitation of mobilization. In contrast, plasma from some vigorous mobolizers (over 5 x 10(exp 6)CD34+cells/collection) enhanced

mobilization. These data suggest that circulating inhibitor(s) and potentially, stimulator(s) of mobilization are generated as a result of cytokine injection. Genetic factors and prior therapy may influence this response. The inhibitor(s) might be TGF-beta. The identity of the simulator(s) is unknown. Characterization and manipulation of these factors might permit adequate mobilization of all breast cancer patient.
Author
Cancer; Dosage; Hematopoiesis; Inhibitors; Stimulation; Therapy

20000117703 Sloan-Kettering Inst. for Cancer Research, New York, NY USA
Enhancement of Breast Cancer Therapy by 6-Aminonicotinamide *Annual Report, 6 Apr. 1998 - 5 Apr. 1999*
Koutcher, Jason A., Sloan-Kettering Inst. for Cancer Research, USA; May 1999; 14p; In English
Contract(s)/Grant(s): DAMD17-98-1-8153
Report No.(s): AD-A381102; No Copyright; Avail: Defense Technical Information Center (DTIC)

6-Aminonicotinamide (6AN) has been shown to enhance the effect of radiation both in vivo and in vitro in a murine tumor models. This study was undertaken to determine whether enhanced efficacy of radiation, adriamycin and taxol could be obtained by pretreating with 6AN. MCF-7 cells were grown on beads and perfused in the NMR magnet. P31 NMR spectra were obtained on cells at 4.7 T (81.03 MHz) which were treated with 6AN or control. Treatment with 6AN caused a new peak to be detected which has been previously assigned to 6-phosphogluconate. In addition, a decrease in phosphocreatine was noted. These results were analygous to results found with murine RIF-1 tumor cells. Surviving fraction studies were subsequently done. Cells were perfused for four hours with 6AN, the 6AN washed out and the cells incubated for three hours before being treated with radiation, adriamycin or taxol. Enhanced efficacy to radiation (2 Gy dose) and adriamycin (10 nM) was noted. 6AN inhibited the effect of Taxol. In vivo studies have been started and it appears that the maximum tolerance dose for 6AN will be between 10 and 12 mg/kg.
Author
Antibiotics; Augmentation; Cancer; Cells (Biology); Dosage; Radiation Effects; Therapy; Mammary Glands

20000117706 Dana Farber Cancer Inst., Boston, MA USA
Differential Regulation of Cell Cycle Progression in Human Breast Cancer Cell Lines by the Estrogen Receptor *Annual Report, 1 Aug. 1998 - 31 Jul. 1999*
Direnzo, James, Dana Farber Cancer Inst., USA; Brown, Myles, Dana Farber Cancer Inst., USA; August 1999; 11p; In English
Contract(s)/Grant(s): DAMD17-97-1-7069
Report No.(s): AD-A381101; No Copyright; Avail: Defense Technical Information Center (DTIC)

Critical predictions as to the biological behavior, and thus the therapeutic strategy, of breast cancer can be made based upon the estrogen receptor (ER). In support of DOD grant no. DAMD17-97-1-7069, our goal is to better understand the mechanisms by which ER controls the expression of target genes and therefore mediates the biological effects upon gene regulation and cell cycle progression. Our detailed studies of the regions of ER that control cell cycle progression in breast cancer cell lines have indicated an absolute requirement for the Activating Function-2 (AF-2) region of ER for hormone-dependent cell cycle progression. In many different cases of nuclear receptors, this area has been vigorously studied and has been shown to be important for the physical interaction between hormone bound receptors and coactivators. Our studies have demonstrated that mechanisms involving the chemical and structural modification of chromatin are critical for transcriptional responses to estrogen and may also be important for estrogen-dependent cell cycle progression.
Author
Cancer; Mammary Glands; Gene Expression; Hormones

20000118210 NASA Ames Research Center, Moffett Field, CA USA
Low LBNP Tolerance in Men is Associated With Attenuated Activation of The Renin-Angiotensin System
Greenleaf, J. E., NASA Ames Research Center, USA; Petersen, T. W., NASA Ames Research Center, USA; Gabrielsen, A., NASA Ames Research Center, USA; Pump, B., NASA Ames Research Center, USA; Bie, P., NASA Ames Research Center, USA; Christensen, N.–J., NASA Ames Research Center, USA; Warberg, J., NASA Ames Research Center, USA; Videbaeck, R., NASA Ames Research Center, USA; Simonson, S. R., NASA Ames Research Center, USA; Norsk, P., NASA Ames Research Center, USA; [1999]; 1p; In English; No Copyright; Avail: Issuing Activity; Abstract Only

Vasoactive hormone concentrations [epinephrine (pE), norepinephrine (pNE), angiotensin II (pATII), vasopressin (pVP), endothelin 1 (pET1)] and plasma renin activity (pRA) were measured during lower body negative pressure (LBNP) to test the hypothesis that responsiveness of the renin-angiotensin system is related to LBNP tolerance. Healthy men (2,822 cal/day(exp -1), 2 mmol*kg(exp -1)*day(exp -1)) Na(+)) were exposed to 30 minutes of progressive LBNP to -50 mmHg. LBNP was uneventful for seven men (25 +/- 2 years, HiTol group), but eight men (26 +/- 3 years) reached pre-syncope after 11 +/- 1 minutes (P is less

than 0.001, LoTol group). Mean arterial pressure was unchanged. Central venous pressure and left atrial diameter decreased in both groups (5-6 mmHg by approx. 30%, P is less than 0.05). Control [hormone] were similar but, pRA differed between groups (LoTol 0.6 +/- 0.1, HiTol 1.2 +/- 0.1 ng Ang1/(ml(exp -1)*h(exp -1)), P is less than 0.05). LBNP increased (P is less than 0.05) pRA and pATII more in HiTol (9.9 +/- 2.2 ng Ang1/(ml(exp -1)*h(exp -1)) and 58 +/- 12 pg/ml(exp -1)) than LoTol (4.3 +/- 0.9 ng Ang1/(ml*h) and 28 +/- 6 pg/ml(exp -1)). In contrast, pVP was higher (P is less than 0.05) in LoTol than in HiTol. The response of the renin-angiotensin system seems linked to the occurrence of pre-syncope, and measurement of resting pRA may be predictive.

Author

Epinephrine; Hormones; Lower Body Negative Pressure; Norepinephrine; Peptides; Vasoconstrictor Drugs; Medical Science

20000118212 NASA Langley Research Center, Hampton, VA USA

Aerospace Medicine and Biology: A Continuing Bibliography With Indexes, Supplement 506

November 2000; 94p; In English

Report No.(s): NASA/SP-2000-7011/SUPPL506; NAS 1.21:7011/SUPPL506; No Copyright; Avail: CASI; A05, Hardcopy

This supplemental issue of Aerospace Medicine and Biology, A Continuing Bibliography with Indexes (NASA/SP#2000-7011) lists reports, articles, and other documents recently announced in the NASA STI Database. In its subject coverage, Aerospace Medicine and Biology concentrates on the biological, physiological, psychological, and environmental effects to which humans are subjected during and following simulated or actual flight in the Earth's atmosphere or in interplanetary space. References describing similar effects on biological organisms of lower order are also included. Such related topics as sanitary problems, pharmacology, toxicology, safety and survival, life support systems, exobiology, and personnel factors receive appropriate attention. Applied research receives the most emphasis, but references to fundamental studies and theoretical principles related to experimental development also qualify for inclusion. Each entry in the publication consists of a standard bibliographic citation accompanied, in most cases, by an abstract. The NASA CASI price code table, addresses of organizations, and document availability information are included before the abstract section. Two indexes- subject and author are included after the abstract section.

CASI

Aerospace Medicine; Bibliographies; Bioastronautics; Biological Effects; Indexes (Documentation); Exobiology

20000118237 Naval Postgraduate School, Monterey, CA USA

Impact Analysis of a Biomechanical Model of the Human Thorax

Jolly, Johannes E.; Jun. 2000; 134p; In English

Report No.(s): AD-A379713; No Copyright; Avail: CASI; A07, Hardcopy; A02, Microfiche

The biomechanical response of a finite element model of the human thorax and a protective body armor system was studied under impact loading from a projectile. The objective of the study was to create a viable finite element model of the human thorax. This objective was accomplished through the construction of a three-dimensional finite element model in DYNA3D, a finite element analysis program. The model was validated by comparing the results of tests of body armor systems conducted on cadavers to results obtained from finite element analysis. A parametric study was undertaken to determine the essential components of the model. The results from this investigation determined that the path of force propagation from a body armor system to the thorax upon bullet impact is directly through the vest to the sternum and then through the skeleton to the rest of the body. Thus, any parameters that affect the components in this pathway were essential to the model. This included the muscles, their geometries, material properties, and viscosity, as well as the Young's modulus of the sternochondral cartilage and the bones themselves.

DTIC

Finite Element Method; Biodynamics; Thorax; Computer Programs; Impact Loads; Musculoskeletal System; Biological Models (Mathematics)

20000119038 California Univ., Berkeley, CA USA

Does Vigorous Exercise Prevent Breast Cancer in Women? *Final Report, 30 Sep. 1997-29 Sep. 1999*

Williams, Paul T.; Oct. 1999; 12p; In English

Contract(s)/Grant(s): DAMD17-97-1-7297

Report No.(s): AD-A383009; No Copyright; Avail: CASI; A03, Hardcopy; A01, Microfiche

The original purpose of the IDEA award was to recruit 36,000 additional runners to add to an existing cohort of 14,000 runners in order to create a total cohort of 50,000 who vigorously exercise. (Funding for surveillance was deferred to a future funding application.) We completed the design of the initial survey questionnaire and recruited the sample through direct mail solicitation

of female running magazine subscribers and race participants. To date, we have received 31,647 questionnaires under DOD funding and should receive at least 1,800 of the additional 4,353 needed to achieve the target of 36,000 women runners. At least one mechanism for the protection of breast cancer is suggested by our baseline questionnaires. The onset of menopause (or amenorrhea) occurred significantly earlier in association with longer distances run per week. Cessation of periods was reported to occur 5 years earlier in women running 40 or more miles per week (39.5 + and - 10.2 years) compared to those running less than 10 (44.43 + and - 8.54 years). There was also a tendency (significant at Pis less than 0.0001) for menses to have started about three months later in the higher mileage runners. The effect is however small compared to the apparent acceleration of menopause. DTIC

Physical Exercise; Mammary Glands; Cancer; Females; Protection

20000119039 Illinois Univ. at Urbana-Champaign, Urbana, IL USA

Gallium-Containing Estrogens as Receptor-Based Breast Tumor Imaging Agents *Annual Report, 1 Oct. 1998-30 Sep. 1999*

Cesati, Richard; Oct. 1999; 22p; In English

Contract(s)/Grant(s): DAMD17-97-1-7292

Report No.(s): AD-A383026; No Copyright; Avail: CASI; A03, Hardcopy; A01, Microfiche

We have conceived of an approach to prepare novel compounds for the estrogen receptor that might be useful in the imaging and diagnosis of breast cancer, by the creation of steroidal-based imaging agents which take advantage of the desirable properties of gallium as a radioisotope. We have completed the preparation of the carbon skeletons needed to assemble several of these compounds. Synthetic routes to ligands for model gallocycles have also been completed. Initial RBA data for several of these compounds have also been obtained. Future efforts will be directed at completing the synthesis of the gallium-containing compounds of the D- ring class, which appear to be the most promising, and preparation of these compounds in radioactive form. DTIC

Cancer; Mammary Glands; Estrogens; Diagnosis; Image Processing; Gallium; Receptors (Physiology)

20000119040 Cincinnati Univ., OH USA

Signal Transduction and Gene Regulation During Hypoxic Stress: A Potential Role in Neurodegenerative Disease *Annual Report, 9 Jul. 1999-8 Jul. 2000*

Millhorn, David E.; Aug. 2000; 23p; In English

Contract(s)/Grant(s): DAMD17-99-1-9544

Report No.(s): AD-A383039; No Copyright; Avail: CASI; A03, Hardcopy; A01, Microfiche

The primary objective of this research project is to determine the role of the mitogen-activated protein kinase (MAPK) pathways (specifically p38 kinase) in mediating the cellular response to hypoxia-stress. The overall scope of this project is to understand how neurons adapt to chronic hypoxia. The neural-like PC12 cell line is used as a model system to identify the molecular mechanisms that mediate tolerance to hypoxia. The inability to develop tolerance can lead to neurodegeneration and possibly cell death. Our work on this project resulted in the publication of 4 original papers, 1 review paper, and 1 book chapter. DTIC

Gene Expression; Physiological Responses; Proteins; Hypoxia; Stress (Physiology); Diseases; Genetics

20000119041 George Washington Univ., Washington, DC USA

Physiological Stress-Induced Drug Resistance and Its Reversal *Annual Report, 1 Jul. 1999-30 Jun. 2000*

Kennedy, Katherine; Jul. 2000; 27p; In English

Contract(s)/Grant(s): DAMD17-99-1-9186

Report No.(s): AD-A383040; No Copyright; Avail: CASI; A03, Hardcopy; A01, Microfiche

Physiological stress conditions associated with solid tumors play a role in chemotherapeutic resistance. Treatment with hypoxia or chemical stress agents causes EMT6 mouse mammary tumor cells to develop resistance to teniposide and etoposide, a topoisomerase II inhibitor. We have shown that prostaglandin A1 can fully reverse stress-induced resistance to teniposide or etoposide and the PGA1 can reverse this resistance when given either prior to or after the stress. PGA1 could also block activation of the transcription factor, NF-kB, as measured by gel shift assays or a luciferase reporter gene. to test whether NF-kB was directly involved in stress-induced resistance, an inducible promoter plasmid system containing a mutant IkB gene (which was non-phosphorylatable) was introduced into EMT6 cells as a dominant negative mutant. Expression of the dominant negative mutant prevented the stress activation of NE-kB and reverted the resistant phenotype to a drug sensitive phenotype. These results imply

that NE-kE directly mediates both chemical and physiological stress-induced drug resistance in cancer cells and suggest that agents like PGA1 which prevent NP-kB activation may improve the efficacy of topoisomerase II inhibitors.
DTIC
Cancer; Mammary Glands; Stress (Physiology); Assaying; Inhibitors; Drugs

20000119044 California Univ., Davis, CA USA
Computer Simulation of Breast Cancer Screening *Annual Report, 1 Jul. 1998-30 Jun. 1999*
Boone, John M.; Jul. 1999; 78p; In English
Contract(s)/Grant(s): DAMD17-98-1-8176
Report No.(s): AD-A383107; No Copyright; Avail: CASI; A05, Hardcopy; A01, Microfiche

Breast cancer will affect approximately 12.5% of the women in the United States, and currently mammographic screening is considered the best way to reduce mortality from this disease through early detection. There is much controversy concerning the most appropriate screening parameters such as starting age, the screening interval, and the stopping age. Long term multi-center clinical trials are the traditional approach to evaluating the efficacy of a medical test such as mammography, however clinical trials are expensive and lengthy. This grant focuses on the use of computer simulation techniques for evaluating the screening efficacy of mammography. Breast cancer growth rates, incidence rates, multiracial population demographics, death rates, breast cancer prognosis factors, breast density considerations, detection versus diameter probabilities, and other pertinent data have been computer fit and incorporated into a breast cancer screening simulator. The simulator is capable of producing many types of results data, including survival curves, tumor size distributions at detection, and "years of life saved" statistics. We are currently in the process of validating the simulator output with the results from respected clinical trials. Once validated, the screening simulator will be useful for studying ways in which the timing of the mammography examination can be optimized.
DTIC
Cancer; Computerized Simulation; Females

20000119045 Duke Univ., Durham, NC USA
Computer Aided Breast Cancer Diagnosis *Annual Report, 23 Sep. 1998-1999*
Floyd, Carey E.; Oct. 1999; 16p; In English
Contract(s)/Grant(s): DAMD17-94-J-4371
Report No.(s): AD-A383108; No Copyright; Avail: CASI; A03, Hardcopy; A01, Microfiche

While biopsy is a sensitive and specific test for breast cancer, to achieve a high sensitivity for cancer, many women with mammographic findings due to benign processes undergo biopsy. to improve the specificity of the decision to recommend biopsy and reduce the number of benign biopsies performed, a computer decision aid is being developed. ANN (ARTIFICIAL NEURAL NETWORKS) systems for prediction have been evaluated using a database of mammographic cases that were sent to biopsy with the results known. A case findings matching algorithm was implemented using a relational database to simplify and speed the coding. A Case-Based Reasoning approach was selected for this study since we wished to examine the cases and the similarity between them. to classify a given test case as benign or malignant, the case is compared to all previous cases, selecting those cases with were similar with regards to their findings. A decision variable was formed as the "malignancy ratio" computed as the ratio of the number of malignant cases to the total number of similar or "matched" cases. The system performed with an ROC area of 0.77. As described here, the system performs better than chance but poorer than the performance reported for radiologists on these data.
DTIC
Cancer; Decision Support Systems; Diagnosis; Relational Data Bases; Clinical Medicine

20000119974 John Wayne Inst. for Cancer Treatment and Research, Santa Monica, CA USA
A New Immunologic Method for Detection of Occult Breast Cancer *Final Report, 1 Oct. 1994 - 31 Aug. 1999*
Gupta, Rishab K., John Wayne Inst. for Cancer Treatment and Research, USA; September 1999; 150p; In English
Contract(s)/Grant(s): DAMD17-94-J-4459
Report No.(s): AD-A382599; No Copyright; Avail: CASI; A02, Microfiche; A07, Hardcopy

The overall objective of this research proposal was to develop laboratory tests that are meaningful diagnostic/prognostic indicators for the physician's use in the battle against human breast cancer. We worked towards the establishment of sensitive immunologic assays, which could reliably detect and quantify antigen-specific IC in the sera of patients with breast cancer. Therefore, our objectives were to define breast tumor associated antigens to which patients respond immunologically, and develop human and marine monoclonal antibodies to these immunogenic breast cancer antigens. It was expected that human monoclonal antibodies would be used to increase the level of tumor- associated antigen (TAA)-specific IC in samples from breast cancer

patients who might have no or low levels of anti-tumor antibodies, and thus no or low levels of TAA-specific IC. We also proposed to develop an IC detection assay that would be specific for tumor associated antigen.
DTIC
Antibodies; Immunology; Antigens; Mammary Glands; Cancer

20000120021 Kentucky Univ., Coll. of Pharmacy, Lexington, KY USA
Allosteric Modifiers of Hemoglobin: Potential Applications in Red Cell Storage and Liposome-Encapsulated Hemoglobin Development *Final Report, 1 Feb. - 30 Oct. 1998*
Burke, Thomas G., Kentucky Univ., USA; Kruszewski, Stefan, Kentucky Univ., USA; Yang, Danzhou, Kentucky Univ., USA; Sep. 12, 2000; 15p; In English
Contract(s)/Grant(s): N00014-98-1-0504
Report No.(s): AD-A382644; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

The overall objective of the research program is to develop allosteric modifiers of hemoglobin, that are effective in vivo. The ability of a novel agent 02-50, a trifluoromethyl substituted analog of LRl6, was found to strongly modulate the P10 value of purified hemoglobin. 02-50 displayed activity greater than that of LRl6. However, the presence of human serum albumin (HSA) strongly modulated the pharmacological properties of LRl6 and 02-50 agents. Experiments with denatured HSA also revealed that the albumin interactions with LR-16 were not specific in nature and both LR-16 and 02-50 are lipophilic and capable of diffusing from LEH particles.
DTIC
Methyl Compounds; Hemoglobin; Erythrocytes; Proteins

20000120023 New Mexico Univ., Albuquerque, NM USA
Delays and Refusals in Treatment for Breast Cancer Among Native American and Hispanic Women With Breast Cancer *Annual Report, 1 Aug. 1998 - 31 Jul. 1999*
Saavedra, Elba, New Mexico Univ., USA; Duryea, Elias, New Mexico Univ., USA; August 1999; 9p; In English
Contract(s)/Grant(s): DAMD17-96-1-6191
Report No.(s): AD-A382693; No Copyright; Avail: CASI; A01, Microfiche; A02, Hardcopy

The aim of this study is to describe the factors associated with delays in breast cancer treatment among New Mexico Hispanic, Native American and non-Hispanic white women. Scope: The study is enrolling a total of 70 participants, 35 patients and 35 care givers identified by the patient. This ethnographic study will gather data on the psychosocial, cultural, atitudinal, spiritual and demographic variables associated with delays in breast cancer treatment. The focus of the semi-structured interview is to encourage the women in story-telling about their breast cancer experiences. Interviews will be conducted for a minimum of two sessions. The study has received input from regional community health advisors, breast cancer survivors, The Gathering of Cancer Support, and People Living Through Cancer. Other organizations supporting the study include; the New Mexico Breast and Cervical Cancer Detection and Control B&CC) Program, the Mexico Tumor Registry, the Health Promotion and Disease Prevention Programs (HPDP) at the Gallup Indian Medical Center, the Northern Navajo Medical Center in Shiprock, and the Crownpoint Health care Facility. Summary: Accomplishments for this project period include; 1) review and identification of 178 additional cases from the NM B&CC Program breast cancer database (potential participants) 2) increased community support and approval from the Churchlock Chapter House in Gallup, New Mexico 3) increased support and input from Hispanic and Native American breast cancer survivors, and community health advisors working with Hispanic and Native American women 4) submission of the study for Navajo Nation IRB approval.
DTIC
Cancer; Females; Mammary Glands; American Indians; Health; Patients; Clinical Medicine

20000120024 Pennsylvania Univ., Philadelphia, PA USA
Gene Therapy Mediated Breast Cancer Immunity *Final Report, 15 Aug. 1996 - 14 Aug. 1999*
Nesbit, Heinke K., Pennsylvania Univ., USA; September 1999; 68p; In English
Contract(s)/Grant(s): DAMD17-96-1-6287
Report No.(s): AD-A382694; No Copyright; Avail: CASI; A01, Microfiche; A04, Hardcopy

The goat of the study was to assess the efficiency of B7-1 expressing breast cancer cells as a tumor vaccine. We showed that adenovirally delivered B7-1 expression on mammary carcinoma cells did not result in tumor relection in vivo and failed to activate allogeneic T cells in vitro. We provided evidence that the lack of T cell stimulation by B7-1 expressing breast cancer cells was due to secretion of PGE2. POE2 is produced by the cyclooxygenase (COX) mediated oxidation of arachidonic acid. The inhibition of COX activity in B7-1 expressing MDA-MB 231 cells restored the proliferative response of T cells. to further support the finding

that POE2 inhibits B7-i induced T cell responses we created B7-i positive, COX-i expressing HBL-100 breast epithelial cells and WM9 melanoma cells. T cells were stimulated to proliferate by B7-i expressing HBL-i00 cells or WM9 cells, whereas T cell proliferation was inhibited when both P7-1 and COX- 1 were expressed. Therefore, POE2 may limit the use of breast cancer vaccines based on B7-1 expressing breast cancer cells.
DTIC
Cancer; Mammary Glands; Therapy; Genes; Immunity

20000120025 Miami Univ., FL USA
Role of Human DNA Polymerase and Its Accessory Proteins in Breast Cancer *Annual Report, 1 Sep. 1997 - 31 Aug. 1998*
Lee, Marietta, Miami Univ., USA; September 1998; 24p; In English
Contract(s)/Grant(s): DAMD17-96-1-6166
Report No.(s): AD-A382695; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

Thus far the mechanisms for genetic errors and genomic instability in breast cancer cells have not been fully delineated. Defects in DNA polymerase delta and its accessory proteins could contribute to the molecular etiology of breast cancer. DNA polymerase delta and its accessory proteins are involved in both DNA replication, repair, recombination and transcription. There are linkages between polymerase delta and cell cycle regulation via protein-protein interaction of polymerase processivity factor PCNA with p21, a cyclin dependent kinase inhibitor. We are approaching this study in a multifaceted manner at the protein, message and gene level. It is hoped that the results from these studies will provide a deeper understanding of the linkage between regulation of polymerase delta and its accessory proteins and carcinogenesis in breast cancer.
DTIC
Cancer; Deoxyribonucleic Acid; Mammary Glands; Genetics; Carcinogens; Proteins

20000120026 Georgetown Univ., Washington, DC USA
Identification of Proteins Required for Repair of Double-Strand Chromosome Breaks, a Predisposing Factor in Breast Cancer *Annual Report, 15 May 1999 - 14 May 2000*
Jones, Jessica, Georgetown Univ., USA; Nakai, Hiroshi, Georgetown Univ., USA; June 2000; 35p; In English
Contract(s)/Grant(s): DAMD17-98-1-8090
Report No.(s): AD-A382696; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

Defects in repair of double-strand chromosomal breaks (DSB) are critical factors in familial and sporadic breast tumors. In model bacterial systems, such lesions can be ascribed to defects in homologous recombination proteins, which can support chromosomal replication by promoting restart of DNA synthesis when replication forks become arrested. This project has focused on developing a bacterial model for DSB repair by characterizing the enzymatic apparatus needed to initiate DNA replication on recombination intermediates. Escherichia coli PriA protein was found to play a critical function in the transition from recombination to DNA replication. PriA specifically binds to forked DNA structures created by recombination or replication fork arrest and promotes the assembly of protein components needed to load the major replicative helicase DoaB onto the template, a critical step in initiation. DnaB requires single-stranded DNA to bind, and this could be created by the helicase action of PriA, an activity that is suppressed by single-stranded binding protein if a duplex opening is already available. These data indicate that PriA can function in the repair of damaged DNA templates by promoting assembly of replication proteins on a wide variety of forked templates, preventing catastrophic loss or alteration of genetic information.
DTIC
Cancer; Chromosomes; Mammary Glands; Proteins

20000120097 National Chin-Yi Inst. of Tech., Dept. of Electronic Engineering, Taichung, Taiwan, Province of China
Segmentation of Medical Images through a Penalized Fuzzy Hopfield Network with Moments Preservation
Lin, Jzau–Sheng, National Chin-Yi Inst. of Tech., Taiwan, Province of China; Journal of The Chinese Institute of Engineers. Special Issue: Chemical Engineering; September 2000; Volume 23, No. 5, pp. 633-643; In English; See also 20000120087; Copyright; Avail: Issuing Activity

Segmentation of medical images, including Computerized Tomography (CT), Magnetic Resonance Imaging (MRI), mammographic imaging, and x-ray imaging, is in important step in the identification of tissue organization for analysis of the human body. Segmentation can also be cast as an optimization problem that call be regarded as the minimization of a criterion function defined as a function of the Euclidean distance between two pixels with their local constraints. In this paper, the Hopfield neural network with penalized fuzzy c-means technique (called PFHNN) is proposed for medical image segmentation. Instead of using global information (such as histogram), the pixels with their first and second order moments constructed from their n nearest neighbors as a training vector are mapped to a two-dimensional Hopfield neural network for the purpose of classifying

the image into suitable regions. The penalized fuzzy c-means technique is also applied to eliminate searching for weighting factors and to update training efficiency with additional bias input. In the experimental result, segmented data are obtained from test phantoms with added noise and MRI images.
Author
Imaging Techniques; Research and Development; Segments; Medical Science

20000120133 Prins Maurits Lab. TNO, Rijswijk, Netherlands
Detection of Long-Term Low-Dose Radiation Damage in DNA *Final Report*
Broekhuijsen, M. P., Prins Maurits Lab. TNO, Netherlands; Timmerman, A. J., Prins Maurits Lab. TNO, Netherlands; vanderSchans, G. P., Prins Maurits Lab. TNO, Netherlands; October 2000; 37p; In English
Contract(s)/Grant(s): A98/M4/23; TNO Proj. 014.10539
Report No.(s): TD-2000-0059; TNO-PML-2000-A57; Copyright; Avail: Issuing Activity

A newly designed, modified polymerase chain reaction (PCR) method was tested for its ability to detect deletions in DNA in a high background of unmutated DNA. The method was shown to be very effective with a small artificial DNA containing a known deletion. Using this system, the deletion could be reliably detected in a background of 100,000 times as much of unmutated DNA. With total DNA from cultured cells, the method also performs well, but needs further optimization to achieve the same efficiency as with the small artificial DNA. Future development should focus on optimization and use with irradiated human DNA from blood cells.
Author
Cells (Biology); Deletion; Deoxyribonucleic Acid; Radiation Damage

20000120138 Prins Maurits Lab. TNO, Rijswijk, Netherlands
Sleep and Alertness Management in Military Operations: Pharmacology, Methods and Animal Models *Final Report*
Busker, R. W., Prins Maurits Lab. TNO, Netherlands; Melchers, B. P. C., Prins Maurits Lab. TNO, Netherlands; Philippens, I. H. C. H. M., Prins Maurits Lab. TNO, Netherlands; Bruijnzeel, P. L. B., Prins Maurits Lab. TNO, Netherlands; April 2000; 46p; In English
Contract(s)/Grant(s): B99/D4/89; TNO Proj. 014.11589
Report No.(s): TD-2000-0004; TNO-PML-2000-A2; Copyright; Avail: Issuing Activity

Military missions are often associated with prolonged duty, night shifts, high stress levels, and transmeridian transport. This results in disrupted sleep habits and possibly in decreased alertness. It is becoming more and more accepted to manage sleep and alertness in order to guarantee fitness of military personnel. This study gives an overview of pharmacological means to regulate sleep and alertness. The focus is on methods to study the effectiveness and safety of hypnotics and stimulants in monkeys. A research approach is designed, in parallel with human volunteer studies, to eventually come to practical protocols for sleep and alertness management in military operations.
Author
Alertness; Sleep; Pharmacology; Research and Development; Human Performance

20000120152 Aeromedical Inst., Soesterberg, Netherlands
G-CARE Project *Progress Report*
Ersoy, G. A., Aeromedical Inst., Netherlands; March 1999; 21p; In English
Contract(s)/Grant(s): A95/KLu/03
Report No.(s): Rept-1999-KI; Copyright; Avail: Issuing Activity

The Computer Assisted Registration and Evaluation of electrocardiograms measured during G-training (G-CARE) software is being developed to assist the medical supervisor in monitoring the electrocardiogram (ECG) of the trainee during centrifuge trainings. An update on the project status is presented. A major developement was a new graphical user interface (GUI) under Windows 95, an integrated database and ECG annotation edit review environment. The edit and review possibilities have also been expanded, as compared to the former DOS version. Recommendations are given for improvement of the performance of the heart beat classifier, by employing new methods of feature extraction. In the next phase of the project, the database module has to be implemented into the new GUI framework.
Author
Computer Techniques; Graphical User Interface; Computer Programs; Data Bases; Progress

20000120155 Lockheed Martin Engineering and Sciences Co., Moffett Field, CA USA

Bioimpedance Measurement of Segmental Fluid Volumes and Hemodynamics

Montgomery, Leslie D., Lockheed Martin Engineering and Sciences Co., USA; Wu, Yi–Chang, Duke Univ., USA; Ku, Yu–Tsuan E., Lockheed Martin Engineering and Sciences Co., USA; Gerth, Wayne A., Duke Univ., USA; [2000]; 29p; In English

Contract(s)/Grant(s): N00014-87-C-0166; No Copyright; Avail: CASI; A03, Hardcopy; A01, Microfiche

Bioimpedance has become a useful tool to measure changes in body fluid compartment volumes. An Electrical Impedance Spectroscopic (EIS) system is described that extends the capabilities of conventional fixed frequency impedance plethysmographic (IPG) methods to allow examination of the redistribution of fluids between the intracellular and extracellular compartments of body segments. The combination of EIS and IPG techniques was evaluated in the human calf, thigh, and torso segments of eight healthy men during 90 minutes of six degree head-down tilt (HDT). After 90 minutes HDT the calf and thigh segments significantly (P is less than 0.05) lost conductive volume (eight and four percent, respectively) while the torso significantly (P is less than 0.05) gained volume (approximately three percent). Hemodynamic responses calculated from pulsatile IPG data also showed a segmental pattern consistent with vascular fluid loss from the lower extremities and vascular engorgement in the torso. Lumped-parameter equivalent circuit analyses of EIS data for the calf and thigh indicated that the overall volume decreases in these segments arose from reduced extracellular volume that was not completely balanced by increased intracellular volume. The combined use of IPG and EIS techniques enables noninvasive tracking of multi-segment volumetric and hemodynamic responses to environmental and physiological stresses.

Author

Body Fluids; Compartments; Hemodynamic Responses; Hemodynamics; Hypokinesia; Physiological Responses

20000120422 Pennsylvania Univ., Philadelphia, PA USA

Predoctoral Training in Breast Cancer Detection and Treatment *Final Report, 1 Aug. 1994 - 31 Jul. 1999*

Leigh, John S., Pennsylvania Univ., USA; August 1999; 18p; In English

Contract(s)/Grant(s): DAMD17-94-J-4027

Report No.(s): AD-A382660; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

Our training program in the detection and treatment of breast cancer has provided an excellent training opportunity to those interested in pursuing research careers in this interdisciplinary area. We have structured our program so that each of the four predoctoral trainees were assigned dual advisors. Each trainee was supervised by a well trained basic scientists as well as a clinician. In addition, each trainee attended weekly journal club meetings and monthly seminars. The field of research encompassed a wide variety of disciplines including Genetics, Biophysics, Biochemistry, Physiology, Tumor Biology, Electrical Engineering, and Computer Science as well as many clinical fields (including Surgery, Radiology, Oncology, Radiation Therapy). The University of Pennsylvania has developed a unique broadly based interdisciplinary program of graduate education aimed at applying physical principles to the clinical problems inherent in the detection and treatment of breast cancer. During the past year our main research effort was aimed at improving the detection and treatment of breast cancer. This effort involved many aspects of detection both by imaging breast cancers as well as genetic screening. We began the development of improved treatment protocols based on increased knowledge of the metabolism of breast disease.

DTIC

Detection; Education; Cancer; Mammary Glands; Occupation; Diseases

20000120423 Jefferson Medical Coll., Philadelphia, PA USA

Mammary Tumor Development: Stromal-Epithelial Interactions in Oncogenesis *Final Report, 1 Sep. 1994 - 31 Aug. 1999*

Strayer, David S., Jefferson Medical Coll., USA; September 1999; 49p; In English

Contract(s)/Grant(s): DAMD17-94-J-4434

Report No.(s): AD-A382595; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

The purpose of this grant was to study mammary oncogenesis in transgenic mice that expressed a virus-derived growth factor, Shope growth factor (SGF), which resembles epidermal growth factor (EGF). Shope growth factor (SGF). Lines of SGF transgenic mice expressed this cytokine using inducible (metallothionein, MT) and constitutive (RSV-LTR) promoters. We have found that expression of SGF in transgenic mice under the control of the RSV-LTR as a promoter led to profound changes in mammary gland histology, resulting in a pathologic and molecular phenotype that shows changes characteristic of%late pregnancy or lactation. These changes include mammary gland differentiation: acinar proliferation, distention of glands and ducts by proteinaceous material consistent in appearance with lactation products (i.e., milk production), and comparable changes in mammary ducts. Corresponding alterations have been seen in patterns of gene expression in these mammary glands: expression of lactation- associated genes such as whey acidic protein, t3-casein, and WDNMI, was increased in SGF-transgenic mice. Transgenic mice expressing SCF under the control of metallothionein promoter (MT-SGF) generally showed similar findings

when MT promoter activity was induced by feeding with Zn2+. These findings have profound implications for understanding mammary oncogenesis and, in particular, its inhibition. 1% qiRi%rT Th%M%
DTIC
Epithelium; Mammary Glands; Cancer; Genes; Cells (Biology)

20000120424 Pittsburgh Univ., Pittsburgh, PA USA
Development of an Integrated Program of Health-Related Quality-of-Life Research for the National Surgical Adjuvant Breast and Bowel Project *Annual Report, 1 Sep. 1998 - 31 Aug. 1999*
Day, Richard D., Pittsburgh Univ., USA; September 1999; 76p; In English
Contract(s)/Grant(s): DAMD17-97-1-7058
Report No.(s): AD-A382570; No Copyright; Avail: CASI; A01, Microfiche; A05, Hardcopy

This is the 2nd Year (months 13-24) Report for a Career Development Award for the development of a Health-Related Quality of Life (HRQL) Program for the National Surgical Adjuvant Breast and Bowel Project (NSABP). Specific aims proposed for the award included: (a) Design and implementation of new HRQL components for planned NSABP treatment and prevention trials; (b) testing and implementation of data collection methods to be used in treatment and prevention trials; (c) analysis of HRQL data collected in the NSABP prevention and treatment trials; (d) refinement and extension of HRQL methods to analyze the data from new treatment and prevention studies; (e) enhancement of minority participation in NSABP trials. Primary achievements for the months 13-24 described in this report include: (i) Implementation of two new NSABP protocols with HRQL components (P-2, B-30); (ii) completion of patient recruitment in the first two NSABP treatment protocols with a HRQL component (B-23, C-O6); (iii) conducting successful NSABP HRQL Workshop; (iv) development of real-time monitoring methods to reduce missing data in NSABP HRQL studies; (v) publication of initial quality of life communication from the NSABP P-i protocol; (vi) development of a minority recruitment program for the P-2 (STAR) HRQL component.
DTIC
Health; Mammary Glands; Cancer; Prevention; Detection; Medical Services

20000120425 Pennsylvania Univ., Philadelphia, PA USA
Developing a System for Directed Gene Introduction into Mammary Gland Via Targeted Infection of Retrovirus Receptor Transgenics *Final Report, 1 Sep. 1994 - 31 Aug. 1998*
Bates, Paul, Pennsylvania Univ., USA; September 1998; 26p; In English
Contract(s)/Grant(s): DAMD17-94-J-4183
Report No.(s): AD-A382556; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

The long term goal of this project is to develop a novel method to target infection of retroviral vectors in vivo utilizing mice expressing a retroviral receptor transgene (the Rous sarcoma virus receptor). Directed infection, and thus directed gene expression of cells expressing the viral receptor should provide a rapid and efficient method to test the mammary tumorigenic potential of genes in an animal model. Unlike the traditional method of testing gene function in transgenic mice, directed infection can be temporally controlled allowing assessment of differences in oncogenic potential at different stages of mammary gland development. Finally, multiple oncogenes can be introduced by co-infection allowing questions of synergy to be addressed. Toward this long term goal, we produced two transgenic mouse lines carrying the RSV receptor. However before characterization of receptor expression or in vivo targeting, both transgenic lines were lost. Considerable progress on development of viral vectors for use in this targeting system was achieved. Vectors and procedures for the production of high titer murine leukemia virus (RSV) pseudotypes were established. These MLV(RSV) vectors allow greater flexibility and capability compared to available RSV vectors and will be of great utility for directed infection of mammary epithelial cells in transgenic mice when the mice become available.
DTIC
Genes; Infectious Diseases; Cells (Biology); Receptors (Physiology); Mammary Glands; Cancer; Viruses; In Vivo Methods and Tests

20000120426 Michigan Univ., Ann Arbor, MI USA
Improved Mammographic Technique for Breast Cancer Diagnosis *Final Report, 11 Jul. 1994 - 10 Jul. 1999*
Chan, Heang–Ping, Michigan Univ., USA; August 1999; 75p; In English
Contract(s)/Grant(s): DAMD17-94-J-4292
Report No.(s): AD-A382555; No Copyright; Avail: CASI; A01, Microfiche; A04, Hardcopy

During the entire project period, we have completed the following tasks: (1) Develop computerized breast border detection and classification scheme. (2) Develop and evaluate exposure equalization filters. (3) Monte Carlo modeling of mammographic

imaging systems and optimization of imaging techniques. (4) Design and build breast-tissue-equivalent phantoms for x-ray and ultrasound imaging. (5) Evaluate effects of equalization on image quality. (6) Develop a novel combined x-ray equalization and ultrasound imaging system for improved evaluation of dense breasts and mammographic lesions. (7) Design and build a compressible tank and a special compression paddle for combined imaging. (8) Evaluate tissue-equivalent fluids for x-ray equalization and ultrasound coupling. (9) Perform phantom study to evaluate the feasibility of combined imaging. (10) Develop breast density segmentation program for automated localization of dense tissue regions on digitized mammograms. (11) Design and build a prototype motorized ultrasound scanning device for the combined imaging system. These studies are consistent with the goals of our proposed project. Our new approach of using a compressible tank containing tissue-equivalent fluid for x%ay equalization in a prone mammography system provides truly patient-specific equalization for breasts of any size and shape, and for any mammographic view. Our studies indicate that x-ray equalization can improve visibility of breast lesions on mammograms. We also demonstrated that the feasibility of developing a combined x-ray and ultrasound imaging system for improved breast imaging. The capability of allowing ultrasound scanning in the same geometry as mammography has the promise to improve breast cancer detection and diagnosis in dense breasts.
DTIC
Mammary Glands; Cancer; Diagnosis; Detection; Imaging Techniques; X Ray Imagery; Ultrasonics; Monte Carlo Method

20000120427 Tufts Univ., Boston, MA USA
The Role of EMMPRIN in Tumor Angiogenesis and Metastasis *Annual Report, 1 May 1999 - 30 Apr. 2000*
Marieb, Erica, Tufts Univ., USA; Toole, Bryan, Tufts Univ., USA; May 2000; 10p; In English
Contract(s)/Grant(s): DAMD17-99-1-9411
Report No.(s): AD-A382545; No Copyright; Avail: CASI; A01, Microfiche; A02, Hardcopy

A critical step in tumorigenesis is proteolytic modification of the peri-cellular matrix surrounding tumor cells by matrix metalloproteinases (MMPs) . Stromal cells associated with tumors, not the tumor cells themselves, are responsible for the production of most tumor MMPs. Studies from our laboratory and those of our collaborators have shown that EMMPRIN (extracellular matrix metalloproteinase inducer), a tumor cell surface glycoprotein, stimulates the production of several MMPs by fibroblasts and endothelial cells. Antisense cDNA and ribozyme constructs were utilized in an attempt to inhibit EMMPRIN expression in TA3/ST cells, a murine breast carcinoma cell line. These constructs were not efficient in blocking EMMPRIN expression and consequently, were inactive in vivo. However, transfection and injection experiments done in collaboration with Dr. Stanley Zucker have shown that MDA-MB-436 human breast cancer cells transfected with GFP-EMMPRIN can produce much larger tumors in nude mice than vector-transfected cells. Also, EMMPRIN can stimulate the production of MMPs 1, 2 and 3 by endothelial cells; MMPs 1, 2 and 9 have been shown previously to promote angiogenesis. Therefore, we proposed that a possible explanation of the increased tumor growth obtained with EMMPRIN-transfected cells is an efficient nutrient supply resulting from angiogenesis. to assay whether EMMPRIN is capable of inducing angiogenesis, we treated HUVECs on type I collagen with either EMMPRIN or bFGF, a known angiogenic factor. As opposed to controls which maintained their cobblestone-like monolayer arrangement, treated HUVECs formed capillary-like tubules, lending Support to EMMPRIN as an angiogenic factor.
DTIC
Cells (Biology); Mammary Glands; Cancer; Assaying; Endothelium; Regeneration (Physiology)

20000120428 Toronto Hospital, Toronto, Ontario Canada
Dominant-Active Alleles of Rb as Universal Tumor Suppressors of Mammary Carcinoma *Annual Report, 1 Sep. 1998 - 1 Sep. 1999*
Zacksenhaus, Eldad, Toronto Hospital, Canada; October 1999; 19p; In English
Contract(s)/Grant(s): DAMD17-97-1-7321
Report No.(s): AD-A382540; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

The tumor suppressor Rb is a nuclear-phosphoprotein that controls cell proliferation, survival and differentiation and is thought to be either mutated or functionally inactivated by phosphorylation in virtually all human cancer including breast cancer. We developed transgenic mouse models to study the outcomes of upregulating the Rb pathway in the mammary gland and test whether Rb is a universal tumor suppressor. Unphosphorylatable alleles of Rb (RbDeltap34 and RbDeltaKl 1, with 8 and 11 CDK sites mutated) were targeted to the mammary epithelium under control of the MMTV-LTR (proliferating and differentiating mammary epithelium) and WAP (differentiating epithelial cells) promoters. Pre-pubertal MMTV-RbDeltap34 and MMTV-RbDeltaKl 1 transgenic female mice exhibited suppression of ductal growth and branching. During estrus, these transgenic females displayed enlargement of the alveolar compartment. Intriguingly, some MMTV-RbDeltap34 and MMTV-RbDeltaKl 1 transgenic females developed focal hyperplasia as well as full-blown mammary adenocarcinomas. In accord with

the more restricted pattern of expression, WAP-RbDeltaKl 1 transgenic mice did not exhibit the early suppression of ductal growth, seen in MMTV-RbDeltaK females, but about 20% developed focal hyperplasia and some developed breast tumors by one year. Though exactly the opposite of what we expect, these provocative and novel results are in accord with our emerging understanding of Rb as a major regulator of both cell proliferation and survival. to determined synergistic or suppressing effects on breast cancer, genetic crosses outlined in the Statement of Work will be carried out by breeding the RbDeltaK transgenic mice with MMTV- Neu and MMTV- wnt mice that are predisosed to breast cancer.
DTIC
Mammary Glands; Cancer; Suppressors; Cells (Biology); Regeneration (Physiology)

20000120759 Rutgers Univ., Dept. of Mathematical Sciences, Camden, NJ USA
Reliability Stress-Strength Models for Dependent Observations with Applications in Clinical Trials
Kushary, Debashis, Rutgers Univ., USA; Kulkarni, Pandurang M., University of South Alabama, USA; [1995]; 23p; In English; No Copyright; Avail: CASI; A03, Hardcopy; A01, Microfiche

We consider the applications of stress-strength models in studies involving clinical trials. When studying the effects and side effects of certain procedures (treatments), it is often the case that observations are correlated due to subject effect, repeated measurements and observing many characteristics simultaneously. We develop maximum likelihood estimator (MLE) and uniform minimum variance unbiased estimator (UMVUE) of the reliability which in clinical trial studies could be considered as the chances of increased side effects due to a particular procedure compared to another. The results developed apply to both univariate and multivariate situations. Also, for the univariate situations we develop simple to use lower confidence bounds for the reliability. Further, we consider the cases when both stress and strength constitute time dependent processes. We define the future reliability and obtain methods of constructing lower confidence bounds for this reliability. Finally, we conduct simulation studies to evaluate all the procedures developed and also to compare the MLE and the UMVUE.
Author
Maximum Likelihood Estimates; Reliability Analysis; Stress Analysis; Medical Science

20000120858 Fundacao Ceiliano Abel de Almeida, Vitoria, Brazil
Research and Training in Tropical and Emerging Infectious Diseases in Brazil *Final Report, 1 Jan. 1998 - 31 Jan. 2000*
Dietze, Reynaldo, Fundacao Ceiliano Abel de Almeida, Brazil; January 2000; 18p; In English
Contract(s)/Grant(s): DAMD17-98-2-8004
Report No.(s): AD-A382544; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

Evaluation of the cellular immune responses on patients with febrile illnesses during a Dengue epidemic in the State of Minas Gerais, Brazil: Preliminary results: In the present study we evaluated by flow cytometry the activation of both CD4+ and CD8+ T cells through the analysis of CD3+ cells co- expressing either CD4+ CD69+ or CD8+ CD69+ in patients with primary Dengue infection.
DTIC
Patients; Infectious Diseases; Tropical Regions; Education; Research; Viruses

20000120859 Iowa Univ., Iowa City, IA USA
Role of the erbB3 Gene Product in Breast Cancer Cell Proliferation *Final Report, 1 Sep. 1994 - 31 Aug. 1999*
Koland, John G., Iowa Univ., USA; September 1999; 77p; In English
Contract(s)/Grant(s): DAMD17-94-J-4185
Report No.(s): AD-A382807; No Copyright; Avail: CASI; A01, Microfiche; A05, Hardcopy

The role of the heregulin receptor ErbB3 in breast cancer cell proliferation was examined. In the first year of funding, we discovered that ErbB3, although possessing a protein tyrosine kinase (PTK) homology domain, is in fact devoid of intrinsic PTK activity. In year two, we demonstrated the critical dependence of heregulin signaling upon the PTK activity of ErbB2 and characterized the interaction of ErbB3 with phosphoinositide (PI) 3-kinase in breast cancer cells. In year three, we identified a single tyrosine residue in ErbB3 responsible for binding the Shc adapter protein, clarified the role of Shc in activation of the Ras/mitogen-activated protein kinase (MAPK) pathway, and began an examination of other ErbB3 tyrosine residues. In the fourth year, we implicated six specific ErbB3 tyrosine residues in mediating interactions with PI 3-kinase and activating its downstream signaling target, the protein kinase Akt. In the fifth year of the project, we investigated a novel mechanism by which the Akt kinase was activated in the absence of a direct interaction of PI 3-kinase with either ErbB2 or ErbB3. Subsequently, we compared the

respective contributions of the Ras/MAPK and PI 3-kinase signaling pathways in mediating the cell proliferation and transformation responses resulting from ErbB2/ErbB3 activity.
DTIC
Genes; Genetic Code; Mammary Glands; Cancer; Cells (Biology); Regeneration (Physiology)

20000120900 Dartmouth Coll., Hanover, NH USA
Butyrate Therapy for Poorly Differentiated Breast Cancer *Final Report, 15 Sep. 1997 - 14 Sep. 1999*
McBain, John, Dartmouth Coll., USA; October 1999; 9p; In English
Contract(s)/Grant(s): DAMD17-97-1-7245
Report No.(s): AD-A382836; No Copyright; Avail: CASI; A01, Microfiche; A02, Hardcopy

This project aims to devise a strategy for maintaining butyric acidemia in mice over a 24 hour period of time, so as to achieve a nearly complete inhibition of histone deacetylase activity. The basic approach is to use butyryglycerides as a prodrug to butyrate and MCPA as an inhibitor of butyrate metabolism (MCPA). We monitor for both vital signs and blood chemistries to assure survival during the prolong metabolic acidosis. Our hypothesis is that such a scheme will allow maintenance of butyrate blood levels between 1 and 5 mM, and that the mice will develop hyperacetylation of chromatin core histones sufficient to cause extensive cytolysis in xenografted tumors with known sensitivity to butyrate-induced apoptosis.
DTIC
Butyric Acid; Cancer; Mammary Glands

20000120901 Utah Univ., Salt Lake City, UT USA
Identification and Genetic Mapping of Genes for Hereditary Breast Cancer and Ovarian Cancer in Families Unlinked to BRCA1 *Final Report, 22 Aug. 1994 - 21 Aug. 1999*
Neuhausen, Susan L., Utah Univ., USA; Sep. 15, 1999; 182p; In English
Contract(s)/Grant(s): DAMD17-94-1-4260
Report No.(s): AD-A382834; No Copyright; Avail: CASI; A02, Microfiche; A09, Hardcopy

A family history of breast cancer is a major risk factor for developing breast cancer, with estimates that up to 10% of breast cancer is due to a genetic predisposition. The original objective of this grant was to localize BRCA2. At the time the grant was funded, we had localized BRCA2, so we modified the aims to isolate BRCA2. Our collaborator on this grant, Dr. Stratton, isolated BRCA2 at the end of 1995. The aims were modified to characterize BRCA2, including identifying mutations in high-risk breast cancer families, identifying BRCA2 mutation carriers, investigating mutation origin of recurrent mutations, examining age-specific penetrance and risks of other cancers, and exploring other factors which may modulate risks of developing cancer in BRCA2 mutation carriers. These aims were accomplished, resulting in 20 publications of research results and four reviews. Highlights include: cloning BRCA2; identifying founder mutations 6174delT in Ashkenazi Jews and 999del5 in Icelanders; investigating origins of recurrent mutations; identifying mutations and mutation carriers for studies of penetrance and risks of other cancers; examining the effect of oral contraceptive use on reducing risk of ovarian cancer; and the effect of bilateral prophylactic oophorectomy on reducing risk of breast cancer.
DTIC
Cancer; Mammary Glands; Ovaries

20000120903 Health Research, Inc., Buffalo, NY USA
Role of a Placenta-Specific Gene in Mammary Tumorigenesis *Annual Report, 1 Jul. 1996 - 1 Jul. 1999*
VanHouten, Joshua N., Health Research, Inc., USA; August 1999; 14p; In English
Contract(s)/Grant(s): DAMD17-96-1-6048
Report No.(s): AD-A164213; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

A solo long terminal repeat (LTR) of an endogenous retrovirus-like element (intracisternal A particle) present in the mouse MIPP gene placenta-specific expression of a 1.2 kb message. We have previously shown that many mouse mammary preneoplasias and carcinomas ectopically express 2.2 and 5.6 kb MIPP-related nRNAs. We determined that the 3' ends of all MIPP transcripts, which are homologous to the kelch repeat motif, have the same sequence. PCR-based techniques were employed to clone the 5' end of the 2.2 kb transcript. Sequence analysis revealed a 1.7 kb open reading frame with an N-terminal BTB/POZ protein-protein interaction domain and six C-terminal kelch repeats. Using recombinant proteins from bacteria, we showed that MIPP co-sediments with microfilaments in vitro. Furthermore, MIPP and actin co-immunoprecipitate from MOD mouse mammary tumor cells. Western blotting with an antiserum we raised against recombinant MIPP protein indicates that only one MIPP protein, about 70kDa, is translated in mouse mammary tumor cells, despite expression of two transcripts. Immunofluorescence has localized the protein to the cytoplasm, with a non-filamentous staining reminiscent of endoplasmic

reticulum. We have transfected MIPP into normal mammary epithelial cells, and transformation studies are in progress to determine whether MIPP contributes to mammary tumorigenesis.
DTIC
Mammary Glands; Tumors; Gene Expression; Genes; Ribonucleic Acids

20000120904 State Univ. of New York, Stony Brook, NY USA
Splicing Variants of Estrogen Receptor in Breast Cancer *Final Report, 30 Sep. 1994 - 29 Sep. 1999*
Miksicek, Richard J., State Univ. of New York, USA; October 1999; 39p; In English
Contract(s)/Grant(s): DAMD17-94-J-4372
Report No.(s): AD-A381693; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

Results are summarized from the analysis of ER-alpha splicing variants in breast tumor cells. A highly diverse population of variants were observed representing primarily exon-skipped transcripts, but also including novel variants resulting from promiscuous or cryptic splicing. Techniques and reagents suited for the analysis of ER-alpha splicing variants were developed and described. Splicing variants were observed to be much more prevalent for ER-alpha than for most other genes including the progesterone receptor gene. The biochemical properties and transcriptional activities of the major ER-alpha splicing variants were also characterized. Two variants (ER.DELTA.E3 & ER.DELTA.E5) were identified that share significant residual function with intact ER-alpha. These properties confer on the ER.DELTA.E3 and ER.DELTA.E5 receptor variants the ability to inhibit the activity of some genes, but to stimulate the transcription of other genes. Genes that represent targets for induction by these ER-alpha splicing variants appear to lack consensus DNA-binding sites for ER-alpha, but instead they are regulated indirectly through interactions with other transcription factors such as AP-1. ER-alpha splicing variants thus function primarily through a recently proposed non-classical pathway for estrogen action. A variety of potential gene targets for regulation by the ER.DELTA.E3 and ER.DELTA.E5 variants are described.
DTIC
Mammary Glands; Cancer; Estrogens; Receptors (Physiology)

20000120905 Manitoba Univ., Winnipeg, Manitoba Canada
Identification of Markers of the Invasive Phenotype in Human Breast Cancer *Annual Report, 1 Sep. 1998 - 1 Sep. 1999*
Watson, Peter, Manitoba Univ., Canada; October 1999; 93p; In English
Contract(s)/Grant(s): DAMD17-97-1-7320
Report No.(s): AD-A382826; No Copyright; Avail: CASI; A01, Microfiche; A05, Hardcopy

Our goal is to identify genes involved in the development of the invasive phenotype as these may offer predictive markers and markers of risk of invasive disease in pre-invasive lesions. We have applied our tissue based strategy to directly identify differentially expressed genes between pre-invasive in-situ (DCIS) and adjacent early invasive tumor cell populations and have completed assessment of 5 tumors and identified two promising candidate 'invasion' genes. Psoriasin (S100 A7) has been pursued by assessment of persistent expression in invasive tumors, showing that high levels correlate with ER-ve and node +ve status. The functional role has been pursued by transfection and overexpression in invasive (MDA-MB-231) and pre-neoplastic (MCF10AT) breast cell lines, and yeast 2-hybrid assay to search for interacting proteins. Lumican is a small leucine-rich proteoglycan, overexpressed in stroma adjacent to in-situ elements and at the margin of invasive elements. Lumican has been pursued by detailed study of expression pattern in-vivo and comparison with expression profiles of related proteoglycans. The functional role is being pursued by study of transfection to achieve overexpression in fibroblasts, to assess the effect of this on epithelial cells in in-vitro assays.
DTIC
Human Beings; Mammary Glands; Cancer

20000120906 Salk Inst. for Biological Studies, San Diego, CA USA
Amplified Genes in Breast Cancer: Molecular Targets for Investigation and Therapy *Final Report, 1 Sep. 1994 - 31 Aug. 1999*
Wahl, Geoffrey M., Salk Inst. for Biological Studies, USA; September 1999; 158p; In English
Contract(s)/Grant(s): DAMD17-94-J-4359
Report No.(s): AD-A382811; No Copyright; Avail: CASI; A02, Microfiche; A08, Hardcopy

Our research focussed on investigating acentric, autonomously replicating DNA containing amplified oncogenes (double minute chromosomes, DMs) as such structures occur in a significant fraction of human cancers. We proposed to develop methods to rapidly isolate and genotype DMs, to identify drugs to eliminate DMs, and to identify the mechanism(s) by which they are eliminated. We developed strategies to specifically tag DMs in living cells to enable analysis of their behavior during the cell cycle

to enable us to ascertain differences between acentric structures and normal chromosomes to aid in the development of DM elimination reagents. We also devised and implemented novel cell labeling strategies to develop tumor models to determine how DM containing cells contribute to tumorigenesis, and to ascertain whether agents that effect DM elimination in vitro reduces tumor cell viability in vivo. Powerful new strategies and molecular tools were made available to the research community to enable sophisticated analyses of normal and abnormal chromosomes in cancer cells, and to allow studies of the relationship between genotype, phenotype and drug sensitivity in vivo.
DTIC
Mammary Glands; Cancer; Therapy

20000120908 California Univ., San Francisco, CA USA
Human Monoclonal Antibodies for Neutralization of Botulinum Neurotoxin *Final Report, 1 May 1998 - 30 Apr. 2000*
Marks, James D., California Univ., USA; May 2000; 28p; In English
Contract(s)/Grant(s): DAMD17-98-C-8030
Report No.(s): AD-A382808; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

The purpose of this work is to regenerate neutralizing human monoclonal antibodies to Botulinum neurotoxins (BoNT) A, B, and E. to generate a large panel of antibodies, mice transgenic for the human immunoglobulin were immunized with BoNT/A, B, and E binding domain (H(sub C)). RNA was prepared, the human variable regions amplified by PCR and used to construct human single chain Fv (scFv) antibody fragment gene repertoires. The repertories were cloned to create phage antibody libraries. Selection of the libraries on BoNT/A, B, and E H(sub C) resulted in the isolation of a large panel of human monoclonal scFv antibody fragments. to demonstrate in vivo toxin neutralization, it was necessary to express the scFv as fusions with the human IgG1 Fc region from the yeast Pichia pastoris due to the rapid serum clearance of scFv. ScFv-Fc fusion showed increased serum half life compared to scFv, but had a significantly shorter half life than IgG. Previously isolated murine and human scFv showed toxin neutralization in vivo as Fc fusions, with a combination of two neutralizing scFv-Fc fusions able to neutralize 100 toxin LD(sub 50)s. Since the serum half life of the Fc fusions was significantly shorter than IgG's, the immunoglobulin V(sub H) and V(sub L) genes of neutralizing scFv were subcloned into a mammalian vector for expression as human IgG (in the case of human scFv) or mouse-human chimeric IgG (in the case of murine scFv). to date, three IgG have been constructed from the three neutralizing scFv and stable cell lines are being constructed from scFv derived from transgenic mice immunized with BoNT/A, B, and E H(sub C). Our plan is to purify IgG from each clone and evaluate in vivo neutralization potency for each unique antibody and for combinations of antibodies. In this way, we anticipate identifying panels of antibodies capable of neutralizing BonT/A, B, and E.
DTIC
Antibodies; Fragments; Immunology; Tumors; Antigens

20000120909 University of Southern California, Los Angeles, CA USA
Molecular Epidemiology of Breast Carcinoma In Situ *Annual Report, 1 Sep. 1998 - 31 Aug. 1999*
Press, Michael F., University of Southern California, USA; September 1999; 10p; In English
Contract(s)/Grant(s): DAMD17-96-1-6156
Report No.(s): AD-A382806; No Copyright; Avail: CASI; A01, Microfiche; A02, Hardcopy

This is a molecular epidemiologic case-control study of breast carcinoma in situ in Los Angeles County designed to address issues related to the cause and progression of breast CIS by determining epidemiologic risk factors, characterizing selected molecular genetic alterations and prospectively assessing disease progression. The specific aims of the research are 1.) to assess epidemiologic risk factors associated with development of breast CIS, 2.) to determine how frequently specific oncogenes or the p53 tumor suppressor gene are altered in breast CIS, 3.) to investigate potential relationship between various epidemiologic risk factors and sematic genetic alterations and 4.) to assess long-term the association of these factors with disease progression. During the four-year grant period we plan to interview approximately 100 black women and 426 white women (including Hispanics) aged 35-64 years who are diagnosed with breast CIS and who are residents of Los Angeles County, are US-born, and English speaking. The study will utilize 490 black and 490 white control subjects selected by random digit dialing in Los Angeles County who will have been interviewed as part of the Women's CARE Study, a multicentered case-control study of invasive breast cancer being conducted concurrently with this proposed study. We will obtain parafin-embedded tumor tissue from the pathology laboratories where the patients were diagnosed for analysis of alterations in selected oncogene and tumor suppressor gene expression. Epidemiologic risk factors (reproductive history, lack of participation in physical activity/exercise, positive family history, race, high body mass and exposure to hormones) will be compared with oncogene and tumor suppresor gene expression in breast CIS.
DTIC
Epidemiology; Cancer; Mammary Glands; Risk

20000121147 California Univ., San Francisco, CA USA

Human Monoclonal Antibodies for Neutralization of Botulinum Neurotoxin *Annual Report, 1 May 1998 - 30 Apr. 1999*

Marks, James D., California Univ., USA; May 1999; 22p; In English

Contract(s)/Grant(s): DAMD17-98-C-8030

Report No.(s): AD-A380394; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

The overall goal of this proposal is to produce neutralizing human monoclonal antibodies against Botulinum neurotoxins for immunoprophylaxis and immunotherapy. Antibodies will be generated using a novel approach, phage display, which overcomes the limitations of conventional hybridoma technology. The proposal represents a continuation of work begun under DAMD17-94-C-4034 titled "Production of Human Antibodies which Neutralize Botulinum Neurotoxin Type A". In the sections below, we first describe the problem, the limitations of currently available reagents, the novel approach we have used for this work (phage display), results obtained to date under DAMD17-94-C-4034, and specific aims and experimental design for the current preproposal.

DTIC

Antibodies; Clostridium Botulinum; Immunology

20000121149 Kazusa Akademia Park Co. Ltd., Kisarazu, Japan

Third International Meeting on the Molecular Genetics and Pathogenesis of the Clostridia

August 2000; 108p; In English; 3rd; Molecular Genetics and Pathogenesis of the Clostridia, 8-11 Jun. 2000, Chiba, Japan

Contract(s)/Grant(s): DAMD17-00-1-0593

Report No.(s): AD-A380358; No Copyright; Avail: CASI; A02, Microfiche; A06, Hardcopy; Abstracts Only; Abstracts Only

The program and abstracts of the Third International Meeting on the Molecular Genetics and Pathogenesis of the Clostridia is presented.

DTIC

Genetics; Pathogenesis; Clostridium; Enzymes; Molecular Biology

20000121158 Air Force Academy, Human-Environmental Research Center, CO USA

Circadian Rhythm Amplitude Effects on Nocturnal Brain Electrical Activity and Mental Performance, *Jun. 1999 - May 2000*

Terry, Laura, Air Force Academy, USA; Miller, James C., Air Force Academy, USA; May 31, 2000; 25p; In English

Report No.(s): AD-A381802; USAFA-TR-2000-04; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

This report describes an evaluation of the ability to detect changes in mental state, indicated by changes in performance, using electroencephalograms (EEGs). Sixteen subjects performed the Multi-Attribute Task Battery (MATB) task during an overnight testing session. Body temperature, performance data, and EEG signals were acquired and analyzed. We grouped subjects by the circadian amplitude characteristic of body temperature, and found group differences in EEG activity and mental performance. Several significant differences across session occurred in both performance and EEG activities. Three significant correlations between performance and EEG activity occurred between theta activity at Fz compared to monitor response time and monitor error percent, and beta activity compared to monitor error percent. The finding lent credibility to the idea that body temperature circadian amplitude predicts nocturnal mental performance and that changes in performance are associated with EEG activity.

DTIC

Mental Health; Mental Performance; Nocturnal Variations; Circadian Rhythms; Brain; Electroencephalography

20000121161 City of Hope Medical Center, Beckman Research Inst., Duarte, CA USA

Novel RNA- or Antibody-Based Strategies Targeting Growth Factors in Prostate Cancer *Annual Report, 1 Sep. 1998 - 31 Aug. 1999*

Fujita–Yamaguchi, Yoko, City of Hope Medical Center, USA; September 1999; 31p; In English

Contract(s)/Grant(s): DAMD17-98-1-8579

Report No.(s): AD-A380322; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

RNA- or antibody-based strategies may provide novel strategies for inhibiting the expression of specific gene products that may be involved in prostate cancer cell growth and progression. Prostate cancer cells could escape hormonal control by constitutively expressing growth factors such as insulin- like growth factors (IGFs). This proposal is to test the hypothesis that IGF-II/ IGF receptor signaling plays an important role in prostate cancer growth and progression. to prove the hypothesis, our newly constructed IGF-II ribozymes and single-chain antibodies against the IGF-I receptor (alpha IGFIR scFvs) are being used. Specific Aim 1 is to test our hypothesis using already available PC-3 prostate cancer cell transfectants and control cells. Effects of intracellular expression of IGF-II ribozyme or alpha IGFIR scFv on cell growth, anticancer- drug induced apoptosis, and

tumorigenesis will be investigated in cell culture and in athymic mice. Specific Aim 2 is to take alternative approaches towards testing our hypothesis and developing novel gene and/or immunotherapy approaches for prostate cancer treatment. RNA- or antibody-based strategies targeting growth factors in prostate cancer have never been evaluated. The proposed studies should thus lay the foundation for the development of novel strategies for prostate cancer treatment.
DTIC
Ribonucleic Acids; Prostate Gland; Cancer; Culture Techniques; Cell Division; Antibodies

20000121162 California Univ., Berkeley, CA USA
Modulation of T-Cell Activation in an Experimental Model of Mammary Carcinoma *Final Report, 1 Jul. 1997 - 30 Jun. 1999*
Hurwitz, Arthur, California Univ., USA; July 1999; 53p; In English
Contract(s)/Grant(s): DAMD17-97-1-7054
Report No.(s): AD-A380385; No Copyright; Avail: CASI; A01, Microfiche; A04, Hardcopy

The goal of this research project was to study the requirements for T cell activation in generating a potent anti-tumor immune response. In the first year, using a transplantable mammary carcinoma model, we demonstrated that the combination of CTLA-4 blockade and a GM-CSF-expressing vaccine was effective for treatment of recently established tumors. This funded year, these findings were to be expanded to 2 additional models: a transplantable melanoma model and a primary prostate cancer model, resulting in one manuscript recently published (1), and one submitted (2). In the melanoma model, we demonstrated that CTLA-4 blockade, in combination with a GM-CSF-expressing vaccine, could eradicate both sub- cutaneous tumors as well as lung metastases. More strikingly, mice that rejected tumors underwent a progressive depigmentation, reminiscent of the vitiligo that occurs in melanoma patients undergoing immunotherapy (3). In the transgenic prostate cancer model, we demonstrated that primary, autoch- thonous prostate tumor incidence is reduced and the histologic severity of tumor lesions is reduced in mice treated with anti-CTLA-4 and a tumor cell vaccine. Interestingly, similarly treated, non-transgenic mice developed a destructive prostatitis. Taken together, our findings demonstrate the potency of this approach: by combining these synergistic therapies, both a potent anti-tumor and autoimmune response can occur. Future studies will address the link between tumor immunity and autoimmunity.
DTIC
Mammary Glands; Prostate Gland; Cancer; Lymphocytes; Immunity

20000121163 California Univ., San Diego, La Jolla, CA USA
Assessment of the Activation State of RAS and Map Kinase in Human Breast Cancer Specimens (96Breast) *Annual Report, 1 Sep. 1998 - 31 Aug. 1999*
Boss, Gerry, California Univ., San Diego, USA; September 1999; 46p; In English
Contract(s)/Grant(s): DAMD17-97-1-7031
Report No.(s): AD-A380388; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

We found that Ras was highly activated in 11 of 20 breast cancers compared to normal tissue; 7 of these 11 cancers expressed both the epidermal growth factor (EGF) and ErbB-2/neu/HER-2 receptors with the remaining four cancers with high Ras activation expressing one of these two receptors. In the other 9 cancers, Ras activation was similar to that observed in normal breast tissue with none of these cancers expressing the E&F receptor while one expressed the ErbB-2 receptor. None of the cancers tested had an activating K- ras mutation nor did any of the cancers express a truncated E(iF receptor or the c-FMS receptor. The activity of mitogen- activated protein (MAP) kinase was high in the cancers and reflected the degree of Ras activation. In cultured mammary tumor cell lines, we showed that Ras activation was ligand dependent in cells overexpressing the ErbB-2 receptor. Thus, Ras was abnormally activated in breast cancers overexpressing the EGF and/or ErbB-2 receptors indicating there are sufficient ligands in vivo to activate these receptors and this work provides a basis for new target-based treatments of this disease. Using a newly-developed assay, we are now in the process of measuring the activation state of Rho, a Ras-related protein that has been shown to play a role in carcinogenesis.
DTIC
Cancer; Mammary Glands; Tissues (Biology); Proteins; Carcinogens; Assaying

20000121164 California Univ., San Francisco, CA USA
Estrogen-Modulated Response of Breast Cancer to Vitamin D and Its Analogs: Role of IGF *Annual Report, 1 Oct. 1998 - 30 Sep. 1999*
Dolezalova, Hana, California Univ., USA; Goetzl, Edward J., California Univ., USA; October 1999; 14p; In English
Contract(s)/Grant(s): DAMD17-96-1-6218

Report No.(s): AD-A380441; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

The principal goal of the proposed studies is to determine if 1,25- dihydroxy-vitamin D3 and some of its analogues inhibit proliferation of human breast cancer cells by altering the expression and function of endothelial differentiation gene-encoded G protein-coupled receptors (Edg Rs) for lysophosphatidic acid (LPA) and sphingosine 1-phosphate (S1P). Estrogen receptor positive and estrogen receptor negative cells express predominantly Edg-2 and Edg-4 Rs for LPA and Edg-3 for Sip, which transduce proliferative responses by direct nuclear signaling, through MAP kinase, and stimulate secretion of type II insulin-like growth factor (IGF-II). The proliferation of breast cancer cells induced by LPA and S1P is inhibited significantly by 10-10-10-8 M 1,25- dihydroxy-vitamin D3 analogue. We aim to delineate the effects of 1,25- dihydroxy- vitamin D3 analogues on Edg R expression and biochemical signaling, IGF-II receptor expression and secretion of IGF-II. Results are expected to further our understanding of abnormal growth regulatory mechanisms in breast cancer and may lead to Edg R directed modalities of treatment.

DTIC

Vitamins; Mammary Glands; Cancer; Estrogens; Biochemistry; Proteins

20000121215 Institute for Nutrition and Food Research TNO, Zeist, Netherlands

The Effect of a Breakfast with High and Low Glycemic Index on Postprandial Blood Glucose and Insulin Concentration, Appetite, Satisfaction, and Well-Being ***Final Report Het Effect Van Een Ontbijt Met Een Hoge- en Een Lage Glycemische Index op Postprandiale Bloedglucose en Insulineconcentratie, Honger en Verzadigingsgevoeiens en Welbevinden***

Pasman, W. J., Institute for Nutrition and Food Research TNO, Netherlands; vandenBerg, H., Institute for Nutrition and Food Research TNO, Netherlands; Aug. 29, 2000; 157p; In Dutch

Contract(s)/Grant(s): A98/KL/111; TNO Proj. 010.20084

Report No.(s): TD-99-0439; TNO-Voeding-V99.729; Copyright; Avail: Issuing Activity

In this randomized, cross-over study, the influence of a breakfast with a high and low glycemic index (GI) on glucose- and insulin concentration in the serum was examined in healthy male volunteers. Also, the effects on appetite, satisfaction and well-being were assessed. No differences were found in glucose and insulin serum concentrations, three hours after breakfast. However, the low GI breakfast induced significantly less appetite and a higher extent of satisfaction in comparison to the high GI breakfast. Furthermore, the fatigue reported after the low GI breakfast was significantly less compared to the high GI breakfast. The incidence of hypoglycemias did not differ between the two breakfasts, indicating that healthy men are able to digest differing carbohydrate loads without any negative side effects. The results of this study indicate that a breakfast with a low GI may have a possitive effect on performance.

Author

Carbohydrates; Glucose; Nutritional Requirements; Insulin; Diets

20000121230 Johns Hopkins Univ., Baltimore, MD USA

Anti-Ecitotoxic and Antioxidant TGF-BETA Family Neurotrophic Factors: In Vitro Screening Models of Motor Neuron Degeneration ***Annual Report, 1 Jun. 1999 - 31 May 2000***

Rothstein, Jeffrey D., Johns Hopkins Univ., USA; June 2000; 19p; In English

Contract(s)/Grant(s): DAMD17-99-1-9490

Report No.(s): AD-A379851; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

TGF beta-like trophic factors have been shown to be protective in acute neuronal injury paradigms. In the current study, we analyzed and compared members of this growing family, including GDNF, neurturin, nodal, persephin, as well as TGF beta 1, for protection against chronic glutamate toxicity. In parallel, we developed a novel organotypic spinal cord culture system to study the ability of these factors to promote motor axon outgrowth. Using these systems, we were able to differentiate the neuroprotective effect of the TGF beta-like factors from their motor axon outgrowth-promoting activity. GDNF, neurturin, persephin, and nodal all protect against excitotoxic motor neuron degeneration. Low amounts of GDNF (1 ng/ml) and high concentrations of neurturin induced vigorous motor axon outgrowth. In contrast, nodal, persephin and TGF beta 1 did not induce motor axon outgrowth. Both GDNF and neurturin bind to Ret receptor complexes and are capable of activating MAP kinase (MAPK) pathway. A specific inhibitor of MAP kinase kinase (MEK), PD98059, inhibits the motor axon outgrowth-promoting activity of the GDNF but not the neuroprotective activity. Similarity, specific PI3K inhibitors, LY294OO2 and Wortmannin , are able to stop the motor axon outgrowth-promoting activity of the GDNF but not the neuroprotective activity. Our results suggest that the neurite outgrowth promoting effect of GDNF is mediated through the PI3K and MAP kinase pathways. The neuroprotective effect of GDNF appears to mediate through a different pathway.

DTIC

Neurophysiology; Nervous System; Antioxidants; Toxicity; Beta Factor; Glutamates

20000121231 Army Research Inst. of Environmental Medicine, Thermal and Mountain Medicine Div., Natick, MA USA
Effect of Hypercholesterolernia on Cutaneous Vascular Responses to Exercise in Healthy, Exercise-Trained, Heat-Acclimated Humans
Stephenson, Lou A., Army Research Inst. of Environmental Medicine, USA; Mair, Brent S., Army Research Inst. of Environmental Medicine, USA; Boulant, Catherine Gabaree, Army Research Inst. of Environmental Medicine, USA; Staab, Janet, Army Research Inst. of Environmental Medicine, USA; Robinson, Scott B., Army Research Inst. of Environmental Medicine, USA; Kesick, Christina M., Army Research Inst. of Environmental Medicine, USA; Kolka, Margaret A., Army Research Inst. of Environmental Medicine, USA; July 2000; 28p; In English
Report No.(s): AD-A379853; USARIEM-TR-T00/21; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

The purpose of this research was to determine whether healthy, exercise-trained, heat-acclimated people with one major risk factor for coronary artery disease (high total cholesterol/high-density lipoprotein cholesterol (TC/ HDL-C)) would have different cutaneous vascular responses to exercise in a warm environment compared to people who were of similar age and gender who did not share the risk factor. It was hypothesized that individuals who had an elevated TC/HDL-C would have similar deleterious effects on the cutaneous vasculature as the coronary arteries and aorta as observed in pathological studies. That is, individuals who have a high TC/HDL-C ratio might have less compliant cutaneous vessels and therefore impaired sensible heat loss than individuals who have a low TC/HDL-C ratio. In the current study, we measured cutaneous vascular responses using noninvasive instruments during rest and exercise in a warm environment in individuals with either a high or low TC/HDL-C ratio. Obtaining evidence for impaired heat dissipation was limited by the conservative study design because the volunteers were studied in a moderately hot environment with a moderate humidity rather than a hot environment because half of the study population, by definition, was at risk for coronary artery disease. Subjects in both groups routinely exercised and were heat-acclimated.
DTIC
Cholesterol; Physical Exercise; High Temperature Environments; Physiological Responses; Coronary Artery Disease

20000121245 Florida Univ., Gainesville, FL USA
Wavelet Representations for Digital Mammography *Final Report, 16 Nov. 1992 - 15 Mar. 1999*
Laine, Andrew F., Florida Univ., USA; Taylor, Fred, Florida Univ., USA; April 1999; 57p; In English
Contract(s)/Grant(s): DAMD17-93-J-3003
Report No.(s): AD-A381680; No Copyright; Avail: CASI; A01, Microfiche; A04, Hardcopy

We report on a receiver operating characteristics (ROC) study focusing on dyadic wavelets for enhancement of mammographic features in digitized mammograms. The enhancement protocol was based on multiscale expansions and non-linear enhancement functions described previously in our annual reports. In this study, dyadic spline wavelet functions were used together with a sigmoidal non-linear enhancement function. We designed a prototype test bed interface and performed a ROC study with three radiologists specialized in mammography. Data was obtained from the national mammography database of digitized radiographs from the University of South Florida. An initial analysis of the data counted the number of false-positives and true-positives in each of two cases: Enhanced and Original. Lesions with a LOC greater or equal 3 were considered malignant. The average TPF was found to be 0.667 with enhancement, and TPF = 0.569 without enhancement. This observed increase in sensitivity is encouraging, but accompanied by a slight increase in the fraction of false-positives (0.222 compared to 0.178). However, when the analysis of the data only focused on micro-calcifications alone, we observed a TPF = 0.417 with enhancement compared to TPF = 0.222 without enhancement. No increase or decrease in FPF was observed. This finding reinforces our hypothesis that feature specific enhancement protocols are indeed useful for visualizing subtle mammographic features.
DTIC
Wavelet Analysis; Medical Services; Public Health; Cancer

20000121260 National Center for Microgravity Research on Fluids and Combusiton, Cleveland, OH USA
A New Clinical Instrument for The Early Detection of Cataract Using Dynamic Light Scattering and Corneal Topography
Ansari, Rafat R., National Center for Microgravity Research on Fluids and Combusiton, USA; Datiles, Manuel B., III, National Inst. of Health, USA; King, James F., DYNACS Engineering Co., Inc., USA; September 2000; 18p; In English
Contract(s)/Grant(s): NCC3-544; RTOP 101-51-00
Report No.(s): NASA/CR-2000-209955; E-12161; NAS 1.26:209955; No Copyright; Avail: CASI; A03, Hardcopy; A01, Microfiche

A growing cataract can be detected at the molecular level using the technique of dynamic light scattering (DLS). However, the success of this method in clinical use depends upon the precise control of the scattering volume inside a patient's eye and especially during patient's repeat visits. This is important because the scattering volume (cross-over region between the scattered fight and incident light) inside the eye in a high-quality DLS set-up is very small (few microns in dimension). This precise control

holds the key for success in the longitudinal studies of cataract and during anti-cataract drug screening. We have circumvented these problems by fabricating a new DLS fiber optic probe with a working distance of 40 mm and by mounting it inside a cone of a corneal analyzer. This analyzer is frequently used in mapping the corneal topography during PRK (photorefractive keratectomy) and LASIK (laser in situ keratomileusis) procedures in shaping of the cornea to correct myopia. This new instrument and some preliminary clinical tests on one of us (RRA) showing the data reproducibility are described.
Author
Cataracts; Cornea; Detection; Eye (Anatomy); Fiber Optics; Fabrication; Lasers; Myopia; Ophthalmology; Light Scattering

20000121268 Katholieke Univ., Dept. of Biochemistry, Nijmegen, Netherlands
A Novel Visual Pigment Family: Circadian Implications *Final Report*
deGrip, Willem J., Katholieke Univ., Netherlands; 2000; 8p; In English
Contract(s)/Grant(s): F61708-98-W-0026
Report No.(s): AD-A379843; SPC-98-4007; No Copyright; Avail: CASI; A01, Microfiche; A02, Hardcopy

The objectives of this report are: (1) Production of an antiserum against melanopsin, a putative circadian photoreceptor, permitting analysis of its expression pattern in mammalian retina. (2) Heterologous expression of melanopsin using recombinant baculovirus for a first characterization of its biochemical properties.
DTIC
Biochemistry; Circadian Rhythms; Mammals; Peptides; Visual Pigments

20000121303 Alabama Univ., Birmingham, AL USA
Conditionally Replicative Adenovirus for Prostate Cancer Therapy *Annual Report, 1 Oct. 1998 - 30 Sep. 1999*
Curiel, David T., Alabama Univ., USA; October 1999; 128p; In English
Contract(s)/Grant(s): DAMD17-98-1-8571
Report No.(s): AD-A380975; No Copyright; Avail: CASI; A02, Microfiche; A07, Hardcopy

Quantitative tumor transduction represents a major limitation to the achievement of meaningful clinical results in cancer gene therapy protocols. Approaches directed towards the goal of enhancing or amplifying the effects of a genetic transduction event may further enhance the potential efficacy of cancer gene therapy strategies. One way to achieve this amplification effect would be via replication of the delivered viral vector. In this approach, a conditionally replicative competent virus would be utilized to selectively replicate within the transduced tumor cells and not in normal tissues. Adenoviral vectors possess the unique attribute with respect to the in vivo gene delivery recommending their employment as conditionally replicative vectors. It is our hypothesis that a conditionally adenovirus that would replicate selectively and specifically into tumor cells could be developed and utilized as an experimental tumor therapy modality for prostate cancer. In these initial studies, we have shown that improving the infectivity of adenoviral vectors dramatically augments the oncolytic potency of CRAD agents. The establishment of this key principal now feasibilize our original goal to improve the replicative specificity of the CRADs for carcinoma of the prostate.
DTIC
Prostate Gland; Cancer; Tissues (Biology); Clinical Medicine; Genetics

20000121309 NASA Ames Research Center, Moffett Field, CA USA
The Influence of Passive Acceleration and Exercise+Acceleration on Work Capacity and Orthostasis
Simonson, S. R., Lockheed Martin Space Operations, USA; Cowell, S. A., Lockheed Martin Space Operations, USA; Stocks, J. M., Australian Catholic Univ., Australia; Biagini, H. W., NASA Ames Research Center, USA; Vener, J. M., Utah Univ., USA; Evetts, S. N., Kings Coll., UK; Bailey, K. N., San Francisco State Univ., USA; Evans, J., Kentucky Univ., USA; Knapp, C., Kentucky Univ., USA; Greenleaf, J. E., NASA Ames Research Center, USA; [1999]; 2p; In English; 13th; Exploring Space, 20-26 May 2000, Santorini, Greece; Sponsored by International Academy of Astronautics, France
Contract(s)/Grant(s): UPN-111-10-20; NRA-96-HEDS-04; UPN-111-30-10-00; No Copyright; Avail: Issuing Activity; Abstract Only

The losses of aerobic power and orthostatic tolerance are significant effects of manned C) spaceflight that can negatively impact crew health and safety. Daily acceleration and aerobic training may ameliorate these effects. To determine the influence of passive intermittent +Gz acceleration (PA) training and active acceleration + interval exercise (AE) training on work 0 0 capacity and the acute (1 min) response to 70 deg head-up tilt, 6 men (X-Bar SD: age, 33 +/- 6 y; height, 178.3 +/- 4.6 cm; mass,

86.3 +/- 6.6 kg) participated in two 3-wk training protocols. It was hypothesized that PA and AE training would improve orthostatic tolerance and that the addition of aerobic conditioning, would not alter this effect.
Author
Acceleration Tolerance; Aerospace Medicine; Hemodynamic Responses; Orthostatic Tolerance; Physical Exercise; Spacecrews; Work Capacity

20000121330 Manitoba Univ., Faculty of Medicine, Winnipeg, Manitoba Canada
Detection of Genetic Lesions in Breast Cancer *Annual Report, 1 Sep. 1998 - 31 Aug. 1999*
Davie, James, Manitoba Univ., Canada; September 1999; 124p; In English
Contract(s)/Grant(s): DAMD17-97-1-7179
Report No.(s): AD-A382537; No Copyright; Avail: CASI; A02, Microfiche; A06, Hardcopy

The purpose of this proposal is to develop a "next generation" representational difference analysis protocol that uses transcribing nuclear DNA. A chromatin immunoprecipitation (ChIPs) technique is being established to isolate active chromatin by its association with highly acetylated hi stones. Before embarking with the ChIPs procedure, it was important to understand the dynamics of histone acetylation in breast cancer cells, and the effect of estradiol on these processes. In the past year, we determined the kinetics of histone acetylation in hormone dependent (T47D5) and hormone independent (MDA MB 231) breast cancer cells. For both cell lines, a small population (10%) of core histones is engaged in rapid hyperacetylation and rapid deacetylation. This population of core histones is thought to be associated with transcriptionally active DNA. The bulk of the acetylated core histones is slowly acetylated. We made the novel observation that estradiol increases the steady state level of histone acetylation in hormone dependent T47D5 breast cancer cells. Estradiol increased the steady state level of hi stone acetylation by decreasing the rate of histone deacetylation. The ChIPs protocol with anti-acetylated H3 antibodies was used to isolate transcriptionally active DNA from breast cancer cells.
DTIC
Hormones; Deoxyribonucleic Acid; Cells (Biology); Genetics; Estrogens; Cancer; Mammary Glands

20000121331 National Inst. of Health, Bethesda, MD USA
Identification of Tumor Suppressor Genes in Breast Cancer by Insertional; Mutagenesis and Functional Inactivation (96 Breast) *Annual Report, 25 Aug. 1998 - 24 Aug. 1999*
Su, Yan A., National Inst. of Health, USA; September 1999; 19p; In English
Contract(s)/Grant(s): DAMD17-97-1-7236
Report No.(s): AD-A382536; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

The development and progression of cancer result from multiple genetic changes accumulated in the cells. The identification of tumor suppressor genes inactivated and proto-oncogenes activated in mammary epithelial cells is essential to understand the genetic basis of breast cancer and is a prerequisite for development of strategies for prevention, diagnosis, and treatment. In breast cancer, loss of heterozygosity (LOR) was detected frequently on chromosome 17 and other chromosomes, suggesting unrecognized tumor suppressor genes. We are applying the novel retroviral-tagging strategy to identify the genes using chromosome 17-suppressed (independent of p53 and ERCAl) breast cancer cell lines. In contrast to the parental tumorigenic cell line CAL51, the suppressed sublines CAL/17-1, CAL/17-3 and CAL/17-5 display insulin-dependent growth in flasks, no growth in soft-agar culture and athymic nude mice. In this annual report, we present our results on selection for the anchorage-independent cell sublines induced by retroviral transduction of the chromosome 17-mediated suppressed cell lines CAL/17, in addition to successful selection for insulin-independent cell sublines. We are now in the process to conduct tumorigenicity tests in athymic nude mice and to clone genomic sequences flanking the integrated retroviral vectors.
DTIC
Genes; Cells (Biology); Mammary Glands; Cancer; Chromosomes

20000121332 Arizona Univ., Tucson, AZ USA
Enzyme Inhibitors of Cell-Surface Carbohydrates: Insects as Model Systems for Neuronal Development and Repair Mechanisms *Annual Report, 1 Jul. 1999 - 30 Jun. 2000*
Polt, Robin, Arizona Univ., USA; July 2000; 28p; In English
Contract(s)/Grant(s): DAMD17-99-1-9539
Report No.(s): AD-A382533; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

An experimental drug, PDMP, has been shown to block metastasis by inhibiting the display of carbohydrates on tumor cell surfaces. Further work with PDMP and related drugs to prevent the spread of cancer now seems justified. This work is intended to show that rapidly growing insect nerve cells can serve as a model for cancer in humans, and simple assays based on this approach

should permit the testing of a large number of new drugs based on PDMP. Drugs that block the outgrowth of the insect nerve cells should also block the outgrowth of cancer cells in humans, or other vertebrate organisms. Using this approach we should be able to rapidly develop potent new drugs which will block metastasis in human cancers.
DTIC
Cells (Biology); Assaying; Cancer; Vertebrates; Nervous System; Drugs; Carbohydrates

20000121340 California Univ., San Francisco, CA USA
Selection of Human Antibody Fragments which Bind Novel Breast Tumor Antigens *Final Report, 15 Aug. 1994 - 14 Aug. 1999*
Marks, James D., California Univ., USA; September 1999; 73p; In English
Contract(s)/Grant(s): DAMD17-94-J-4433
Report No.(s): AD-A382534; No Copyright; Avail: CASI; A01, Microfiche; A04, Hardcopy

A major goal of cancer research has been to identify tumor antigens which are qualitatively or quantitatively different from normal cells. The presence of such antigens could be detected by monoclonal antibodies that would form the basis of diagnostic tests and therapeutic agents. For this project, we developed novel technology, antibody phage display, to produce a new generation of tumor specific antibodies. We produced a library of human antibodies from which we can isolate panels of monoclonal antibodies to any purified antigen within 2 weeks. Methodologies have been developed to increase antibody affinity to values not previously achievable. Finally, we have developed methodologies which permit direct selection of libraries on tumor cells for the purpose of generating antibodies with desirable functional properties, such as endocytosis and growth inhibition. A panel of antibodies have been isolated which are breast tumor cell specific and a method has been developed where the antibody can be used to identify the receptor bound. We have applied these technologies to produce several human antibodies that bind the ErbB2 receptor overexpressed in one third of breast cancers. With collaborators at UCSF, we have used these antibodies to target doxorubicin containing liposomes, which can cure tumors in mice. The National Cancer Institute Decision Network is supporting further pre-clinical development for anticipated clinical trials for breast cancer.
DTIC
Antibodies; Antigens; Cancer; Mammary Glands; Cells (Biology)

20000121341 State Univ. of New York, Albany, NY USA
Measurements of X-Ray Capillary Optics for Digital Mammography (96 Breast) *Annual Report, 1 Sep. 1998 - 31 Aug. 1999*
Padiyar, Sushil, State Univ. of New York, USA; September 1999; 36p; In English
Contract(s)/Grant(s): DAMD17-97-1-7166
Report No.(s): AD-A382529; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

X-ray capillary optics present great potential in designing a mammographic imaging system with high resolution, enhanced contrast, a high dynamic range and a low absorbed dose to the patient. Well engineered optics can collimate, locus and filter x-rays. Optics can magnify images or demagnify images to mate them to a direct x-ray detector. Measurements on two collimating prototypes as pre-patient optics and two linearly tapered optics as post-patient "scatter-rejection" devices are reported here. Preliminary scatter fraction measurements demonstrate an excellent ability to reject Compton scattered photons, implying enhanced contrast in medical imaging systems.
DTIC
Digital Systems; Medical Services; Radiography; Mammary Glands; X Ray Optics; Diagnosis

20000121343 Michigan Univ., Ann Arbor, MI USA
Stress and Coping in Genetic Testing for Cancer Risk *Annual Report, 15 Jun. 1998 - 14 Jun. 1999*
Coyne, James C., Michigan Univ., USA; Sonis, Jeffrey H., Michigan Univ., USA; July 1999; 405p; In English
Contract(s)/Grant(s): DAMD17-96-1-6157
Report No.(s): AD-A382520; No Copyright; Avail: CASI; A04, Microfiche; A18, Hardcopy

This project involves a prospective study of women who are at high risk for early-onset breast cancer, and their husbands and siblings. Proband women are assessed at entry into the study, immediately before receiving results, and 2 months, 6 months, and 12 months after receiving results. Among women for whom test results are not available within one year of study entry, yearly assessments are administered to track changes in functioning over time. The main objectives of the study have been to describe psychological functioning among high-risk women and their families; to evaluate the performance of screening instruments in detecting clinical depression; to describe social support processes among high-risk women; and as follow-up data become available, to assess the impact of genetic testing on women and their families. In general, both extensive baseline data and preliminary follow-up data suggest that women and their families manage the process of genetic testing well, exhibiting relatively

low levels of distress and worry, and reporting few negative effects of testing. Ongoing analyses are beginning to clarify predictors of health behaviors, risk perception, response to testing, marital functioning, and other indicators of adjustment. Future analyses will clarify causal relationships among personality, functioning, and other variables, as follow-up data become available.
DTIC
Stress (Psychology); Genetics; Cancer; Mammary Glands; Risk

20000121345 California Univ., San Francisco, CA USA
Cell Type-Specific mRNA Amplification and Expression Profiling from Breast Tumor Sections *Annual Report, 30 Sep. 1998 - 29 Sep. 1999*
Albertson, Donna G., California Univ., USA; October 1999; 11p; In English
Contract(s)/Grant(s): DAMD17-97-1-7122
Report No.(s): AD-A382518; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

The evolution of solid tumors involves acquisition of genetic abnormalities, which result in changes in both the set of genes expressed and the relative levels of gene expression. However, the increasing number of candidate genes whose expression needs to be evaluated for prognostic, diagnostic, therapeutic, or research purposes will require obtaining material from numerous tissue sections. Therefore this proposal is motivated by the need for more effective use of clinical specimens, and will address the problem of obtaining sufficient and cell type specific mRNA from clinical breast tumor specimens. This will entail adapting/developing procedures to amplify with fidelity the mRNA repertoire expressed in small numbers of normal, pre-cancerous and malignant breast epithelia. to this end, in this project period, we have concentrated effort on establishing and validating microarray-based assays for measuring gene expression levels and have demonstrated the capability to isolate and amplify mRNA from cultured cells. Realization of these objectives will allow, in the future, development of a resource, consisting of amplified mRNA populations from individual cells from normal and tumor material, that can be used for evaluation of the prognostic, diagnostic and/or therapeutic importance of genes expressed in breast cancer.
DTIC
Ribonucleic Acids; Genetics; Cancer; Mammary Glands; Gene Expression; Tissues (Biology); Epithelium

20000121350 Sloan-Kettering Inst. for Cancer Research, New York, NY USA
Psychobehavioral Impact of Genetic Counseling and Breast Cancer Gene Testing in Healthy Women of African Descent *Annual Report, 16 Sep. 1998 - 15 Sep. 1999*
Offit, Kenneth, Sloan-Kettering Inst. for Cancer Research, USA; October 1999; 51p; In English
Contract(s)/Grant(s): DAMD17-96-1-6293
Report No.(s): AD-A381142; No Copyright; Avail: CASI; A01, Microfiche; A04, Hardcopy

Recent molecular studies have identified two large genes, BRCAl on chromosome 17 and BRCA2 on chromosome 13; mutations in these genes are now thought to be responsible for the majority of breast cancer cases in families with four or more affected relatives (Ford et al., 1995). Depending on the population studied, women with mutation in BRCAl/2 have 40% to 85% cumulative risk of developing breast cancer and 5% to 60% cumulative risk of developing ovarian cancer (Struewing et al., 1997; Whittemore et al., 1997; Schrag et al., 1997). There are several benefits associated with genetic testing for breast cancer susceptibility (Baum et al., 1997). For example, women found to be mutation carriers can increase the probability that breast cancer will be detected at early stage by increasing their breast cancer surveillance behavior and women who learn that they do not carry a cancer-predisposition mutation may experience relief and improvements in quality of life (Baum et al., 1997). However, genetic testing can also have adverse psychological consequences including loss of insurance, stigmatization, and increased psychological distress (Croyle et al., 1997; Bankowski et al., 1991, Holtzman, 1989). Most of the studies of the impact of counseling and genetic testing have
DTIC
Stress (Psychology); Human Behavior; Race Factors; Mammary Glands; Cancer; Diagnosis; Genes; Chromosomes

20000121352 Baylor Coll. of Medicine, Houston, TX USA
Tissue Specific Chromosome Deletions: An In Vivo Genetic Screen for Tumor Suppressor Genes in the Mammary Glands *Annual Report, 20 Apr. 1998 - 19 Apr. 1999*
Bradley, Allan, Baylor Coll. of Medicine, USA; May 1999; 37p; In English
Contract(s)/Grant(s): DAMD17-98-1-8280
Report No.(s): AD-A381229; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

Breast cancer is a genetic disease involving both gain and loss of function mutations in many different genes. It is important to define which genes are significant mutational targets in sporadic breast tumors so that treatments can be directed based on the

knowledge of the genetic changes in the tumor. This proposal is focused on identifying tumor suppressor genes which are mutated in sporadic breast cancer. We proposed to identify these tumor suppressor genes by a novel genetic screen in vivo. This genetic screen involves the adaptation of our chromosome engineering technology to delete specific chromosomal regions in mouse mammary epithelial cells in vivo. We planned to use tissue specific expression of Cre in mammary epithelial cells to induce these deletion events in vivo. When combined with insertional mutagenesis this technology has the power to identify tumor suppressor genes mutated in breast cancer. In the first year of this proposal we have constructed several "pre-deletion" chromosomes, transmitted them into the germ line and tested recombination event in vivo. We have also evidence of tissue specific recombination in heart muscle. We have also generated a MMTV-Cre transgene in the hprt locus which is also in the mouse germ line.
DTIC
Mammary Glands; Cancer; Chromosomes; Genes; Mutations; In Vivo Methods and Tests

20000121354 University of Southern California, Los Angeles, CA USA
Radiographic Density, Cancer, Inheritance and Acquired Risk in Twins *Final Report, 15 Mar. 1998 - 14 Mar. 1999*
Mack, Thomas M., University of Southern California, USA; March 1999; 6p; In English
Contract(s)/Grant(s): DAMD17-98-1-8360
Report No.(s): AD-A381130; No Copyright; Avail: CASI; A01, Microfiche; A02, Hardcopy

Computerized mammographic density measurements have been linked to breast cancer risk; the greater the breast density, the higher the risk of breast cancer. Our goals are to confirm if these observations are true within pairs of identical twins, to determine the heritability mammographic density, and to determine if adult exposures and experiences related to breast cancer risk result in modifications of mammographic density. We are interviewing both members of up to 2500 twin pairs registered in the California Twin Program about the risk factors of interest, collecting mammograms from each twin, scanning the films and measuring the densities, and comparing the measurements between co- twins in light of zygosity, past experiences, and the appearance of subsequent breast cancer. Thus far we have identified 1922 potentially eligible individuals from 961 pairs, contacted 1255, and have obtained the cooperation of 1043 or 83%. We have received formal signed consents for (temporary) release of the mammograms from 806 twins, and have received and scanned 1319 of the 1364 mammograms from 646 of these, including both twins from 307 pairs. Cooperation from twins and their providers has been excellent. Results will not be available until blinded readings of the scanned films are available.
DTIC
Cancer; Mammary Glands; Radiography; Risk; Exposure; Genetics

20000121355 Thomas Jefferson Univ., Philadelphia, PA USA
Cell-Cell Adhesion and Insulin-Like Growth Factor I Receptor in Breast Cancer *Annual Report, 15 Aug. 1998 - 14 Aug. 1999*
Guvakova, Marina A., Thomas Jefferson Univ., USA; Surmacz, Ewa, Thomas Jefferson Univ., USA; September 1999; 65p; In English
Contract(s)/Grant(s): DAMD17-97-1-7211
Report No.(s): AD-A381131; No Copyright; Avail: CASI; A01, Microfiche; A04, Hardcopy

The structural disintegration of normal epithelium is an early manifestation of cancer in mammary gland. Yet our knowledge on mechanisms controlling breast epithelial cell adhesion is still rudimentary. The increased content of the insulin-like growth factor I receptor (IGF-IR) and its close homologue the insulin receptor (IR) has been well documented in human breast cancer specimens. In this study we investigated how these hormone receptors modulate cell adhesion in breast carcinoma cells. Previously we developed MCF-7 human breast cancer cells overexpressing the IGF-IR. The major achievement of this work is the establishment of a new model consisting of MCF-7-derived cells overexpressing the IR that allowed the comparison of IR and IGF-IR functions. Our results strongly confirmed the specificity of the IGF-IR in promoting the large non-invasive tumor aggregates on biological matrix. For the first time we demonstrated that in breast cancer cells IGF-IR tyrosine kinase modulates the intercellular balance of Beta-catenin, the element of E-cadherin/catenin cell- cell adhesion complex. We continued to explore anti-tumor potentials of the antiestrogens and found that a synthetic steroid analog ICI 182,780 is a potent inhibitor of non-invasive breast tumor aggregates in three-dimensional culture.
DTIC
Epithelium; Hormones; Cells (Biology); Mammary Glands; Cancer; Receptors (Physiology)

20000121356 Michigan State Univ., East Lansing, MI USA
Improved Follow-Up of Breast Abnormalities Through Comprehensive Breast Care in Women 40 to 70 Years of Age *Annual Report, 1 Mar. 1999 - 28 Feb. 2000*
Pathak, Dorothy R., Michigan State Univ., USA; March 2000; 455p; In English
Contract(s)/Grant(s): DAMD17-98-1-8318
Report No.(s): AD-A381114; No Copyright; Avail: CASI; A04, Microfiche; A20, Hardcopy

To address inconsistencies among health care providers in breast cancer screening and management of abnormal findings, we randomized eight Family Practice residencies into control and intervention groups. The intervention has multiple components addressing skill, knowledge and management of breast cancer related issues. Additionally, a chart reminder system assists physicians in daily breast care management. Physician performance in clinical settings is assessed through chart audits. We have successfully completed the training and baseline assessment of cognitive and clinical skills and implemented the chart reminder system for the intervention sites. Chart audits are 95% complete. The analysis of the immediate effect of the training session found that in the short term the curriculum significantly improved cognitive and clinical skills. Assessment of the long-term effect of the curriculum is planned for May and June 2000. The curriculum will be provided to the control sites in August and September 2000. One unexpected outcome is that we have been asked to provide this curriculum to other health care professionals (Nurse Practitioners, OB/Gyn residents, etc.). Over all we are on target for the successful completion of the project according to the scope of work statement in the original grant.
DTIC
Medical Services; Cancer; Mammary Glands; Cognition; Health

20000121357 Baylor Coll. of Medicine, Houston, TX USA
Functional Study of Maspin in Breast Cancer *Annual Report, 13 Apr. 1998 - 12 Apr. 1999*
Zhang, Ming, Baylor Coll. of Medicine, USA; May 1999; 13p; In English
Contract(s)/Grant(s): DAMD17-98-1-8029
Report No.(s): AD-A381036; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

The object of this proposal is to understand the tumor suppressor function of maspin, a novel serine protease inhibitor, and to test directly maspin as a therapeutic agent for breast cancer. Transgenic and knockout mouse models will be employed to study the effects of gain and loss of maspin function on mouse mammary tumorigenesis and development. We hypothesize that overexpression of maspin should be protective against mammary tumorigenesis and metastasis, while loss of maspin will render mice more susceptible to tumor formation and metastasis. The proposal is based upon our previous experiments, primarily performed in conventional cell culture models, demonstrating that maspin has tumor suppressor activity. Recently, we have established transgenic mice overexpressing maspin in the mammary gland, and generated maspin knockout mice. We have crossed maspin transgenic mice with a breast tumor WAP-Tag strain. Our data suggest that maspin functions directly as a metastasis inhibitor. We have also shown in this report the mechanism by which maspin inhibits normal mammary development during pregnancy in WAP-maspin transgenic mice, and we are testing maspin against tumor progression in mice. Continuation of these tasks in the next few years will help us understand the role of maspin in tumor metastasis and angiogenesis, and hopefully leading to the development of new therapies for the treatment of breast cancer.
DTIC
Cancer; Mammary Glands; Culture Techniques; Inhibitors; Enzymes; Protease; Cells (Biology)

20000121358 Childrens Hospital Medical Center, Boston, MA USA
WNT-1 Signaling in Mammary Carcinogenesis *Annual Report, 16 Mar. 1998 - 15 Mar. 1999*
He, Xi, Childrens Hospital Medical Center, USA; April 1999; 16p; In English
Contract(s)/Grant(s): DAMD17-98-1-8047
Report No.(s): AD-A381046; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

WNT genes encode a large family of secreted signaling molecules essential for development and oncogenesis. wnt-1, the founding member of the wnt gene family, was initially identified as an oncogene which, upon ectopic expression induced by viral insertion, causes mammary tumorigenesis in mice, providing a potential model for studying human breast cancer. However, the Wnt- 1 receptor, an essential component mediating Wnt- 1 function, has not been identified, and the molecular and biochemical nature of the Wnt signaling pathway is not fully understood. In this proposal for the Career Development Award, we propose experiments combining molecular techniques and the axis duplication assay in the Xenopus embryo to answer the following two critical questions: 1) What is the receptor mediating Wnt-1 oncogenic function? 2) How does the Dishevelled protein, which is

an essential Wnt signaling component, transduce Wnt-1 signal? These experiments should provide a better understanding of the molecular nature of Wnt-1 signaling in mammary malignancy.
DTIC
Cancer; Mammary Glands; Genes; Proteins; Assaying

20000121359 RAND Corp., Santa Monica, CA USA
Prostate Cancer Patient Outcomes and Choice of Providers: Development of an Infrastructure for Quality Assessment
Litwin, Mark S., RAND Corp., USA; Steinberg, Michael, RAND Corp., USA; Malin, Jennifer, RAND Corp., USA; Naitoh, John, RAND Corp., USA; McGuigan, Kimberly A., RAND Corp., USA; Steinfeld, Rebecca, RAND Corp., USA; Adams, John, RAND Corp., USA; Brook, Robert H., RAND Corp., USA; 2000; 252p; In English; Sponsored in part by the Bing Fund
Report No.(s): AD-A381288; ISBN 0-8330-2873-1; Copyright; Avail: Defense Technical Information Center (DTIC)

Prostate cancer is the most common solid malignancy diagnosed in American men. More than half of the new cases identified each year are localized prostate cancer, an early stage of the disease in which the tumor is confined to the prostate. The usual approach to localized prostate cancer includes radical prostatectomy, radiation therapy, or watchful waiting. Unfortunately, clear evidence about the comparative efficacy of these treatments is lacking; and, even untreated, most men with early stage prostate cancer have a life expectancy comparable to similarly aged men without prostate cancer. The most common potential long-term complications after treatment include urinary incontinence, impotence, and bowel dysfunction. The rates of these complications reported by different researchers and institutions in the scientific literature vary substantially. Although this variability may simply reflect differences in the patients included (case-mix) or the ways in which the data were collected, it does raise concern that widespread variation exists in the quality of treatment provided for men with prostate cancer across the USA.
DTIC
Diagnosis; Cancer; Prostate Gland; Radiation Therapy

20000121360 Charles R. Drew Univ. of Medicine and Science, Los Angeles, CA USA
Using Breast Cancer Survivors to Increase Mammography Use *Annual Report, 1 Aug. 1998 - 31 Jul. 1999*
Robinson, Susan, Charles R. Drew Univ. of Medicine and Science, USA; August 1999; 23p; In English
Contract(s)/Grant(s): DAMD17-97-1-7189
Report No.(s): AD-A382430; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

The primary objectives for year two were to: recruit and train 6 breast cancer survivors and 6 community women without breast cancer for a program to train women to become breast health educators and to implement breast health education programs (Breast Health Symposia) in community churches. The goal of the program is to encourage participation in mammography among women, ages 40 and older, who have not had a mammogram within 12 months. A total of 8 breast cancer survivors and 9 women without the disease successfully completed a training program that was designed to enable them to effectively conduct breast health symposiums among churches located in South Central Los Angeles. The educators are similar in age, race and education. All trainees received a standardized training program that was led by the research team. Twenty churches were randomly assigned to one of two intervention groups. Group A, the control group, received breast health education from community educators. Group B received breast health education from breast cancer survivors.
DTIC
Education; Mammary Glands; Cancer; Diseases; Diagnosis; Tests

53
BEHAVIORAL SCIENCES

Includes psychological factors; individual and group behavior; crew training and evaluation; and psychiatric research.

20000115495 Air Force Academy, Dept. of Behavioral Sciences and Leadership, CO USA
Development of a Basic Flight Instruction Tutoring System (BFITS) Research Station
Miller, James C.; Kirk, Michael T.; Flynn, John S.; Hurt, Morgan P.; Schlueter, Jeffrey C.; Apr. 2000; 48p; In English
Report No.(s): AD-A381920; HERC-2000-03; No Copyright; Avail: CASI; A03, Hardcopy; A01, Microfiche

The Basic Flight Instruction Tutoring System (BFITS) was designed to observe and track the behavior of students as they attempt to learn basic flight procedures. Several modifications were required to adapt the BFITS to the needs of researchers at the USA Air Force Academy. These modifications were accomplished by a team of five cadets enrolled in Behavioral Sciences 473, Human Factors Engineering, and their instructor. A limited test and evaluation assured that the BFITS research station

worked as desired. The BFITS is a rich resource for investigations of fundamental learning processes associated with novice pilot learning. It may be used extensively as a tool to support faculty and cadet investigations of those processes.
DTIC
Flight Training; Human Factors Engineering; Flight Simulators; Flight Simulation; Universities

20000115618 San Jose State Univ., CA USA
Evaluation of a Computational Model of Situational Awareness
Burdick, Mark D., San Jose State Univ., USA; Shively, R. Jay, Army Aviation and Missile Command, USA; [2000]; 5p; In English; 14th, 30 Jul. 4 Aug. 2000, San Diego, CA, USA; Sponsored by Human Factors and Ergonomics Society, USA
Contract(s)/Grant(s): 21-1614-2360; RTOP 581-31-22; No Copyright; Avail: CASI; A01, Hardcopy; A01, Microfiche

Although the use of the psychological construct of situational awareness (SA) assists researchers in creating a flight environment that is safer and more predictable, its true potential remains untapped until a valid means of predicting SA a priori becomes available. Previous work proposed a computational model of SA (CSA) that sought to Fill that void. The current line of research is aimed at validating that model. The results show that the model accurately predicted SA in a piloted simulation.
Author
Evaluation; Simulation; Computerized Simulation; Physiological Factors

20000120151 Institute for Human Factors TNO, Soesterberg, Netherlands
Cognitive Task Load: A Function of Time Occupied, Level of Information Processing and Task Set Switches ***Cognitieve Taakbelasting: Een Functie Van Bezettingstijd, Niveau Van Informatieverwerking en Taaksetwisselingen***
Neerincx, M. A., Institute for Human Factors TNO, Netherlands; vanBesouw, N. J. P., Institute for Human Factors TNO, Netherlands; Sep. 29, 2000; 90p; In Dutch; Original contains color illustrations
Contract(s)/Grant(s): A99/KM/328; TNO Proj. 787.3
Report No.(s): TD-2000-0321; TM-00-A047; Copyright; Avail: Issuing Activity

For the Royal Netherlands Navy, the Netherlands Organization for Applied Scientific Research (TNO) Human Factors is developing a method for Cognitive Task Analysis that guides the early stages of the software development process, aiming at an optimal mental load. This method is based on a practical theory of cognitive task load. In addition to the classical measure percentage time occupied, this theory distinguishes two load factors that affect cognitive task performance and mental effort: (1) the level of information processing and (2) the number of task-set switches. Experiments should provide evidence for the factors' effects. We developed a 'Ship Control Center' computer-task in which the user plays the role of damage control manager, supervising the platform systems on the ship. When alarms appear (e.g. fire), the manager has to provide (virtual) assistants with adequate operation instructions as fast as possible. A task consists of several actions. The task performance measure is task time, divided into action selection time (i.e. the choice what to do) and action execution time. In a first experiment, the task time and the subjective mental effort proved to be substantially higher when the level of information processing (i.e. the number of knowledge-based actions) was relatively high. The second experiment showed that all three factors had their individual effects on performance and mental effort. The action execution time proved to be more than two times larger for the knowledge-based actions than for the rule-based actions. The action selection time proved to be larger when the number of task-set switches was high, when the percentage time occupied was high and when the number of knowledge-based actions was high. For knowledge-based actions, the effect of time occupied on total action time was larger than for rule-based actions, showing that the load factors can enforce each other's effects. A regression analysis showed that the three factors together explain the variance in task time up to 80%. The subjective mental effort was higher when the number of knowledge-based actions was high and when the number of task-set switches was high. A regression analysis showed that these two factors together explain the variance in mental effort for 32%. The experiments provide empirical support for the three-dimensional model of cognitive task load. In the damage control tasks of the experiment, the cognitive factors 'level of information processing' and 'task-set switches' had a larger effect on performance time and mental effort than the classical 'time occupied' factor, whereas the three factors together predict the task time very well. The model can be used for the analyses of current and future tasks in order to improve mental load by task re-allocation and the provision of cognitive support.
Author
Mental Performance; Human Performance; Research and Development; Data Processing; Tasks

20000120156 Research Inst. for Advanced Computer Science, Computational Science Div., Moffett Field, CA USA
What the Logs Can Tell You: Mediation to Implement Feedback in Training
Maluf, David, Research Inst. for Advanced Computer Science, USA; Wiederhold, Gio, Stanford Univ., USA; Abou–Khalil, Ali, Caelum Research Corp., USA; [2000]; 7p; In English

Contract(s)/Grant(s): NAS2-14217; NCC2-1006; N66001-95-C-08618; No Copyright; Avail: CASI; A02, Hardcopy; A01, Microfiche

The problem addressed by Mediation to Implement Feedback in Training (MIFT) is to customize the feedback from training exercizes by exploiting knowledge about the training scenario, training objectives, and specific student/teacher needs. We achieve this by inserting an intelligent mediation layer into the information flow from observations collected during training exercises to the display and user interface. Knowledge about training objectives, scenarios, and tasks is maintained in the mediating layer. A designer constraint is that domain experts must be able to extend mediators by adding domain-specific knowledge that supports additional aggregations, abstractions, and views of the results of training exercises. The MIFT mediation concept is intended to be integrated with existing military training exercise management tools and reduce the cost of developing and maintaining separate feedback and evaluation tools for every training simulator and every set of customer needs. The MIFT Architecture is designed as a set of independently reusable components which interact with each other through standardized formalisms such as the Knowledge Interchange Format (KIF) and Knowledge Query and Manipulation Language (KQML).
Author

Education; Feedback; Military Technology; Computer Programs

20000120210 Institute for Human Factors TNO, Soesterberg, Netherlands

Testing Task Situation Awareness? *Final Report EenTest Voor Taaksituatiebewustzijn?*

Boer, L. C., Institute for Human Factors TNO, Netherlands; vanSchie, C. C., Institute for Human Factors TNO, Netherlands; Apr. 17, 2000; 26p; In Dutch

Contract(s)/Grant(s): A96/KLu/366; TNO Proj. 787.1

Report No.(s): TD-2000-0136; TNO-TM-00-A027; Copyright; Avail: Issuing Activity

The objective of the study was to see whether task awareness (part of the general concept SA) could be measured with a experimental test developed by the Netherlands Organization for Applied Scientific Research (TNO). During testing, people have to solve errors (at times, double errors) while guarding a temperature. Forgetting the temperature indicated poor task situation awareness. Taken as a more or less stable characteristic of the individual, the score on the experimental test is of major importance for predicting adequate functioning in the cockpit on the long term, and can be used as a test for personnel selection. In an investigation, 80 pilot candidates of the Royal Netherlands Air Force were tested on task forgetting. They were also tested on an existing battery including a flight simulator test, the only test where several tasks were executed simultaneously. Task forgetting during double experimental errors correlated 0.33 (n = 44) with the performance quality of the simulated flight at the time that the transponder code had to be changed. (Another study revealed a correlation of 0.53; n = 32 with task forgetting on the ship's bridge.) The discussion indicates that task forgetting is not always the result of poor SA. Task forgetting in the simulator can be the result of depletion of capacity due to mental overload; task forgetting in the TNO test may reflect unnecessary risk taking. The recommendation is to improve the concept validity of the TNO test by: (1) reducing the opportunities for risk taking, (2) to try situation awareness even more with more challenging errors, and (3) to refine the scoring procedure by registration of 'near forgetting'. The expectation is that the test has a high potential to bring the quality of someone's task SA to light.
Author

Errors; Risk; Research and Development; Human Performance

20000120372 Institute for Human Factors TNO, Soesterberg, Netherlands

The Effect of Intra-Team Feedback on Team Performance after Developing a Shared Mental Model *Interim Report Het Effect van Intra-Team Feedback op de Team Prestatie Nadat een Gemeenschappelijk Mentaal Model is Ontwikkeld*

Rasker, P. C., Institute for Human Factors TNO, Netherlands; Schraagen, J. M. C., Institute for Human Factors TNO, Netherlands; Stroomer, S. M., Institute for Human Factors TNO, Netherlands; Oct. 16, 2000; 33p; In English

Contract(s)/Grant(s): B00-061; TNO Proj. 731.1

Report No.(s): TD-2000-0325; TM-00-B010; Copyright; Avail: Issuing Activity

This study was conducted to investigate the effect of intra-team feedback (i.e., team members giving each other feedback) on team performance in teams performing a Command & Control task. In this study we wanted to a) replicate our previous findings under enhanced training conditions, b) establish a link between intra-team feedback and the knowledge team members are expected to develop in a shared mental model, and c) investigate whether intra-team feedback is still beneficial when teams have had the opportunity to engage in intra-team feedback to maintain up-to-date knowledge in a shared mental model.
Author

Feedback; Human Performance; Command and Control

20000120410 Institute for Human Factors TNO, Soesterberg, Netherlands

Support for Iteration in Training Program Design *Interim Report Ondersteuning voor Iteratie in het Ontwerp van Training Programma's*

Verstegen, D. M. L., Institute for Human Factors TNO, Netherlands; Steutel, S., Institute for Human Factors TNO, Netherlands; Barnard, Y. F., Institute for Human Factors TNO, Netherlands; Oct. 04, 2000; 66p; In English

Contract(s)/Grant(s): B00-051; TNO Proj. 790.1

Report No.(s): TD-2000-0323; TM-00-B009; Copyright; Avail: Issuing Activity

A methodology for the design of training simulator specifications has been developed in a European defence research project MASTER (EUCLID RTP 1 1. 1) The MASTER methodology meets most of the requirements posed in previous research. However, we have identified four areas where it needs further research and development: 1. Empirical evaluation of the methodology 2. Support for iterative design 3. The content of libraries and guidelines 4. Different kinds of guidance In our research we focus on the first two issues.

Author

Education; Iteration; Training Simulators

20000120412 Institute for Human Factors TNO, Soesterberg, Netherlands

Teams Under Stress: A Literature Review *Interim Report Teams Onder Strees: Een Literatuuroverzicht*

Hoeksema–vanOrden, C. Y. D., Institute for Human Factors TNO, Netherlands; vanDuijne, F. H., Institute for Human Factors TNO, Netherlands; vanVliet, A. J., Institute for Human Factors TNO, Netherlands; Jun. 27, 2000; 88p; In Dutch

Contract(s)/Grant(s): A98/KL/302; TNO Proj. 731.2

Report No.(s): TD-2000-0145; TM-00-A035; Copyright; Avail: Issuing Activity

This report describes a literature study for the project Teams under Stress. A theoretical framework is proposed in order to describe the functioning of combat units in demanding situations. The core of the framework is as follows: the individual can cope with situational demand by means of individual- and team resources. The outcome of the process will be measured in terms of performance and health, The literature is used to investigate the relations between the concepts of the framework. It has been found that exposure to traditional combat situations, confrontations with the local population and frustrations of peacekeeping were major predictors of stress reactions. Good leadership, cohesion and military pride have proven to be good protectors against stress reactions. Problem-focused coping, planning, supporting mates, being able to postpone rewards and regulating or temporary ignoring emotions proved to be healthy coping strategies. Most studies describe just a part of the framework. Moreover, only a constrained number of studies have been carried out in the military field. The majority of the results have been found in student populations, occupational groups and other sub-populations. This study pleads for further research in the military field, in which all the concepts of proposed theoretical framework should be investigated together. In preparation of such an empirical study, validated questionnaires are brought together for all concepts in the theoretical framework. These are included in an appendix.

Author

Teams; Organizations; Stress (Biology); Human Performance; Health

20000121198 Air Force Research Lab., Human Effectiveness Directorate, Wright-Patterson AFB, OH USA

Pitfalls of Ability Research in Aviation Psychology *Interim Report, Sep. 1998 - Jan. 1999*

Carretta, Thomas R., Air Force Research Lab., USA; Ree, Malcolm James, Our Lady of the Lake Univ., USA; December 1999; 21p; In English

Contract(s)/Grant(s): AF Proj. 1123

Report No.(s): AD-A372383; AFRL-HE-WP-TR-1999-0232; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

Ability research in aviation psychology can be fraught with pitfalls that lead to inappropriate conclusions. We identify several issues that lead to potential misinterpretation of results and suggest corrective solutions. These issues include lack of construct validity of the measures, misinterpretation of correlations and regression weights, lack of statistical power, failure to estimate cross validation effects, and misinterpretation of factor analytic results.

DTIC

Aviation Psychology; Research; Regression Analysis; Mental Performance

20000121242 Air Force Academy, Human-Environmental Research Center, CO USA

Women in Military Aviation, *Aug. 1999 - May 2000*

Waterman, Katrine M., Air Force Academy, USA; Miller, James C., Air Force Academy, USA; May 31, 2000; 27p; In English

Report No.(s): AD-A381795; USAFA-TR-2000-06; No Copyright; Avail: CASI; A01, Microfiche; A03, Hardcopy

As women become increasingly involved in the world of aviation and combat flying roles, questions concerning gender issues in the cockpit are becoming extremely relevant. Some of the most significant areas of concern dealing with women in the cockpit are behavior, body composition, anthropometry, biomechanics, physiology, health, and learning. This project addresses these seven areas of concern for women in military aviation. We conducted this review through a literature search, and through interviews with both women and men in the operational Air Force and the civilian world. In addition, a computer-based simulator was used to compare the learning characteristics between men and women for basic flying skills. All the research cited reached the same general conclusions. There is no difference in the abilities of men and women to perform successfully and safely in an aviation career. The statistical analysis of the data collected for this experiment produced similar results; there was no significant difference between men and women in any of the four measures used to test basic flying performance. Overall, both men and women are physically and mentally equally qualified to pursue aviation careers.
DTIC
Females; Cockpits; Occupation; Human Performance; Sex Factor; Pilots (Personnel)

20000121325 Naval Postgraduate School, Monterey, CA USA
Determinants of Flight Training Performance: An Analysis of the Impact of Undergraduate Academic Background
Reis, Paul M., Naval Postgraduate School, USA; June 2000; 76p; In English
Report No.(s): Ad-A381146; No Copyright; Avail: CASI; A01, Microfiche; A05, Hardcopy

This thesis uses pre-commissioning academic and demographic factors, along with flight school performance data to measure pilot success in flight school. The goal is to determine if undergraduate major or school attended affect flight school performance. Measure of effectiveness include: (1) Flight School Completion Status, (2) Aviation Pre-Flight Indoctrination Composite Scores, and (3) Primary Flight Training Composite Scores. Recruitment for naval aviators is focused on individuals with "technical majors," according to present policy of the Naval Recruiting Command. This recruiting philosophy is based on the "Rickover Hypothesis," which postulates that naval officers with technical degrees are superior to naval officers with non-technical degrees. The Logit model showed that aviators with engineering degrees have a statistically greater chance of completing flight school than aviators with non-engineering technical or non-technical degrees. In addition, the results showed an association between academic background and flight school performance. This research justifies the current Navy policy of concentrating aviator recruitment efforts on individuals with technical degrees.
DTIC
Aircraft Pilots; Flight Training; Human Performance; Pilot Selection

54
MAN/SYSTEM TECHNOLOGY AND LIFE SUPPORT

Includes human factors engineering; bionics, man-machine, life support, space suits and protective clothing. For related information see also 16 Space Transportation and 52 Aerospace Medicine..

20000116093 Air Force Research Lab., Human Effectiveness Directorate, Brooks AFB, TX USA
Testing and Evaluation of the Northrop Grumman Corporation Model 9602 Life Support for Trauma and Transport (LSTAT) Unit, Part Number ATBX01006A002 ***Final Report, Nov. 98***
Blake, Butch O.; Sylvester, James C.; Mar. 2000; 26p; In English
Contract(s)/Grant(s): Proj-7184
Report No.(s): AD-A377368; AFRL-HE-BR-TR-2000-0027; No Copyright; Avail: CASI; A03, Hardcopy; A01, Microfiche

The Northrop Grumman Corporation Model 9602 Life Support for Trauma and Transport (LSTAT) Unit, Part Number ATBX01006A002 is conceptually designed for use in military medical evacuation on board USAF aeromedical evacuation aircraft. Specific components of the LSTAT that under went the evaluation process included: The Protocol Systems Inc., Propaq Model 106 LCD Physiological Monitor; IMPACT Corporation, Model 326 Continuous/Intermittent Suction Unit (CISU); IMPACT Corporation, Model 754 "Eagle" Transport Ventilator; SurVivaLink Corporation, Automated External Defibrillator (AED); IVAC, Inc. Model MedSystem III Infusion Pump; i-STAT, Inc., Blood Analyzer; Internal 480 Liter Bottle Oxygen System; Display and Data Logging Subsystem (DDLS) to include Fujitsu Model Stylistic 1000 Secondary Display; and Electrical Power Subsystem (EPS).
DTIC
Life Support Systems; Medical Equipment; Armed Forces; Oxygen Supply Equipment; Medical Services; Evacuating (Transportation)

20000116149 Air Force Research Lab., Human Effectiveness Directorate, Wright-Patterson AFB, OH USA
Evaluation of the Effects of the ZetaLiner During Helmet Impact *Interim Report, Aug.-Nov. 1999*
Perry, Chris E.; Nov. 1999; 36p; In English
Contract(s)/Grant(s): Proj-7184
Report No.(s): AD-A382259; AFRL-HE-WP-SR-2000-0005; No Copyright; Avail: CASI; A03, Hardcopy; A01, Microfiche

An experimental effort was conducted to compare the ZetaLiner, a new foam flight helmet liner manufactured by Oregon Aero, to the Thermal Plastic Liner (TPL), the helmet liner used in the USAF's standard flight helmet, the HGU-55/P. The liners were compared based on their effectiveness in attenuating impact acceleration and minimizing head injury potential. A series of vertical drops with a Helmet Drop Tower (HDT) were conducted using HGU-55/P flight helmets, TPLs, and several ZetaLiner samples. In addition to the liner comparison, helmet impacts were also conducted to evaluate Oregon Aero's Ballistic Liner Upgrade (BLU) compared to the rigid foam liner used in the HGU-55/P. All tests exposed the helmet shell to impacts against a hemispherical anvil as outlined in military standard MIL-H-87174. The probability of head injury, as defined by the Head Injury Criteria (HIC), was calculated using measured impact acceleration of the HDT headform for each helmet configuration. Test results indicated that all impact configurations passed the acceleration standard as outlined in MIL-H-87174. The headform acceleration, resulting HIC values, and probability of severe brain injury values for the ZetaLiner tests were less than the comparative values for either the standard ACES II TPL or the HGU-55/P helmet with the BLU.
DTIC
Flight Clothing; Helmets; Head (Anatomy); Linings

20000116335 NASA Johnson Space Center, Houston, TX USA
Spacecraft Minimum Allowable Concentrations: Determination, Application, and Contingency Situations
Marshburn, Thomas H., NASA Johnson Space Center, USA; [1999]; 1p; In English; Hyperbaric Breathing Gas, 30 Sep. Sep. - 1 Oct. 1999, Aberdeen, Scotland, UK; Sponsored by UK Health and Safety Initiative, UK; No Copyright; Avail: Issuing Activity; Abstract Only

This document is an outline of a presentation about the determination of minimum allowable concentrations in spacecraft. The presentation reviews the type of toxins and mechanisms to determine the acceptable concentrations of these toxic substances. The considerations for the unique situation that spaceflight entails including zero gravity, and the intense scrutiny are reviewed. The current measurement hardware is reviewed. The spacecraft atmospheres on the Shuttle, airflow, the Space Station and the EMU in respect to airflow, pressure, constituents are also summarized. Contingency situations and potential hazards are also discussed.
CASI
Toxicity; Spacecraft Environments; Bioastronautics; Spacecraft Cabin Atmospheres; Environmental Control

20000116402 Institut Franco-Allemand de Recherches, Saint-Louis France
Artificial Heads for High-Level Impulse Sound Measurement, 5-8 Jul. 1999
Buck, K.; Parmentier, G.; Jan. 1999; 8p; In English
Report No.(s): AD-A382230; ISL-PU-341/99; No Copyright; Avail: CASI; A01, Microfiche; A02, Hardcopy

If the Insertion Loss (IL) of hearing protectors has to be determined with very high impulse or continuous noise levels, the acoustic insulation of the Artificial Test Fixture has to exceed at least the Insertion Loss (IL) of the hearing protector. An another requirement when evaluating ear muffs, is an adequate reproduction of the pinna and the circumaural area. For the evaluation of ear plugs and hearing protectors using Active Noise Cancellation (ANR) the impedance of the eardrum must be properly reproduced. These requirements have not been always fulfilled by commercially available artificial heads. Therefore, a special device for this type of measurement has been designed and built in our laboratories. The head has been molded with Polyurethane material in a way, that the HEAD Acoustics external ear and circumaural area could be fit. In order to simulate the acoustic impedance of the human ear, a Bruel & Kjaer ear simulator has been used. The acoustic insulation of the ATF is better than the requirements of the different standards. The Transfer Function of the Open Ear (TFOE) is very close to the data published by Shaw. The device is linear up to peak pressure levels of 190 dB. It is possible with this ATF, to evaluate the IL of all types of hearing protectors up to pressure levels of 190 dB.
DTIC
Acoustic Measurement; Ear Protectors; Continuous Noise; High Impulse

20000118223 Institute for Human Factors TNO, Soesterberg, Netherlands

Interfaces in Future Ship Control Centres: Evaluation of Shared Workspaces *Interim Report Interfaces in Toekomstige Technische Centrales: Evaluatie Shared Workspaces*

Passenier, P. O., Institute for Human Factors TNO, Netherlands; Houttuin, K., Institute for Human Factors TNO, Netherlands; Sep. 06, 1999; 32p; In Dutch; Original contains color illustrations

Contract(s)/Grant(s): A97/KM/333; TNO Proj. 787.2

Report No.(s): TD-99-0338; TM-99-A060; Copyright; Avail: Issuing Activity

Under contract to the Royal Netherlands Navy (A97/KM/333), in the experimental Command and Control laboratory (C2-Lab) of TNO-HFRI an evaluation study was conducted regarding the use of shared workspaces for overview and conferencing purposes in the Ship Control Centre ISM on-board future frigates, like the Air Defense and Command frigate (ADCF). The results of the study show that for the SCC-team an added value is offered by the automatically) updated overview presentation according to the 'General Arrangement Plan' (GAP) concept, presenting damage and system-related information at different levels of detail. At the highest level, presenting mainly damage-related information for the whole ship, an additional need was identified for information regarding the ship's operational status and system availability. On the other hand, especially at the lower levels of GAP presentation, care has to be taken that the amount of available information does not make the presentation unclear. Also, the possibility of using the GAP presentation for supporting the communication between team members (e.g. command huddles) is regarded to have a positive effect on the efficiency and unambiguity of the internal information transfer. However, for this purpose, additional facilities are required for a temporary copy of more detailed, mimic-like information from the individual workstations. Regarding the use of a Large Screen Display (LSD), this device is foreseen to be useful for the presentation of a common overview, with direct availability for the visual support of communication between team members (e.g. 'pointing function' during command huddles). Important for this setup is to have a clear protocol for display management, calling for a minimal overhead for the different team members. Further, for communication support within the different domains (damage and technical), in many cases other means of information exchange will be used, for instance based on mimics from individual operator positions. The use of a central overview screen for this purpose might cause unnecessary "crosstalk" with the other team members. On the other hand, regarding conferencing based on individual workstations, a possible danger is recognized of 'discommunication', because of ambiguities in the layer settings on the individual screens. Regarding future research it is proposed to, based on the current findings, further develop the GAP information specification for application on board the ADCF. This follow-up study has to take into account the ADCF specific constraints regarding the implementation of a shared workspace (for instance, the limited possibilities for a large screen presentation for all team members, given the planned dimensions of the SCC).

Author

Air Defense; Command and Control; Decision Making; Process Control (Industry); Workstations; Man Machine Systems; Human Factors Engineering

20000119049 NASA Ames Research Center, Moffett Field, CA USA

Regenerable Air Purification System for Gas-Phase Contaminant Control

Constantinescu, Ileana C., Science Systems and Applications, Inc., USA; Finn, John E., NASA Ames Research Center, USA; LeVan, M. Douglas, Vanderbilt Univ., USA; Jan. 18, 2000; 1p; In English; International Conference on Environmental Systems, 10-13 Jul. 2000, Toulouse, France

Contract(s)/Grant(s): RTOP 131-20-10; No Copyright; Avail: Issuing Activity; Abstract Only

Tests of a pre-prototype regenerable air purification system (RAPS) that uses water vapor to displace adsorbed contaminants from an adsorbent column have been performed at NASA Ames Research Center. A unit based on this design can be used for removing trace gas-phase contaminants from spacecraft cabin air or from polluted process streams including incinerator exhaust. During the normal operation mode, contaminants are removed from the air on the column. Regeneration of the column is performed on-line. During regeneration, contaminants are displaced and destroyed inside the closed oxidation loop. In this presentation we discuss initial experimental results for the performance of RAPS in the removal and treatment of several important spacecraft contaminant species from air.

Author

Air Purification; Contaminants; Phase Control; Vapor Phases; Water Vapor

20000120136 Prins Maurits Lab. TNO, Rijswijk, Netherlands

Monitoring Air Quality on Board of Hare Majesteit Zeeleeuw *Final Report Monitoren Luchtkwaliteit Aan Boord Van Hare Majesteit Zeeleeuw*

vanderGijp, S., Prins Maurits Lab. TNO, Netherlands; Albers, J., Prins Maurits Lab. TNO, Netherlands; August 2000; 18p; In Dutch; Original contains color illustrations

Contract(s)/Grant(s): A95/KM/418; TNO Proj. 014.11377; TNO Proj. 014.11752
Report No.(s): TD-2000-0028; TNO-PML-2000-A26; No Copyright; Avail: CASI; A03, Hardcopy; A01, Microfiche

During a shipping period from September to December on board of Hare Majesteit Zeeleeuw the concentration of saturated hydrocarbons and carbon dioxide was monitored. In contradiction to the expectation no increase in the hydrocarbon concentration was found in this period. Instead the concentration of the hydrocarbon followed a similar pattern as the carbon dioxide concentration. This indicates a strong contribution of snorting or less probable the replacement of Sofholime canisters to the air quality. The concentration propane stayed well below the SMAC level known for other linear alkanes. Based on the results described in this report it is not yet possible to make a statement about the changing frequencies of the carbon filters. The carbon dioxide level was at most 0.8% and had an average of 0.2%.

Author

Air Quality; Carbon Dioxide Concentration; Hydrocarbons; Concentration (Composition)

20000120150 Institute for Human Factors TNO, Soesterberg, Netherlands

Digital Human Modeling: Anthropometric Aspects *Final Report Digitale Mensmodellering: Antropometrische Aspecten*

Delleman, N. J., Institute for Human Factors TNO, Netherlands; Hin, A. J. S., Institute for Human Factors TNO, Netherlands; 20000329; 44p; In English

Contract(s)/Grant(s): B97/040; TNO Proj. 789.1

Report No.(s): TD-2000-0133; TNO-00-B004; Copyright; Avail: Issuing Activity

The 1998 ergonomics research program of the department of Work Environment of the Netherlands Organization for Applied Scientific Research (TNO) Human Factors focused on anthropometric aspects of digital human models. Studies were carried out on the validity of body geometry and reach envelopes in a digital human model. From previous research projects it is already known that the lower trunk and thighs change shape considerably when going from standing to sitting. A pilot study conducted gives reason to expect that the effect of trunk inclination on trunk depth is at least as great as the effect of changing the main body posture from standing to sitting or vice versa. It is recommended to extend the pilot study to research with multiple subjects of different somatic classes. These characteristics can be introduced in human modelling systems with the development of models of specific parts of the body. Whole-body scans are a convenient instrument in developing these models. Reach analyses are part of practically all human factors engineering projects carried out at the department of Work Environment. The department uses the Boeing McDonnell Douglas Human Modeling System (BMD HMS) to perform reach studies. The modelling of the links and joints of the upper extremity is of crucial importance to the reach envelopes produced. An experimental study conducted showed that for producing valid reach envelopes with BMD HMS (version 3.0.4) the upper link structure requires re-modelling, The length and range of motion of the shoulder girdle segment deserve special attention. Ergonomic consults for military and civil assignments of workplace design will make use of the knowledge explored in this study. A next step in improving application of digital human models in design evaluations is to develop models on human motor behaviour and to build a concept of proper positioning of a manikin in a CAD-design. Another challenge for future research is to steer a man model in a virtual design with a multi-tracking system worn by a subject.

Author

Anthropometry; Human Factors Engineering; Research and Development; Posture; Human Body

20000120154 Institute for Human Factors TNO, Soesterberg, Netherlands

Effectiveness of 'Phase Change Materials' in Clothing *Interim Report Effectiviteit Van 'Phase Change Materials' in Kleding*

denHartog, E. A., Institute for Human Factors TNO, Netherlands; Heus, R., Institute for Human Factors TNO, Netherlands; May 02, 2000; 32p; In Dutch

Contract(s)/Grant(s): A98/KL/336; TNO Proj. 789.2

Report No.(s): TD-2000-0138; TNO-TM-00-A029; Copyright; Avail: Issuing Activity

Currently, a lot of attention is given about sweaters and coats in which a so called 'Phase Change Material' (PCM) is used. These PCMs exhibit a phase shift from solid to fluid between 200C and 300C. The idea is that the PCM stores the heat of the wearer during exercise and that this heat is being released as the person rests. As military tasks also often lead to intermittent exposures to heat or cold, the effectiveness of PCMs in currently available clothing was studied at the TNO Human Factors Research Institute. The comparison of heating and cooling of a free hanging normal sweater and one with PCM, showed that the sweater with PCM remained constant at 290 C for two minutes. This at least demonstrated that the PCM was active. The question remained whether this activity was also of practical use. From material measurements at the TNO Textile Technology and Development Institute it was concluded that two percent of the mass of the sweater consisted of the PCM (paraffin derivative). At a total weight of about 750 grams, this would mean 15 grams of the PCM. The heat of fusion of such materials is approximately 150 J/g. The heat storage capacity is then about 2250 J. to a person who would be walking at a leisure pace first and who would then have a

rest, about 60 W of heat should be produced by the PCM to stay at the same comfort temperature. With the capacity that we found in the sweater this person would stay for 2250/60 = 37.5 seconds longer in comfort, after this period he would continue to cool down. Further computations show that the prevention of cooling, using a PCM, under alternating conditions would require about 0.5 kg to 1 kg of the PCM. Such quantities have not been found in commercially available clothing. As relatively large quantities of PCM are required it seems more sensible, also regarding the costs, to take an extra coat with you. In spite of the lack of effectiveness that was found in the commercially available clothing, the application of PCMs in clothing may have a future. Therefore, it is advisable to not only monitor the developments, but also to actively collect information on the possible use of these materials.
Author
Clothing; Heat Storage; Research and Development; Technology Utilization

20000120260 Institute for Human Factors TNO, Soesterberg, Netherlands
Flying with a Head-Mounted Display: Mental Workload Effects ***Final Report Gevolgen Voor de Mentale Werkbelasting Bij Het Vliegen Met Een Head-Mounted Display***
Veltman, J. A., Institute for Human Factors TNO, Netherlands; Verschoor, M. H., Institute for Human Factors TNO, Netherlands; deVries, S. C., Institute for Human Factors TNO, Netherlands; Aug. 04, 2000; 48p; In English
Contract(s)/Grant(s): A97/KLu/311; TNO Proj. 788.1
Report No.(s): TD-2000-0153; TNO-TM-00-A043; Copyright; Avail: Issuing Activity

Compared to a conventional (fixed) display, a Head-Mounted Display (HMD) has the advantage that the availability of information is not dependent on the operator's viewing direction. This is one of the reasons why HMDs are more and more commonly found in military aircraft cockpits. However, there is not much information about the consequences of these systems for task performance and workload. Positive and negative effects of using an HMD compared to a conventional head-up display (HUD) were explored in terms of performance and workload. The experiment was commissioned by the Royal Netherlands Airforce.
Author
Head-Up Displays; Human Factors Engineering; Human Performance; Mental Performance; Physiological Responses; Workloads (Psychophysiology)

20000120409 Institute for Human Factors TNO, Soesterberg, Netherlands
Subjective Tilt by Vection and Centrifugation ***Interim Report Ervaren Zelfkanteling bij Vectie en Centrifugeren***
Bos, J. E., Institute for Human Factors TNO, Netherlands; Jun. 26, 2000; 44p; In Dutch
Contract(s)/Grant(s): B99-043; TNO Proj. 789.3
Report No.(s): TD-2000-0144; TM-00-B007; Copyright; Avail: Issuing Activity

How humans estimate their body motions by signals from the vestibular apparatus and their eyes, can be described with a differential equation. This equation predicts a plain relationship between 1) a time constant of a low-pass filter to discriminate between accelerations due to motion and gravity, 2) the sensed angular velocity, and 3) the sensed tilt angle under constant rotation of the visual field in a vertical plane (roll-vection). by means of a centrifuge experiment to determine the time constant in a relatively direct way (by the somatogravic effect), and two methods to determine the sensed tilt angle under roll-vection, it is examined whether the postulated relationship could be validated. It appeared, however, that the value of that time constant by the vection experiment was significantly smaller than that by the centrifuge experiment, and as known from the literature. On the individual level also no significant correlation between both time constants was found. Two main reasons for the latter are discussed. First, it appeared that the tilt angle under roll-vection did already not behave according to the model and the literature, Second, the effect of rotation in the centrifuge was confounding. by means of improvements to measure the tilt-angle under roll-vection and to circumvent the rotation effect in the centrifuge, it should be possible, however, to validate the relationship also on the individual level in an other experiment.
Author
Attitude (Inclination); Differential Equations; Vertical Perception; Vestibular Tests; Centrifuging; Mathematical Models

20000120862 Defence and Civil Inst. of Environmental Medicine, Downsview, Ontario Canada
1997 Canadian Forces Air Operations Vision Survey Sections III, IV, V and VI Vision Protectors and Enhancers
Heikens, M. F.; Gray, G. W.; O'Neill, H. J.; Salisbury, D. A.; Jul. 2000; 31p; In English
Report No.(s): AD-A382329; DCIEM-TR-2000-065; Copyright; Avail: Defense Technical Information Center (DTIC)

Introduction: In 1997, DCIEM conducted an Operational Vision Survey of current Canadian Forces (CF) pilots. This third report deals with those aspects related to vision protective and enhancement equipment, specifically sunglasses, visors, laser protective devices, and night vision goggles.
DTIC
Night Vision; Protectors; Surveys; Eye Protection

20000121128 Lockheed Martin Engineering and Science Services, Moffett Field, CA USA
A Solid-State Compressor for Integration of CO2 Removal and Reduction Assemblies
Mulloth, Lila M., Lockheed Martin Engineering and Science Services, USA; Finn, John E., NASA Ames Research Center, USA; [2000]; 1p; In English; Environmental Systems, 10-13 Jul. 2000, Toulouse, France
Contract(s)/Grant(s): RTOP 131-20-10; No Copyright; Avail: Issuing Activity; Abstract Only

Integration of CO2 removal and reduction assemblies in a spacecraft air revitalization system requires an interface with the functionality of a vacuum pump/compressor and a buffer tank. The compressor must meet the vacuum needs of the CO2 removal unit and the pressure needs of the CO2 reduction device, and must also store sufficient CO2 to accommodate the differences in cycle times of the two processes. In this presentation, we describe the design and operation of an adsorption-based device sized for use on the International Space Station. The adsorption compressor functions at a power level approximately ten times lower than a comparable mechanical compression/buffer tank system. The unit is also smaller, lighter, and quieter than its mechanical counterpart.
Author
Air Purification; Carbon Dioxide Removal; Compressors; Life Support Systems

20000121171 NASA Ames Research Center, Moffett Field, CA USA
System Design Techniques for Reducing the Power Requirements of Advanced life Support Systems
Finn, Cory, NASA Ames Research Center, USA; Levri, Julie, Orbital Sciences Corp., USA; Pawlowski, Chris, Orbital Sciences Corp., USA; Crawford, Sekou, Orbital Sciences Corp., USA; [2000]; 1p; In English; 4th; Life Support and Biosphere Science, 6-9 Aug. 2000, Baltimore, MD, USA
Contract(s)/Grant(s): RTOP 131-20-10; No Copyright; Avail: Issuing Activity; Abstract Only

The high power requirement associated with overall operation of regenerative life support systems is a critical Z:p technological challenge. Optimization of individual processors alone will not be sufficient to produce an optimized system. System studies must be used in order to improve the overall efficiency of life support systems. Current research efforts at NASA Ames Research Center are aimed at developing approaches for reducing system power and energy usage in advanced life support systems. System energy integration and energy reuse techniques are being applied to advanced life support, in addition to advanced control methods for efficient distribution of power and thermal resources. An overview of current results of this work will be presented. The development of integrated system designs that reuse waste heat from sources such as crop lighting and solid waste processing systems will reduce overall power and cooling requirements. Using an energy integration technique known as Pinch analysis, system heat exchange designs are being developed that match hot and cold streams according to specific design principles. For various designs, the potential savings for power, heating and cooling are being identified and quantified. The use of state-of-the-art control methods for distribution of resources, such as system cooling water or electrical power, will also reduce overall power and cooling requirements. Control algorithms are being developed which dynamically adjust the use of system resources by the various subsystems and components in order to achieve an overall goal, such as smoothing of power usage and/or heat rejection profiles, while maintaining adequate reserves of food, water, oxygen, and other consumables, and preventing excessive build-up of waste materials. Reductions in the peak loading of the power and thermal systems will lead to lower overall requirements. Computer simulation models are being used to test various control system designs.
Author
Design Analysis; Life Support Systems; Systems Engineering; Systems Integration; Environmental Engineering

20000121172 Rutgers Univ., Dept. of Bioresource Engineering, New Brunswick, NJ USA
A Simulation Study Comparing Incineration and Composting in a Mars-Based Advanced Life Support System
Hogan, John, Rutgers Univ., USA; Kang, Sukwon, Rutgers Univ., USA; Cavazzoni, Jim, Rutgers Univ., USA; Levri, Julie, Stevens Inst. of Tech., USA; Finn, Cory, NASA Ames Research Center, USA; [2000]; 1p; In English; 4th; Life Support and Biosphere Science, 6-9 Aug. 2000, Baltimore, MD, USA
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The objective of this study is to compare incineration and composting in a Mars-based advanced life support (ALS) system. The variables explored include waste pre-processing requirements, reactor sizing and buffer capacities. The study incorporates

detailed mathematical models of biomass production and waste processing into an existing dynamic ALS system model. The ALS system and incineration models (written in MATLAB/SIMULINK(c)) were developed at the NASA Ames Research Center. The composting process is modeled using first order kinetics, with different degradation rates for individual waste components (carbohydrates, proteins, fats, cellulose and lignin). The biomass waste streams are generated using modified "Eneray Cascade" crop models, which use light- and dark-cycle temperatures, irradiance, photoperiod, [CO2], planting density, and relative humidity as model inputs. The study also includes an evaluation of equivalent system mass (ESM).
Author
Composting; Life Support Systems; Mathematical Models; Biomass Burning; Bioprocessing; Environmental Engineering

20000121173 NASA Ames Research Center, Moffett Field, CA USA
Modeling Separate and Combined Atmospheres in BIO-Plex
Jones, Harry, NASA Ames Research Center, USA; Finn, Cory, NASA Ames Research Center, USA; Kwauk, Xianmin, Sverdrup Technology, Inc., USA; Blackwell, Charles, Lockheed Martin Engineering and Science Services, USA; [2000]; 1p; In English; 4th; Life Support and Biosphere Science, 6-9 Aug. 2000, Baltimore, MD, USA
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We modeled BIO-Plex designs with separate or combined atmospheres and then simulated controlling the atmosphere composition. The BIO-Plex is the Bioregenerative Planetary Life Support Systems Test Complex, a large regenerative life support test facility under development at NASA Johnson Space Center. Although plants grow better at above-normal carbon dioxide levels, humans can tolerate even higher carbon dioxide levels. Incinerator exhaust has very high levels of carbon dioxide. An elaborate BIO-Plex design would maintain different atmospheres in the crew and plant chambers and isolate the incinerator exhaust in the airlock. This design easily controls the crew and plant carbon dioxide levels but it uses many gas processors, buffers, and controllers. If all the crew's food is grown inside BIO-Plex, all the carbon dioxide required by the plants is supplied by crew respiration and the incineration of plant and food waste. Because the oxygen mass flow must balance in a closed loop, the plants supply all the oxygen required by the crew and the incinerator. Using plants for air revitalization allows using fewer gas processors, buffers, and controllers. In the simplest design, a single combined atmosphere was used for the crew, the plant chamber, and the incinerator. All gas processors, buffers, and controllers were eliminated. The carbon dioxide levels were necessarily similar for the crew and plants. If most of the food is grown, carbon dioxide can be controlled at the desired level by scheduling incineration. An intermediate design uses one atmosphere for the crew and incinerator chambers and a second for the plant chamber. This allows different carbon dioxide levels for the crew and plants. Better control of the atmosphere is obtained by varying the incineration rate. Less gas processing storage and control is needed if more food is grown.
Author
Air Purification; Closed Ecological Systems; Dynamic Models

20000121205 Stevens Inst. of Tech., Hoboken, NJ USA
Application of Energy Integration Techniques to the Design of Advanced Life Support Systems
Levri, Julie, Stevens Inst. of Tech., USA; Finn, Cory, NASA Ames Research Center, USA; Jan. 18, 2000; 1p; In English; 4th; Life Support and Biosphere Science, 6-9 Aug. 2000, Baltimore, MD, USA
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Exchanging heat between hot and cold streams within an advanced life support system can save energy. This savings will reduce the equivalent system mass (ESM) of the system. Different system configurations are examined under steady-state conditions for various percentages of food growth and waste treatment. The scenarios investigated represent possible design options for a Mars reference mission. Reference mission definitions are drawn from the ALSS Modeling and Analysis Reference Missions Document, which includes definitions for space station evolution, Mars landers, and a Mars base. For each scenario, streams requiring heating or cooling are identified and characterized by mass flow, supply and target temperatures and heat capacities. The Pinch Technique is applied to identify good matches for energy exchange between the hot and cold streams and to calculate the minimum external heating and cooling requirements for the system. For each pair of hot and cold streams that are matched, there will be a reduction in the amount of external heating and cooling required, and the original heating and cooling equipment will be replaced with a heat exchanger. The net cost savings can be either positive or negative for each stream pairing, and the priority for implementing each pairing can be ranked according to its potential cost savings. Using the Pinch technique, a complete system heat exchange network is developed and heat exchangers are sized to allow for calculation of ESM. The energy-integrated design typically has a lower total ESM than the original design with no energy integration. A comparison of ESM savings in each of the scenarios is made to direct future Pinch Analysis efforts.
Author
Design Analysis; Mars Missions; Mission Planning; Life Support Systems

20000121347 NASA Ames Research Center, Moffett Field, CA USA
Applying Technology Ranking and Systems Engineering in Advanced Life Support
Jones, Harry, NASA Ames Research Center, USA; [2000]; 1p; In English; 4th; Life Support and Biosphere Science, 6-9 Aug. 2000, Baltimore, MD, USA
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According to the Advanced Life Support (ALS) Program Plan, the Systems Modeling and Analysis Project (SMAP) has two important tasks: 1) prioritizing investments in ALS Research and Technology Development (R&TD), and 2) guiding the evolution of ALS systems. Investments could be prioritized simply by independently ranking different technologies, but we should also consider a technology's impact on system design. Guiding future ALS systems will require SMAP to consider many aspects of systems engineering. R&TD investments can be prioritized using familiar methods for ranking technology. The first step is gathering data on technology performance, safety, readiness level, and cost. Then the technologies are ranked using metrics or by decision analysis using net present economic value. The R&TD portfolio can be optimized to provide the maximum expected payoff in the face of uncertain future events. But more is needed. The optimum ALS system can not be designed simply by selecting the best technology for each predefined subsystem. Incorporating a new technology, such as food plants, can change the specifications of other subsystems, such as air regeneration. Systems must be designed top-down starting from system objectives, not bottom-up from selected technologies. The familiar top-down systems engineering process includes defining mission objectives, mission design, system specification, technology analysis, preliminary design, and detail design. Technology selection is only one part of systems analysis and engineering, and it is strongly related to the subsystem definitions. ALS systems should be designed using top-down systems engineering. R&TD technology selection should consider how the technology affects ALS system design. Technology ranking is useful but it is only a small part of systems engineering.
Author
Life Support Systems; Project Planning; Technology Assessment; Feasibility Analysis

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EXOBIOLOGY

Includes astrobiology; planetary biology; and extraterrestrial life. For the biological effects of aerospace environments on humans see 52 Aerospace medicine; on animals and plants see 51 Life Sciences. For psychological and behavioral effects of aerospace environments see 53 Behavioral Science.

20000115621 NASA Ames Research Center, Moffett Field, CA USA
How Common are Habitable Planets?
Lissauer, Jack J., NASA Ames Research Center, USA; [2000]; 12p; In English
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The Earth is teeming with life, which, occupies a diverse array of environments; other bodies in our Solar System offer fewer, if any, niches which are habitable by life as we know it. Nonetheless, astronomical studies suggest that a large number of habitable planets-are likely to be present within our Galaxy.
Author
Habitability; Earth (Planet); Planets; Extraterrestrial Life

20000121327 NASA Ames Research Center, Moffett Field, CA USA
Ecosystem Modeling of Biological Processes to Global Budgets
Christopher, Potter S., NASA Ames Research Center, USA; [2000]; 1p; In English; Astrobiology Science Conference, 3-5 Apr. 2000, Moffett Field, CA, USA
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From an ecological perspective, the search for life on distant planets begins from several key assumptions. The first of these is that, viewed from a remote location in space, the signature of life on a distant planet will be the result of net gas exchange of organisms with their environment. On the basis of extensive biogeochemical measurements and biogenic trace gas fluxes in modem Earth environments, it is probable that certain groups of organisms both produce and consume the same trace gas(es) within a single bioprofile of Solid (porous) substrate or surface water. The net gas exchange rate with the atmosphere measured at the living surface is frequently the result of competing metabolic reactions, which may carried out by different functional groups of organisms located at dissimilar 'climatic' or chemical microsites within the same bioprofile. Biogenic gases produced at one (deep) level of a bioprofile may be consumed by another functional group of organisms located closer to the level of surface exchange with the atmosphere. A second key assumption is that the net biogenic fluxes of atmospheric gases on Earth can be used

to infer relative abundance and functional composition of the major organisms on a distant planet. Examples of this principle include the presence of methanogenic microorganisms abundant today in freshwater ecosystems worldwide, which are major source of atmospheric methane and its seasonal variability in Earth's atmosphere. A third assumption is that scaling up biogenic gas fluxes from a single biological community to the planetary level requires flux measurements at the whole ecosystem level. This implies that measurements of biogenic gas exchange with the global atmosphere cannot be easily inferred from measurements of gas production rates of single organisms, which may have been isolated in some manner from the setting of their native ecosystem. Hence, the unit of biological organization used in modern Earth Science for scaling up to biosphere effects on atmospheric composition is the ecosystem level. These assumptions are the foundation for developing modern emission budgets for biogenic gases such as carbon dioxide, methane, carbon monoxide, isoprene, nitrous and nitric oxide, and ammonia. Such emission budgets commonly include information on seasonal flux patterns, typical diurnal profiles, and spatial resolution of at least one degree latitude/longitude for the globe. On the basis of these budgets, it is possible to compute 'base emission rates' for the major biogenic trace gases from both terrestrial and ocean sources, which may be useful benchmarks for defining the gas production rates of organisms, especially those from early Earth history, which are required to generate a detectable signal on a global atmosphere. This type of analysis is also the starting point for evaluation of the 'biological processes to global gas budget' extrapolation procedure described above for early Earth ecosystems.

Author

Atmospheric Composition; Biogeochemistry; Ecosystems; Exobiology; Microorganisms

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