**Acronym:** MDS

**Title:** Mice Drawer System

**Principal Investigator(s):**
Ranieri Cancedda, M.D., University of Genoa (Unige) and National Cancer Research Institute, Genoa, Italy

**Co-Investigator(s)\Collaborator(s):**
Stefano Schiaffino, University of Padova, Padua, Italy
Antonio Musaro, University of Rome La Sapienza, Rome Italy
Diana Conte Camerino, University of Bari, Bari, Italy
Angela Maria Rizzo, University of Milano, Milan, Italy
Felice Strollo, Instituto Nazionale Riposo e Cura Anziani (INRCA), Rome, Italy
Daniela Santucci, Istituto Superiore di Sanita, Rome, Italy
Paolo Di Nardo, University of Rome Tor Vergata, Rome, Italy
Giuseppe Miserocchi, University of Milano, Milan, Italy
Proto Pippia, Universiy of Sassari, Sassari, Italy
Michael D. Delp, Ph.D., University of Florida, Gainesville, FL
Yufang Shi, Ph.D., University of Medicine and Dentistry of New Jersey, Newark, NJ
Ted A. Bateman, Ph.D., Clemson University, Clemson, SC
Charles A. Fuller, University of California - Davis, Davis, CA
Yoshinobu Ohira, Osaka University, Osaka, Japan
Ishihara Akihiko, Kyoto University, Kyoto, Japan
Morel, Centre National de la Recherche Scientifique, Toulouse, France
Dieter Blottner, Ph.D., Charite Campus Benjamin Franklin, Berlin, Germany
Betty Nusgens, Ph.D., University of Liege, Wallonia, Belgium
Yi Liu, Ph.D., University of Genoa (Unige) and National Cancer Research Institute, Genoa, Italy
Roberta Biticchi, University of Genoa (Unige) and National Cancer Research Institute, Genoa, Italy

**Contact(s):**
PI - Ranieri Cancedda, +39 010 5737391
Primary - Yi Liu, +39 010 5737213
Secondary - Roberta Biticchi, +39 010 5737393

**Mailing Address(es):**
Professor Ranieri Cancedda
Department of Oncology, Biology and Genetics
University of Genova
Largo R. Benzi 10
16132 Genoa, Italy

**Developer(s):** Thales Alenia Space, Genoa, Italy

**Sponsoring Agency:** Italian Space Agency (ASI)

**Increment(s) Assigned:** 19

**Brief Research Summary (PAO):** Mice Drawer System (MDS) is an Italian Space Agency (ASI) investigation that will use a validated mouse model to investigate the genetic mechanisms underlying bone mass loss in microgravity. Research conducted with the MDS is an analog to the human research program, which has the objective to extend the human presence safely beyond low Earth orbit.

**Research Summary:**

- The Mice Drawer System (MDS) is an Italian Space Agency (ASI) facility which is able to support mice onboard the International Space Station during long-duration exploration missions (from 100 to 150-days) by living space, food, water, ventilation and lighting.

- Mice can be accommodated either individually (maximum 6) or in groups (4 pairs). MDS is integrated in the Space Shuttle middeck during transportation (uploading and downloading) to the ISS and in an EXPRESS Rack in *Destiny*, the US Laboratory during experiment execution.

- Osteoporosis is a debilitating disease that afflicts millions of people worldwide. One of the physiological changes experienced by astronauts during space flight is the accelerated loss of bone mass due to the lack of gravitational loading on the skeleton. This bone loss experienced by astronauts is similar to osteoporosis in the elderly population.

- MDS will help investigate the effects of unloading on transgenic (foreign gene that has been inserted into its genome to exhibit a particular trait) mice with the Osteoblast Stimulating Factor-1, OSF-1, a growth and differentiation factor, and to study the genetic mechanisms underlying the bone mass pathophysiology. MDS will test the hypothesis that mice with an increased bone density are likely to be more protected from osteoporosis, when the increased bone mass is a direct effect of a gene involved in skeletogenesis (skeleton formation).

**Detailed Research Description:** Osteoporosis is a debilitating disease that afflicts millions worldwide. One of the physiological changes experienced by astronauts during space flight is the accelerated loss of bone mass due to the lack of gravitational loading on the skeleton, a loss that is similar to osteoporosis in the elderly population on Earth.

Osteoblast Stimulating Factor-1 (OSF-1), also known as pleiotrophin (PTN) or Heparin-Binding Growth-Associated Molecule (HB-GAM) belongs to a family of secreted heparin binding proteins..OSF-1 is an extracellular matrix-associated growth and differentiation factor that is normally expressed in cartilage; it can stimulate the proliferation and differentiation of human osteoprogenitor cells (cell that differentiate into an osteoblast) *in vitro*.

The Mice Drawer System will study the effects of microgravity on transgenic mouse bones in order to identify genetic mechanisms playing a role in the reduction of the bone mass observed in humans and animals as a consequence of long-duration (greater than 100 days) microgravity exposure. Onboard the ISS, MDS is relatively self-sufficient; a crewmember will check the health status of the rodents on a daily basis, by assessing them through the viewing window. Water levels will be assessed by the crew daily and refilled as needed. Replacement of the food bars and replacement of the waste filters will be conducted inflight by crewmembers every 20-days.

Following return to Earth tissue and molecular analysis will be performed by the investigator team.

- Tissue studies will focus on characterization of the bone composition, turnover and structural changes in trabecular and cortical bones (bones with low density and strength and high surface area) of microgravity exposed and Earth bound mice.

    - Histomorphometry measurements, quantitative study of the microscopic organization and structure of a tissue, will be performed to describe the configuration of bone trabeculae and the extent to which bone trabecular lattice is intact in animals exposed to microgravity in space.
    - Imaging with X-ray microtomography, and with 3D Synchrotron microCT will help to characterize the 3D bone micro-architecture changes. Bone composition will be investigated by X-ray diffraction and Fast Fourier Transform Infrared Spectrophotometry (FTRI). Bone growth rate will be determined by the double calcein labeling.

- Molecular studies will focus on the modulation of biochemical markers at protein level. Protein analysis will be performed on blood samples collected from the mice 4 to 12-hours after landing. Similarly blood will be collected from control animals maintained on the Earth. The studies planned include:
    - Plasma analysis by enzyme linked immunosorbent assay (ELISA) for bone resorption markers (hydroxyproline, pyridinoline, C-telopeptide, calcium, phosphorus) and bone formation markers (type-I procollagen propeptides, bone alkaline phosphatase, osteocalcin).
    - Ribonucleic acid (RNA) analysis by reverse transcription polymerase chain reaction (RT-PCR) for the expression of bone osteogenic markers (ALP, cbfa1, osterix, osteopontin, bone sialoprotein) and for the expression of bone osteoclastic markers (the osteoclast specific alfa-v/beta-3 integrin and cathepsin K as well as calcitonin receptors will be performed on the RNA extracted from bones.
    - A high-density DNA (deoxyribonucleic acid) microarray will be performed to determine the molecular signature of bone cells in mechanical signal transmission and osteogenic differentiation in all its complexity, in this study, we will take advantage of the powerful method, Affymetrix.
    - Total RNA isolated from mice will be synthesized into double-stranded complemetary DNA (cDNA), followed by in vitro transcription to synthesize biotin-labeled cRNA probes.

This research is also expected to contribute data to the current body of research on microgravity effects on the skeletal, cardiovascular, and immune systems, liver and kidney function as well as other physiological systems through a tissue sharing program. Every effort will be made to harvest as many different samples and types of tissue from the mice as possible for other mission specific biomedical research. Positive results from this research may advance our understanding of mechanistic changes that occur in various physiological systems after exposure to microgravity and support overall efforts to reduce health risks to crewmembers. The investigations resulting from the MDS tissue sharing program are as follows:

- A transgenic approach to space osteoporosis
  Ranieri Cancedda, University of Genova, Liguria, Italy
  Tissue: Bone, Blood

  Investigate the effects of microgravity on transgenic (inbred mice) as a tool to study genetic mechanisms underlying bone mass pathophysiology (study of the disturbance of normal mechanical, physical, and biochemical functions caused by a disease). The project is based on the rationale that mice with an increased bone density are likely to be better protected from osteoporosis, when their phenotype is a direct effect of gene(s) involved in skeletogenous (process to produce the sleleton).

- Akt-FoxO signaling and protein degradation pathways during muscle atrophy induced by space flight
  Stefano Schiaffino, University of Padova, Padua, Italy
  Tissue: Anterior tibialis, Gastrocnemius and other muscles

  Muscle wasting occurs in many conditions such as disuse, fasting, cancer, diabetes and renal failure. Space flight is known to cause muscle atrophy. However, the activity of signaling pathways during space flights has never been explored. We will investigate the role of Akt-FoxO signaling pathway as the main cause of muscle loss during space flight.

- Study of the IGF-1 system in mice subjected to spaceflight
  Antonio Musaro, University of Rome La Sapienza, Rome Italy
  Tissue: Soleus, Extensor digitorum longus, Anterior tibialis

  Investigate whether the IGF-1 signaling pathway is affected in the skeletal muscle of mice subjected to space flight. In particular, soon after the mice return to the Earth, the different muscle

will be isolated and immediately frozen in liquid nitrogen and then stored at -70 degrees C until analysis. The gene and protein expression levels of muscle IGF-1, IGF-1R will be assessed in all muscle biopsies and correlated with histological analysis. This analysis will allow correlation to the expression of mIGF-1 as a function of weight loss. This study will also evaluate whether space flight affects specific signal transduction pathways that mediate the IGF-1 actions, such as PI3-Kinase/Akt, MAPK, calcineurin. This study will also determine the potential signal transduction pathways associated with muscle atrophy such as the ubiquitin ligase, atrogin-1/MAFbx, and Foxo. The results obtained will provide useful data to assess the status of IGF-1 pathway in the muscle of mice subjected to space flight; design specific therapeutic tools to counteract muscle atrophy associated to space flight; reduce muscle atrophy in future space explorers.

- Effects of microgravity on ion channel function and expression in mouse skeletal muscle: role in disuse-induced muscle atrophy and phenotype transition, and potential targets for therapeutic intervention
  Diana Conte Camerino, University of Bari, Bari, Italy
  Tissue: Soleus, Extensor digitorum longus, Anterior tibialis, Urine filter

  Using the HU model of simulated microgravity, it appeared that ion channel expression/function is changed by muscle disuse in relation to muscle phenotype transition and/or muscle atrophy, thereby contributing to muscle adaptation/alteration and constituting possible therapeutic targets. The opportunity offered by the MDS facility to study ion channel changes occurring during actual microgravity is very important for two main reasons. First, it is critical to verify that the effects observed with the HU model occur during space flight, in order to further validate the HU mouse as a valuable model of simulated microgravity. Second, the MDS facility will offer a huge opportunity to test drugs acting on sarcolemma ion channels as potential countermeasures against the muscle alteration induced by microgravity, and more generally by Earth conditions such as muscle disuse/immobilization, inherited and acquired muscle dystrophies, or ageing.

- Effects of space flight on erythrocytes and oxidative stress of rodents
  Angela Maria Rizzo, University of Milano, Milan, Italy
  Tissue: Blood

  Erythrocyte and hemoglobin loss has been continuously observed during space missions; these observations have been summarized as “space anemia”. Many studies have demonstrated that erythrocytes exposed to microgravity whether in vivo or in vitro, have a modified rheology and undergo greater hemolysis. We can suppose that microgravity together with space radiation causes variations of cellular shape, plasma membrane composition, and peroxidative stress, that can be responsible of space anemia. The availability of rodents blood and tissues through a biospecimen sharing plan is a good opportunity to investigate the in vivo effects of space environment on erythrocytes, androgens levels and oxidative stress. The aim of our project is to analyze red blood cell membrane composition and to determine the oxidative stress that these animals and their erythrocytes have undergone.

- Endocrine determinants of rodent musculo-skeletal ageing phenomena in space
  Felice Strollo, Instituto Nazionale Riposo e Cura Anziani (INRCA), Rome, Italy
  Tissue: Gonads, Hypophysis, Stomach, Urine filter

  Microgravity causes osteoporosis by an ageing-like mechanism in males and females. In fact, impaired osteogenesis might contribute to it more than enhanced osteolysis, as it happens with ageing. A parallel decrease in muscle mass occurs in space. The aim of this study is to try and go deeper into the overall underlying endocrine-related mechanisms of these phenomena by correlating brain and gonadal function changes with some drivers of metabolic adaptation potentially involved in such changes, including visceral adiposity and circadian rhythm.

- Mouse behavioural observation of mouse under microgravity condition ethogram definition and neurobiological correlates
  Daniela Santucci, Istituto Superiore di Sanita, Rome, Italy
  Tissue: Brain, Adrenal Glands, Tongue

  The aim of the proposed research is the study of role of gravitational environment in mammalian neurobehavioral response. Increasing evidence from both ground-based and space research indicate that nervous system is potentially affected by exposure to hyper/microgravity. We intend to evaluate changes in neurochemical, neuromorphological, hormonal, and behavioral parameters during and following exposure to space flight in mice. In particular, video recorded data obtained by the OSS available on the MDS facility during the experiment will be analyzed in order to finely define the behavioral repertoire (ethogram) of the mice exposed to space environment. Moreover, neurobiological correlates known to be involved in the responses to stress, such as blood or tissue levels of NGF, BDNF, interleukin, and relative receptors, will be evaluated in brain, adrenal glands, tongue and limbs.

- Role of stem cells in cardiac muscle deconditioning in microgravity
  Paolo Di Nardo, University of Rome Tor Vergata, Rome, Italy
  Tissue: Myocardium, Diaphragm

  It has been demonstrated that adult cardiomyocytes can be progressively substituted within the myocardium by newly formed contractile cells originated from stem cells resident in the heart and/or recruited from the blood stream, either in the form of the endogenous cells or following systemic infusion from a donor. This implies that, in microgravity, muscle atrophy could be ascribed, among other factors, to an impaired stem cell/cardiomyocyte turnover. Therefore, the present investigation is aimed at evaluating whether microgravity could modify stem cell activation within the mammalian myocardium. To this end, in a first step, the number and molecular and biochemical features of stem cells embedded in the myocardium of mice exposed to microgravity will be assessed.

- Lungs genomics in mice chronically exposed to microgravity
  Giuseppe Miserocchi, University of Milano, Milan, Italy
  Tissue: Lungs

  The Mice Drawer System (MDS) offers the opportunity to expose mice to long-duration microgravity. This study will evaluate the functional conditions of the lungs after chronic microgravity exposure. This research will be performed based on previous studies on extravascular matrix in experimental interstitial lung edema. This study will develop high resolution morphometry of the lungs; perform gene expression analysis of various pro-inflammatory cytokines and possibly whole transcriptome analysis using microarray; estimate signalling in endothelial and epithelial cells; evaluate the modifications induced on the interstitial macromolecular structure of the extracellular matrix. The integration of data from these four study lines should allow a thorough evaluation of the impact of chronic microgravity exposure on the respiratory function.

- Effect of real microgravity on the expression of proteins involved in the rat intestinal transit
  Proto Pippia, Universiy of Sassari, Sassari, Italy
  Tissue: Stomach and Intestine

  The modification or the loss of the gravitational force vector strongly affects many physiological functions as a result of biological process modifications. Many space missions have shown that prolonged exposure of humans to extended weightlessness may seriously affect their health. The modifications of physiological parameters seem to be a direct consequence of changes in cellular activities, as well as protein expression in many processes involving the regulation of cell growth, metabolism, signal transduction and transcription, apoptosis and tumor suppression. Numerous studies have revealed changes in gastrointestinal secretion, motility, evacuation and absorption in

humans and animals after space missions: among biological alterations, low gravity generates modification of gastrointestinal function as enzyme activity, intestinal mucosa integrity, colonic microflora, and liver activity. The aim of the study is to determine whether real microgravity influence the expression of enzymes involved in the intestinal transit and gastrointestinal homeostasis as the inducibile isoform of nitric oxide synthase (iNOS), ciclooxygenase (COX-1 and COX-2), ICAM-1 and heat shock proteins 70 (HSP 70) and 90 (HSP 90).

- Effects of Microgravity on heart mass and Extracellular Matrix
  Michael D. Delp, Ph.D., University of Florida, Gainesville, FL
  Tissue: Heart

  It is hypothesized that microgravity will induce cardiac atrophy in the flight animal. Total heart mass, as well as right ventricular, left ventricular and septal mass will be measured and compared to that of ground-based vivarium control and animal enclosure module (AEM) control mice. To determine whether microgravity alters cardiac extracellular matrix protein concentration and composition. It is hypothesized that microgravity will decrease total collagen content in the right ventricle, left ventricle and septum; alter the collagen composition of the heart toward the isoform that would favor increased cardiac compliance, i.e., less type I collagen and more type III collagen, and/or decrease the cross-liking among collagen fibers.

- The effect of spaceflight on the immune system and stress response in osteoblast stimulating factor-1 transgenic mice
  Yufang Shi, Ph.D., University of Medicine and Dentistry of New Jersey, Newark, NJ
  Tissue: Thymus, spleen and serum

  Using the mouse hindlimb suspension model, we have found that mice subjected to this condition have significant reductions in lymphocyte numbers, which occurs through apoptosis. These mice also exhibited significant increases in serum levels of haptoglobin and corticosteroid. Increased serum haptoglobin has also been observed in astronauts during space flight, and it is currently being evaluated as a marker for stress levels. Recently, we found that mice deficient in osteopontin (OPN) are resistant to hindlimb unloading-induced increases in corticosteroids. Therefore, we would like to verify these observations in mice flown in space. Since osteoblast stimulating factor-1 (OSF1) has been shown to be an important cell survival factor, we believe that overexpression of OSF1 may affect the survival of lymphocytes. In addition, with the increased bone formation in OSF1 transgenic mice, it is possible that there will be less OPN released from bone under conditions of microgravity during space flight, thus reducing corticosteroid production. Therefore, we will examine the extent of depletion of lymphocytes, and the changes in haptoglobin and corticosteroid levels in wild type and OSF1-transgenic mice immediately after space flight.

- Cellular/molecular causes of skeletal deterioration
  Ted A. Bateman, Ph.D., Clemson University, Clemson, SC
  Tissue: Long bones, Spine

  We would analyze skeletal tissue by assays similar to those used for examining bones from mice flown on CBTM-01 and CBTM-02 payloads. This includes 1) microcomputed tomography (microCT) of both trabecular and cortical bone from multiple sites. As a non-destructive test microCT can proceed and even direct future analysis such as histology, quantitative histomorphometry, mechanical testing, or material property studies. 2) mechanical testing of the femur diaphysis in three- (or four-) point bending. 3) compositional analysis of mineral and organic constituents (this can be performed on non-traditional skeletal tissue like ribs). 4) histology and histomorphometry of decalcified (paraffin and glycol methacrylate techniques) or undecalcified section. 5) Immunohistochemistry of decalcified embedded sections for apoptosis, macrophage activation, inflammation, and osteoclast activation proteins with an emphasis on the RANK/RANKL/OPG pathway. 6) ELISA/CBA analysis of serum for bone formation, bone resorption and inflammatory markers.

- Effects of long-duration spaceflight on the circadian and metabolic systems of mice
  Charles A. Fuller, University of California - Davis, Davis, CA
  Tissue: Eyes, Liver Epididymal fat pad, Brain, Plasma

  Circadian rhythms and body mass regulation/energy metabolism are critical homeostatic systems for the health and well being of organisms. Further, these systems have been demonstrated to be influenced by altered gravity, including space flight. This program is requesting tissues and data to help understand the effects of long-duration space flight on the regulation of these systems. The hypotheses we propose to test are:
    - Mice exposed to 100 days of microgravity will, compared to ground controls, demonstrate altered retinal and hypothalamic morphology, circadian clock gene activity, and reduced sensitivity to light exposure, the primary environmental stimulus for the circadian system.
    - Mice exposed to 100 days of microgravity will, compared to ground controls, demonstrate increased body and fat mass, decreased food intake, altered levels of hypothalamic neuropeptides related to energy balance, and liver function will be shifted to support fat storage.

- Effects of space flight on genes/proteins ex in brain/muscle
  Yoshinobu Ohira, Osaka University
  Tissue: Brain, Muscle, Plasma, Testis

  This experiment will be performed to investigate the adaptation of brain, adductor longus muscle, testis, and blood plasma of rats to gravitational unloading by actual spaceflight and/or simulation model, hindlimb suspension. The major parameters to be analyzed are expression of genes and proteins in various regions of brain and adductor longus muscle and hormones in blood plasma. As for the adductor longus muscle, histochemical analyses, including the size and number of myonuclei and satellite cells, DNA content and number of nucleoli in each myonucleus, cross-sectional area, and length of fibers and specific gene expression, such as heat shock protein, will be also analyzed in longitudinal single fibers and muscle cross-sections. In the whole homogenates of half of the muscle, cut longitudinally, expression of myosin heavy chain (MHC) will be analyzed. Phosphorylation of the ribosomal protein S6 and 27 kD heat shock protein will be also measured to estimate the rate of protein synthesis. As for the estimation of protein degradation, ubiquitination of MHC will be determined. Further, the number of spermatozoon in testis, which is closely associated with testosterone level, will be also measured, since it was suggested that hindlimb suspension of adult male mice caused a decrease in plasma testosterone, which may play some role(s) in the regulation of muscle mass.

- Responses of cell body size and oxidative enzyme activity in motoneurons of the mouse spinal cord following space flight
  Ishihara Akihiko, Kyoto University
  Tissue: Spinal cord

  The major research objective in this study is to compare changes in cell body size and oxidative enzyme activity of motoneurons at the cervical and lumbar segments in the mouse spinal cord following space flight. This study will observe in microgravity a decreased oxidative enzyme activity of motoneurons at the lumbar, but not at the cervical, segment in the mouse spinal cord; no change in cell body size of motoneurons at the cervical or lumbar segment in the mouse spinal cord.

- Effects of microgravity on expression and localization of vascular myocyte calcium release channels and endothelial NOS
  Morel, Centre National de la Recherche Scientifique, Toulouse, France
  Tissue: Brain

  In this project we propose to investigate the effects of microgravity on expression and localization of vascular myocyte calcium release channels and endothelial NOS. Cardiovascular

deconditioning in microgravity may be mediated through adaptation of postganglionic adrenergic neurons and adrenoreceptors. This process, may in turn be modulated by changes in caloric intake.

- Microgravity effects on skeletal muscles
  Dieter Blottner, Ph.D., Charite Campus Benjamin Franklin, Berlin, Germany
  Tissue: Muscles

  In this project we propose to investigate the NOS /NO pathway expression in mouse hind limb skeletal muscle of the MDS mice and to monitor atrophy and selective proteolysis in skeletal muscle myofibers 1 and 2 of the MDS mice. We expect to confirm that the NOS/NO pathway will be affected (i.e., reduced expression, myofiber type specific expression?) by real space flight, and that microgravity-induced muscle atrophy might be monitored by proteolysis biomarkers MuRF1 in slow and fast myofibers of weight bearing or non-weight bearing hind limb muscles in mice. The results may be used to further understand the molecular and cellular adaptation processes to microgravity in vertebrate skeletal muscle. In addition, reliable biomarkers may be helpful to develop effective countermeasure protocols to prevent dramatic muscle atrophy and to ensure performance control for humans in space flight.

- Microgravity-induced skin atrophy
  Betty Nusgens, Ph.D., University of Liege, Wallonia, Belgium
  Tissue: Skin

  We have previously demonstrated that fibroblasts from the dermis sense and react to mechanical forces issued from the surrounding extracellular matrix. Conversely, fibroblasts are able to remodel their environment by a dynamic process of synthesis and degradation. Fibroblasts and cells of the vascular network also react to soluble mediators secreted by the keratinocytes such as IL-1, IL-6, VEGF. Skin fibroblasts upon relaxation of mechanical tension adopt a catabolic phenotype and produce significant amount of IL-1 and IL-6, of various matrix metalloproteinases (MMP) while the collagen synthesis is reduced. In microgravity, we have shown that the expression of MMP-1 and IL-6 by dermal fibroblasts is increased indicating that cell might interpret microgravity as a mechanical relaxation. This concept is supported by a reduction of the actin stress fibers and focal adhesions in fibroblasts in microgravity. The expression of IL-1, IL-6 and MMP-1 is under the control of signaling molecules regulating the cytoskeleton dynamics, such as Cdc42, a member of the RhoGTPases family. Another member, Rac1, modulates keratinocytes differentiation and fibroblasts proliferation. Altogether, microgravity might alter metabolic equilibrium of the skin and perhaps of other soft connective tissues such as tendons or interstitial matrix of internal organs.

The MDS hardware is used for experiments which study the influence of microgravity on rodent physiology and anatomy. The MDS is a self-contained habitat that provides its occupants with living space, food, water, ventilation, and lighting. Its internal waste management system guarantees that animals are isolated from their waste by-products and that these by-products and food crumbs do not escape into the ISS where the crew is living and working.

MDS consists in one external container (dimensions 421 x 480 x 516 mm) in which several subsystems are integrated:

- The Mice Chamber (MC) is divided into two sections. Each section is internally subdivided in three equal cages each one of 116 x 98 mm (floor area) and 85 mm height. A total of 6 cages are available each one providing the following basic services, food bar dispenser, drinking valve and a camera for observation.

- The Liquid Handling Subsystem (LHS) delivers water to each cage independently through the drinking valve. Water is delivered *ad libitum* (free feeding); the LHS includes a water tank of 0.5-liters that, once empty, can be re-filled on orbit.

- The Food Delivery Subsystem (FDS) supplies each cage independently with food bars each one of 149 x 73 x 7.5 mm and a mass of about 90 grams. Once finished, new food bars can be re-supplied through six openings located in the MDS Front Panel.

- The Air Conditioning Subsystem (ACS) generates a continuous air flow of 0.1 m/s through the cages which is used to perform air renewal and remove waste products. About 5 percent of the total air is exchanged with ISS cabin in order to eject generated carbon dioxide and inject consumed oxygen (open loop). HEPA In and Out filters are used to prevent possible microbiological contamination between the ISS cabin and MDS. Removed waste products (urine, feces, food debris etc.) are collected within waste filters located below each MC section. Active control of air temperature is from 25 to 26 degrees C. Passive control of air humidity by means of desiccant is in the range from 40 to 70 percent.

- The Illumination Subsystem (ILS) implements light/dark cycles programmable in steps of 5-minutes starting from nominal 12-hour light/12-hour dark. Light intensity is programmable from 0 to 40 lux in steps of 10 lux. Diffuse light is provided during light periods (no bright spots). Infrared light sources are available for mice observation during dark periods.

- The Observation Subsystem (OSS) permits the observation of mice through the use of 6 video cameras (one/cage). Mice observation is possible also during dark periods. Video data are transmitted to ground in order to permit a near real-time verification of mice health status and behavior.

- The Control Unit (CU) permits the automatic execution of the tasks necessary to perform the experiment according to a command table previously loaded inside its internal memory.

**Project Type:** Payload

**Images and Captions:**


MDS integrated inside the Double Payload Container. Image provided courtesy of ASI.


Lateral side view of MDS, with waste filter partially removed. Image courtesy of ASI.

**Operations Location:** ISS Inflight

**Brief Research Operations:**

- Operations consist of daily status checks by the crew to assess the health and status of the rodents.
- During daily status checks water levels will be checked and filled as needed.
- Every 20-days the food bar and waste filters for each mice chamber will be replaced.

**Operational Requirements:** For the MDS investigation three groups of mice will be utilized. One group of mice will be sent to the ISS housed in an MDS enclosure. Two control groups of mice will remain on Earth in Genoa, Italy, one in a MDS enclosure the other in standard rodent housing.

Onboard the ISS, MDS is relatively self-sufficient; a crewmember will check the health status of the rodents on a daily basis, by assessing them through the viewing window. Water levels will be assessed by the crew daily and refilled as needed. Replacement of the food bars and replacement of the waste filters will be conducted inflight by crewmembers every 20-days or as needed. After landing, the MDS will be returned to the investigator for extensive analysis.

**Operational Protocols:** Once the rodents are in space, a crewmember will check the health status of the rodents on a daily basis, by assessing them through the viewing window on each MDS. Water levels on the water boxes will be assessed by the crew daily and refilled as needed. Replacement of the food bars and replacement of the waste filters will be conducted inflight by crewmembers every 20-days.

**Review Cycle Status:** PI Reviewed

**Category:** Biological Sciences in Microgravity

**Sub-Category:** Animal Biology

**Space Applications:** Astronauts suffer from a significant loss of bone mass during space flight, the ISS Medical Project office has developed some countermeasures to hinder the rapid loss of bone mass. Despite these countermeasures bone mass loss continues to be a problem for astronauts. Finding additional countermeasures will increase the overall health of astronauts on long duration missions.

**Earth Applications:** Microgravity is considered by the scientific community as a accelerated model for studying terrestrial osteoporosis. Results obtained in this space experiment will facilitate the understanding of genetic elements that protect people from osteoporosis. The targeted users are astronauts after a long-term space mission, elderly people especially post-menopause women, and patients after long-time immobilization.

Osteoporosis is a major public health threat for an estimated 44 million people worldwide. Space flight induces a systematic, accelerated bone loss, hence, this investigation will provide a good model for osteoporosis and potential treatments. It will provide scientists further insight into skeletal loss from microgravity and the role of OPG as a potential treatment for osteoporosis.

**Manifest Status:** New

**Supporting Organization:** Space Operations Mission Directorate - Italian Space Agency (SOMD - ASI)

**Previous Missions:** This is the first expedition for MDS, although a similar investigation CBTM flew on STS-108/UF-1.

**Web Sites:**
Italian Mice to Head Into Space

**Related Payload(s):** CBTM

**Last Update:** 10/01/2008