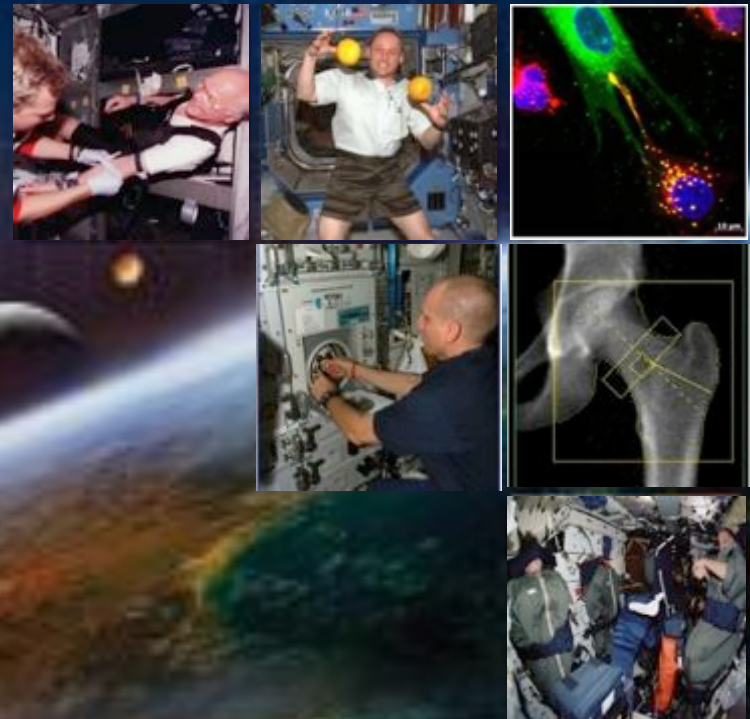




Human Research Program

The Twins Study: NASA's First Foray into 21st Century Omics Research

AsMA
14 May 2015



Craig E. Kundrot, Ph.D.
Deputy Chief Scientist, HRP
SA2/NASA JSC



ISS Crew: Scott Kelly, Mikhail Kornienko Sign On For One-Year Mission

Posted: 11/26/2012 9:28 am EST Updated: 11/26/2012 9:46 am EST

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FOLLOW: Video, Scott Kelly, International Space Station, Top News, No Words, Mikhail Kornienko, International Space Station, Science News

By: Tariq Malik

Published: 11/26/2012 09:27 AM EST on SPACE.com

A veteran NASA space commander and Russian cosmonaut have signed on for the ultimate space voyage: a yearlong trip on the International Space Station.

American astronaut Scott Kelly and Russian cosmonaut Mikhail Kornienko will launch on the one-year space station flight in spring 2015 and return to Earth in spring 2016, NASA officials announced today (Nov. 26). They will begin their mission training in early 2013.

The mission will help NASA understand how the human body adapts to extremely long space missions, such as voyages around the moon, to an asteroid and ultimately to Mars, NASA officials said.

Astronaut Scott Kelly Preparing for Unprecedented One Year in Space; Mission to Experiment on His Bone Mass, Vision, Immune System

By Leah Feller Staff Writer, Dec 07, 2012 05:00 PM EST

0 Comments 12 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78 79 80 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100 101 102 103 104 105 106 107 108 109 110 111 112 113 114 115 116 117 118 119 120 121 122 123 124 125 126 127 128 129 130 131 132 133 134 135 136 137 138 139 140 141 142 143 144 145 146 147 148 149 150 151 152 153 154 155 156 157 158 159 160 161 162 163 164 165 166 167 168 169 170 171 172 173 174 175 176 177 178 179 180 181 182 183 184 185 186 187 188 189 190 191 192 193 194 195 196 197 198 199 200 201 202 203 204 205 206 207 208 209 210 211 212 213 214 215 216 217 218 219 220 221 222 223 224 225 226 227 228 229 230 231 232 233 234 235 236 237 238 239 240 241 242 243 244 245 246 247 248 249 250 251 252 253 254 255 256 257 258 259 260 261 262 263 264 265 266 267 268 269 270 271 272 273 274 275 276 277 278 279 280 281 282 283 284 285 286 287 288 289 290 291 292 293 294 295 296 297 298 299 300 301 302 303 304 305 306 307 308 309 310 311 312 313 314 315 316 317 318 319 320 321 322 323 324 325 326 327 328 329 330 331 332 333 334 335 336 337 338 339 340 341 342 343 344 345 346 347 348 349 350 351 352 353 354 355 356 357 358 359 360 361 362 363 364 365 366 367 368 369 370 371 372 373 374 375 376 377 378 379 380 381 382 383 384 385 386 387 388 389 390 391 392 393 394 395 396 397 398 399 400 401 402 403 404 405 406 407 408 409 410 411 412 413 414 415 416 417 418 419 420 421 422 423 424 425 426 427 428 429 430 431 432 433 434 435 436 437 438 439 440 441 442 443 444 445 446 447 448 449 450 451 452 453 454 455 456 457 458 459 460 461 462 463 464 465 466 467 468 469 470 471 472 473 474 475 476 477 478 479 480 481 482 483 484 485 486 487 488 489 490 491 492 493 494 495 496 497 498 499 500 501 502 503 504 505 506 507 508 509 510 511 512 513 514 515 516 517 518 519 520 521 522 523 524 525 526 527 528 529 530 531 532 533 534 535 536 537 538 539 540 541 542 543 544 545 546 547 548 549 550 551 552 553 554 555 556 557 558 559 560 561 562 563 564 565 566 567 568 569 570 571 572 573 574 575 576 577 578 579 580 581 582 583 584 585 586 587 588 589 590 591 592 593 594 595 596 597 598 599 600 601 602 603 604 605 606 607 608 609 610 611 612 613 614 615 616 617 618 619 620 621 622 623 624 625 626 627 628 629 630 631 632 633 634 635 636 637 638 639 640 641 642 643 644 645 646 647 648 649 650 651 652 653 654 655 656 657 658 659 660 661 662 663 664 665 666 667 668 669 670 671 672 673 674 675 676 677 678 679 680 681 682 683 684 685 686 687 688 689 690 691 692 693 694 695 696 697 698 699 700 701 702 703 704 705 706 707 708 709 710 711 712 713 714 715 716 717 718 719 720 721 722 723 724 725 726 727 728 729 730 731 732 733 734 735 736 737 738 739 740 741 742 743 744 745 746 747 748 749 750 751 752 753 754 755 756 757 758 759 760 761 762 763 764 765 766 767 768 769 770 771 772 773 774 775 776 777 778 779 780 781 782 783 784 785 786 787 788 789 790 791 792 793 794 795 796 797 798 799 800 801 802 803 804 805 806 807 808 809 810 811 812 813 814 815 816 817 818 819 820 821 822 823 824 825 826 827 828 829 830 831 832 833 834 835 836 837 838 839 840 841 842 843 844 845 846 847 848 849 850 851 852 853 854 855 856 857 858 859 860 861 862 863 864 865 866 867 868 869 870 871 872 873 874 875 876 877 878 879 880 881 882 883 884 885 886 887 888 889 890 891 892 893 894 895 896 897 898 899 900 901 902 903 904 905 906 907 908 909 910 911 912 913 914 915 916 917 918 919 920 921 922 923 924 925 926 927 928 929 930 931 932 933 934 935 936 937 938 939 940 941 942 943 944 945 946 947 948 949 950 951 952 953 954 955 956 957 958 959 960 961 962 963 964 965 966 967 968 969 970 971 972 973 974 975 976 977 978 979 980 981 982 983 984 985 986 987 988 989 990 991 992 993 994 995 996 997 998 999 1000



A Chance in a Lifetime Opportunity for a Twins Study





Great Value in n = 1 Omics Study Over Time

Resource

Cell

Personal Omics Profiling Reveals Dynamic Molecular and Medical Phenotypes

Rui Shen,¹ George L. Miao,^{1,2} Jennifer Li-Ping Han,^{1,3} Li-Ping Han,^{1,4} Hugo Yik, Liliang Li,^{1,5} Wang Chen,^{1,6} Baoxi Min,¹ Ronald J. Harpazov,¹ Sheng Huo,^{1,7} Richard E. Green,¹ Wang Zhang,¹ Michael A. Clark,¹ Benjamin Vukobratovic,¹ Susanto Kusumawardana,^{1,8} Mouni Choudhury,¹ and Y. Shirley¹
 Saundharam,^{1,9} Rajan Moolanagar,¹ David Shuman,¹ Gina Kuchel,¹ Fred Luchessa,¹ Kaitlyn Barragoie,¹ Joseph Baga,¹ Mouni Karaman,¹ Nelson Odeh,¹ Scott Eick,¹ Marco Garcia,¹ Wilhelmina M. Griffin,¹ Matthew Delgado,^{1,10} Mark A. Blainey,^{1,11} Qingyong Li,¹ Shuang Wang,¹ Shuang Wang,¹ Tom E. Klein,¹ Peter B. Admon,¹ Adam J. Butte,¹ Ross A. Hwang,¹ Mark Gerstein,^{1,12} Mark H. Nelson,¹ Hua Tang,¹ and Thomas Seydewitz¹

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Mike Snyder

SUMMARY
 Personalized medicine is expected to benefit from combining genomic information with regular monitoring of physiological states by multiple high-throughput methods. Here, we present an integrative personal omics profile (POP), an analysis that combines genomic, transcriptomic, proteomic, metabolomic, and microbiome profiles from a single individual over a 14-month period. Our POP analysis revealed various medical risks, including type 2 diabetes. It also uncovered extensive dynamic changes in diverse molecular components and biological pathways across healthy and diseased conditions. Extensive high-coverage genomic and transcriptomic data, which provide the basis of our POP, revealed extensive interatomic changes during healthy and diseased states and an unexpected RNA editing mechanism. This study demonstrates that longitudinal POP can be used to interpret healthy and diseased states by connecting genomic information with additional dynamic omics activity.

INTRODUCTION
 Personalized medicine aims to assess medical risks, monitor dynamic and static phenotypes according to the specific genetic constitution and molecular phenotype. The extent of genetic constitution and the extent of phenotypic variation are related to the overall genetic background. Research recently demonstrated that integration of genomic and clinical information is a key step. Much of the genome is difficult to explore and many complex diseases, such as diabetes, cardiovascular disease and cancer, each involve a large number of different genes and biological pathways (Shin et al., 2010; Szymanski et al., 2011; Li et al., 2015), as well as environmental conditions that are difficult to assess. As such, the combination of genetic information along with deep molecular profiles of samples will be essential for predicting, diagnosing and treating diseases as well as for understanding disease progression and prevention of disease onset (Snyder et al., 2016). Presently, healthy and diseased states are typically followed using a limited number of assays that sample a small number of markers of disease types. With the advancement of next-generation technologies, it is now possible to analyze several of 10⁷ molecular components. For example, DNA microarrays have allowed the interrogation of hundreds and thousands

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Cell

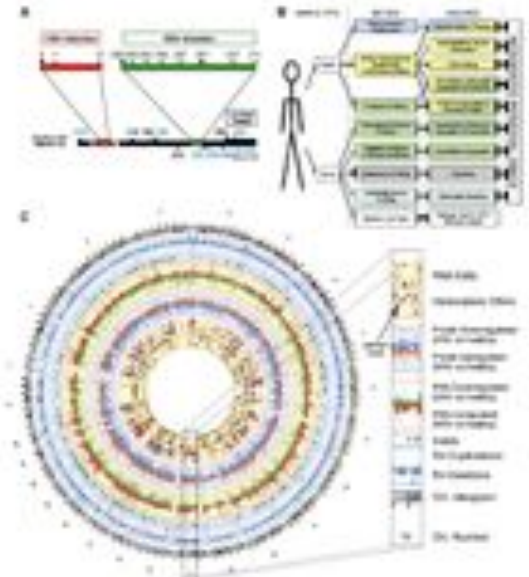
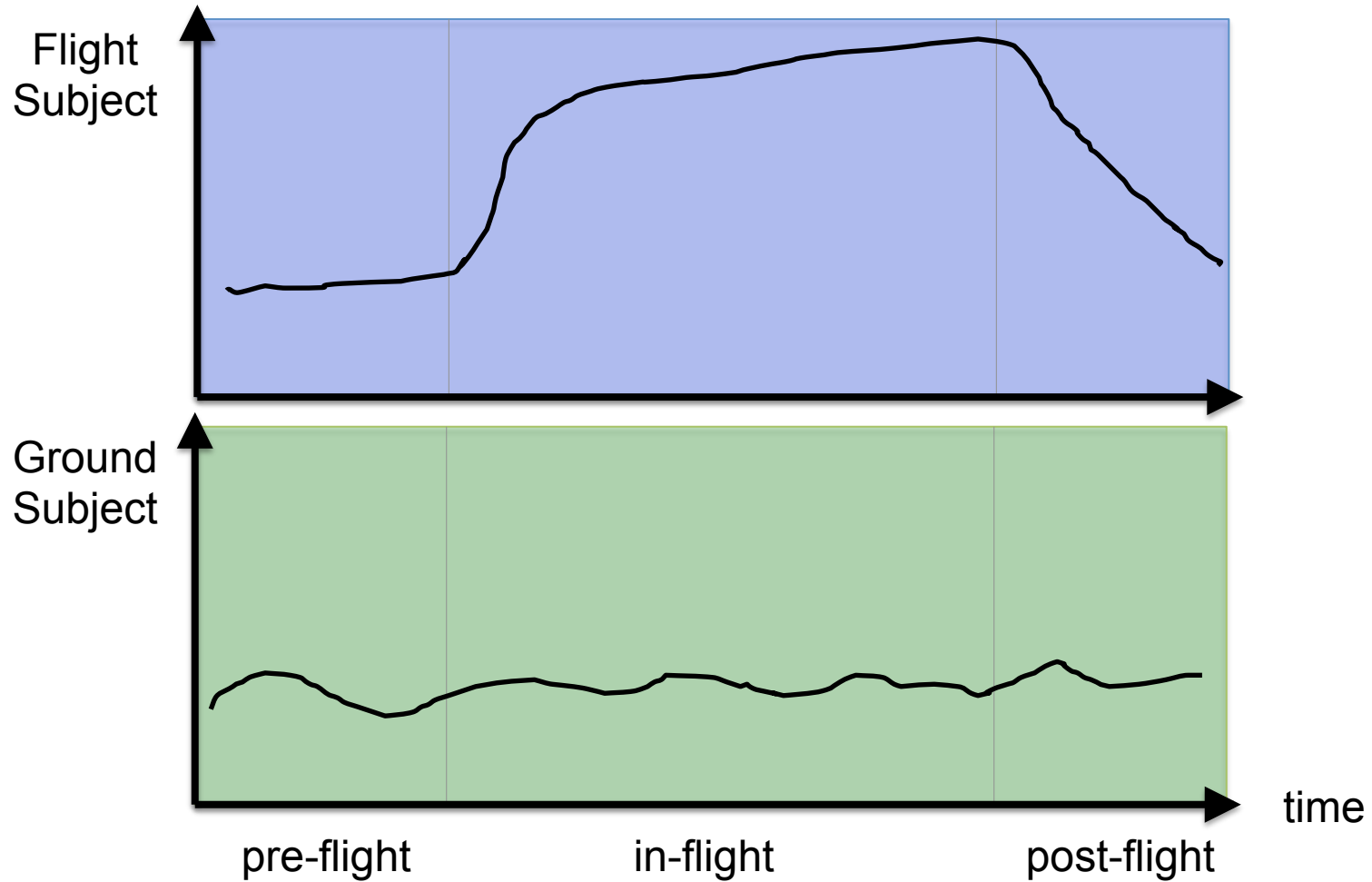


Figure 1. Omics profiles.
 (A) POP workflow. The subject is monitored over 14 months using high-throughput methods across 100 genes, RNA, proteins, metabolites, and microbiome. (B) Integration of transcriptomic and metabolomic data and the clinical data into the POP. (C) POP profiles across 14 months. The POP profiles are integrated into a single profile. The POP profiles are integrated into a single profile. The POP profiles are integrated into a single profile.

POP-based Disease Risk Evaluation
 We sought to identify those to be associated with increased susceptibility to disease (Shin et al., 2015). The list of high confidence (HCR) and middle risk (MR) genes was compared to the changes in gene expression levels (Shin et al., 2015) associated with disease onset (Table 1). We identified 17 and 4 of the HCR and MR genes, respectively, that were associated with disease onset. The list of genes was further analyzed for clinical relevance (Table 2). Disease risks are summarized in Figure 2B, and characterized by disease susceptibility. High-risk genes include (1) mutation (SNP) in the 3'UTR of the gene encoding insulin (INS), (2) a damaging mutation in POP associated with elevated plasma glucose (Muller et al., 2012), and (3) variants associated with type 2 diabetes and obesity, such as FTO.

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One Notion





National Aeronautics and Space Administration
Johnson Space Center
Human Exploration and Operations Mission Directorate
Human Research Program
Houston, TX 77058

Human Exploration Research Opportunities (HERO)

Appendix D

Differential Effects on Homozygous Twin Astronauts Associated with Differences in Exposure to Spaceflight Factors

Response Period: July 30, 2013 – September 17, 2013
Proposals Due: September 17, 2013, 5 PM Eastern Time
Estimated Selection Announcement: January 2014

Appendix D - 1

“To capitalize on this unique opportunity,

NASA’s Human Research Program (HRP) and the
National Space Biomedical Research Institute
(NSBRI) are initiating

a *pilot demonstration project focused on the use of
integrated human -omic analyses* to

better understand the biomolecular responses to

the physical,
physiological, and
environmental stressors

associated with spaceflight.”



Buccal & Saliva



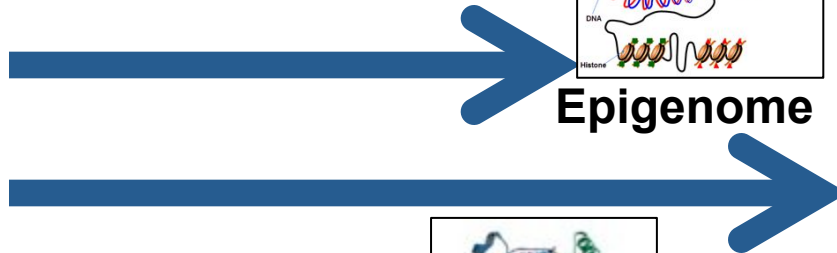
Urine



Blood

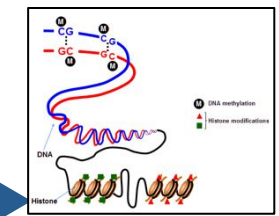


Stool

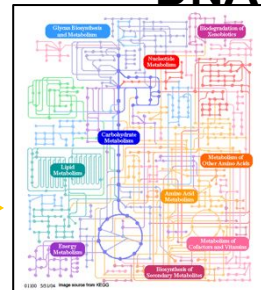


Epigenome

DNA



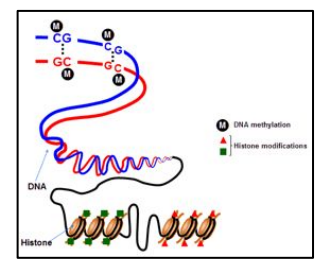
Proteins



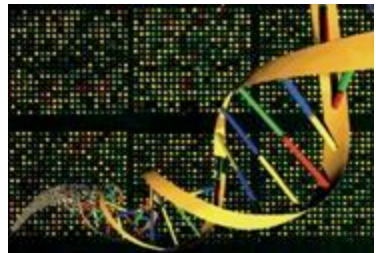
Metabolites



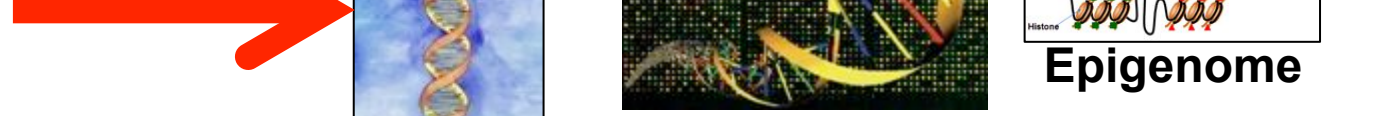
Proteins



Epigenome



RNA



DNA



Metagenome

Differential effects on Telomeres and Telomerase in Twin astronauts associated with spaceflight



Susan Bailey, Ph.D.
Colorado State Univ



Kerry George
Wyle Labs/JSC

Specific Aims

The rate at which telomeres shorten provides an informative biomarker of aging and age-related pathologies (e.g., cardiovascular disease and cancer) that captures the interplay between genetics and lifestyle factors.

We propose that for the astronauts telomere maintenance is particularly relevant, as it reflects the combined exposures (e.g., radiation) and experiences (nutritional, psychological and physical stressors) encountered during space travel.

The Twins study provides the extraordinary opportunity to control variables of individual genetic differences, susceptibilities and lifestyle factors, making differential effects observed between the twins space-flight specific.

Comparisons with unrelated astronauts (separate study), will allow evaluating role of genetics/individual susceptibilities.

Implications of Research for Space & Earth

Space: This twins study will identify space-flight specific factors that influence telomere length and telomerase activity, informative biological indicators of aging and age-related degenerative diseases (e.g., cardiovascular disease and cancer). Our mechanistic investigations will begin to establish relevant relationships and suggest potential mitigation strategies for future study and to improve astronaut overall health.

Earth: Aging and age-related diseases like cardiovascular disease and cancer are an everyday concern on earth as well, therefore this study also seeks to make comparisons with unrelated astronauts (and controls) that will serve to identify individual susceptibility factors that influence telomere length and telomerase activity. Taken together with our mechanistic studies, mitigation strategies will be improved and applicable to all.

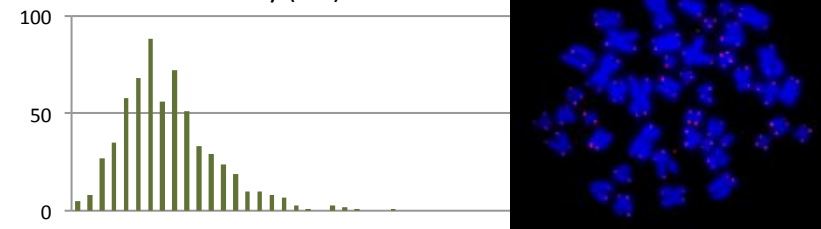
Our goal is to assess changes in telomere length and telomerase activity associated with the upcoming yearlong ISS mission in the space- and earth-bound twin astronauts.

We hypothesize that accelerated telomere shortening and elevated telomerase activity will be associated with space flight as compared to ground based control, in a duration and severity dependent manner.

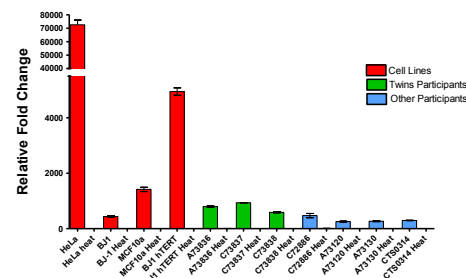
- Blood samples will be taken **pre-flight** (to establish baseline), **in-flight** (to evaluate short-term/temporary changes) and **post-flight** (to evaluate long-term/permanent changes)
- Data sharing for other endpoints will also inform this effort
- *In vitro* studies will investigate potential mechanisms (e.g., oxidative stress) and mitigation strategies (e.g., antioxidants)

Telomere length will be assessed using TELO-FISH

Florescence *in situ* Hybridization (FISH) with telomere probe on chromosomes (and interphase nuclei) is evaluated as Relative Fluorescence Intensity (RFI) distributions.



Telomerase activity will be assessed using qRT-PCR TRAP quantitative Real Time-PCR Telomere Repeat Amplification Protocol



Epigenomics



Specific Aims

Aim 1. We will measure DNA methylation and chromatin at a genome-wide level in biological samples obtained from the space traveler at quarterly intervals, pre- and post-flight, and at times of unexpected exposures such as radiation events, or spacecraft environmental contamination. We also obtain measurements of the ground-based twin.

Aim 2. We will integrate epigenomic data with exposure to spaceflight conditions, looking for exposure-linked changes, and by comparison to the ground-based twin, determine whether these are transient or long-lived effects. We will also determine whether DNA mutations arise secondarily to these epigenetic changes.



Andrew Feinberg, M.D., M.P.H., and Jason Feinberg

Sample Collection and Analysis



Blood mononuclear cells, buccal wash, at all time points

- Whole genome DNA sequencing prior to launch and post-recovery
- Whole genome bisulfite sequencing at several time points, 450K between
- ChIP-seq at all time points
- RNAseq at several time points, arrays between

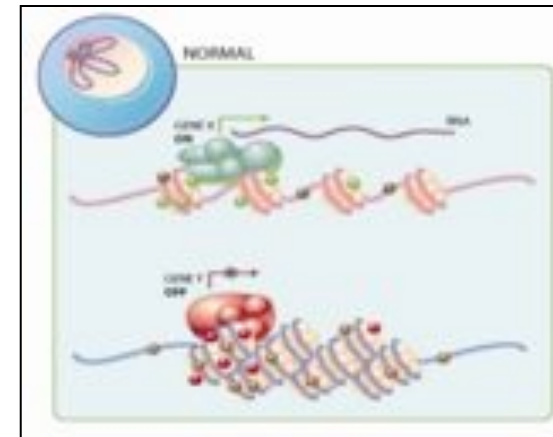
Implications of the Research for Space & Earth



Space: Identify reversible causes of genomic damage in space, e.g. radiation or toxin induced epigenomics change; quantify aging and genomic exposure.

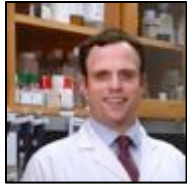


Earth: First human study of the epigenome over time in a defined/controlled environment.



- DNA methylation
- Histone modifications (>200 known)
- Chromatin factor complexes
- Chromatin structure

Landscape of DNA and RNA Methylation



Christopher Mason, Ph.D.

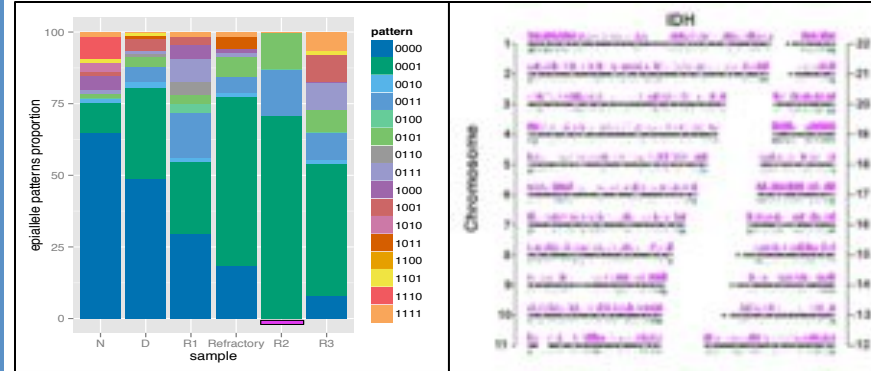


Francine Garrett-Bakelman, M.D. Ph.D.



- #1 – Genome-wide epigenetic profiles of DNA methylation changes
- #2 – A comprehensive catalog of coding and noncoding, small and large RNA
- #3 – Transcriptome-wide maps of RNA methylation sites

Δ in Epigenetics : Loci, regions, and clones



Δ in Transcriptome : Genes, Isoform, Edits, Allele, SNVs, ncRNAs, Fusions, & Methylation

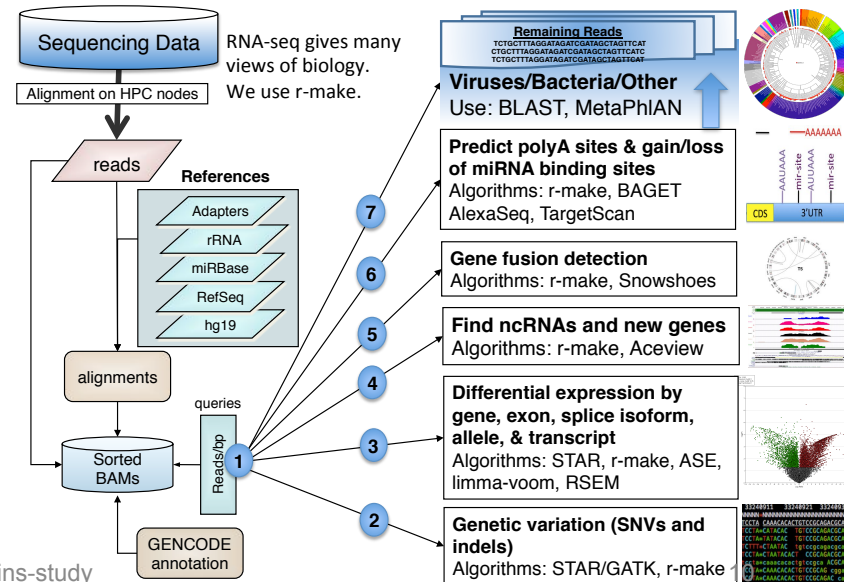
Implications of the Research for Space & Earth



Space: (1) Establish the genetic networks and expression patterns activated by space travel, (2) trace clonality of epigenetic changes, (3) examine the methylation of RNA



Earth: Aid research on aging, cancer, RNA biology, and circadian rhythm, all of which show differences at the (epi)genome & (epi)transcriptome



Biochemical Profile: Homozygous Twin control for a 12 month Space Flight Exposure



Scott M.
Smith, Ph.D.

Specific Aims

To provide a database of biochemical analyses from blood and urine samples. The analyses reflect a broad set of nutritional and physiological variables that may be altered as a result of the space flight environment (including diet, stress, weightlessness). Collecting data on the Ground twin will allow for a more direct comparison of the effects of space flight on human biochemistry and physiology.

Blood and urine collections

Preflight:

L-180, L-45, L-10

In-flight:

FD15, 30, 60, 120, 180, 240, 300, 360

Post flight:

R+0, R+30



Implications of the Research for Space & Earth



Space:

Improve understanding and time course of biochemical changes during flight and how the changes relate to diet during flight.



Earth:

Improve understanding of how diet can impact different biological systems.

Immunome studies in space



Emmanuel Mignot, MD, PhD



Stanford University

Specific Aims

- Study how long term space travel affects the immune system
- We will study how parameters of the immune system change at baseline and after a seasonal flu vaccination
- To do so, we study baseline and post flu parameters before, during and after a one year space flight

Implications of the Research for Space & Earth



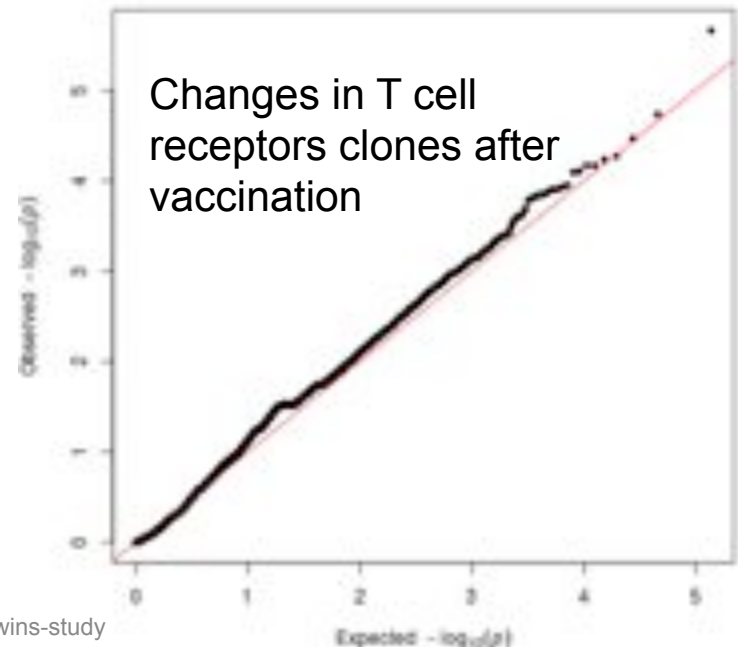
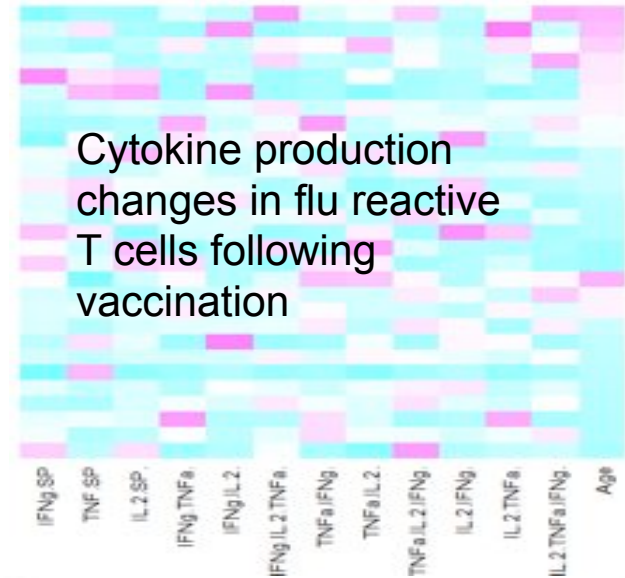
Space:

Will ensure that astronauts keep a healthy immune system during long flight, and stay protected against infections from earth when visitors are coming.

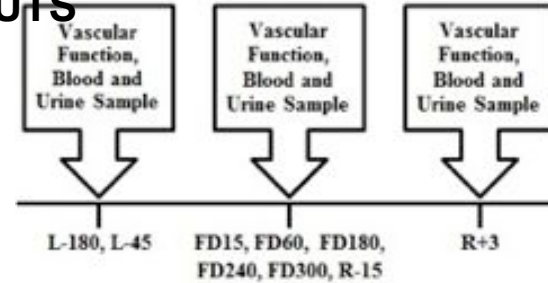
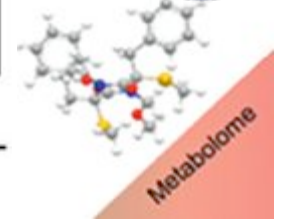


Earth:

Understand how immune response to vaccination differ in twins



METABOLOMIC AND GENOMIC MARKERS OF ATHEROSCLEROSIS IN TWIN ASTRONAUTS



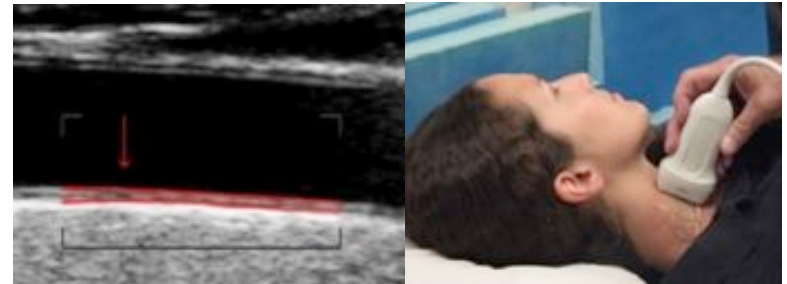
Specific Aims

- To study the effects of long-duration spaceflight on the cardiovascular system independent of genotype
- To investigate relationships between gene expression, metabolomic profiles, biomarkers in blood and urine, and arterial structure and function using the space-flown and the ground-based identical twin



Stuart Lee

Pre- and Post-flight Testing



Inflight Operations



Implications of the Research for Space & Earth

Space: Determine if the spaceflight environment perturbs genomic and metabolomic profiles and accelerates development of atherosclerosis (occupational health)

Earth: Develop novel insights of how longitudinal changes in genomic and metabolomic profiles are related to risk factors for atherosclerosis



PROTEOMIC ASSESSMENT OF FLUID SHIFTS AND ASSOCIATION WITH VISUAL IMPAIRMENTS AND INTRACRANIAL PRESSURE IN TWIN ASTRONAUTS



Brinda Rana, PhD
Mike Stenger, PhD
Vivian Hook, PhD

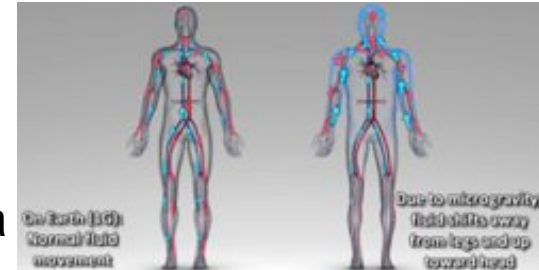
Specific Aims

To explore proteomic and genomic biomarkers underlying space flight-induced fluid shifts and visual impairment & intracranial pressure (VIIP) symptoms.

The proteome is the set of proteins produced by the genome at a given time. Proteomics captures the state of molecular and cellular processes at a specific time point.



Blood Plasma proteins



In-flight Operations



Blood Plasma collection
Ultrasound measures of fluid shifts
Intracranial Pressure
Intraocular Pressure
Ocular Structure
Blood Pressure
Heart Rate
Vascular Resistance

Implications of the Research for Space & Earth

Space: Discovery of molecular pathways involved in the evolution of spaceflight adaptations related to fluid redistribution in-flight and the etiology of visual acuity and ocular changes in-flight and post-flight.

Earth: This project has broader impact on Earth-based clinical areas such as traumatic brain injury-induced elevations of intracranial pressure, hydrocephalus, and glaucoma

Pre- and Post-flight Testing



All in-flight operations and:
Tissue hydration
MRI

Cognitive Performance in Spaceflight



Specific Aims

There are a number of environmental stressors unique to the spaceflight environment that may affect cognitive performance, which is crucial for mission success. Our main objective in the TWINS study is to investigate whether cognitive performance is affected by initial and prolonged exposure to the spaceflight environment and after return to Earth. We will use the *Cognition* test battery, which consists of 10 brief neuropsychological tests that were specifically designed for high performing astronauts. We will compare data within subjects, between twins, relative to astronauts flying 6-month missions, and relative to normative data gathered in astronauts on the ground. The cognitive data will be correlated with markers derived from biological samples taken before, during, and after the 12-month mission.



Mathias Basner, M.D., Ph.D.



Ruben C. Gur, Ph.D.

Implications of the Research for Space & Earth



Space: Exploration-type missions will require humans to spend unprecedented durations in space, yet our knowledge on the effects of prolonged exposure to the spaceflight environment is very limited. After the study, we will have an initial understanding of whether and to what extent prolonged ISS missions are associated with changes in cognitive performance, and how these relate to biologic markers.



Earth: The results have direct implication for other high performing populations exposed to stressful environments for prolonged periods of time on Earth.

	Test	Cognitive Domain	Brain Regions (from fMRI studies)	Avg. Time (Min)
	Motor Praxis (MPT)	Sensory-motor ability	Sensorimotor Cortex	0.51
	Visual Object Learning (VOLT)	Visual object learning and memory	Medial Temporal Cortex - Hippocampus	1.69
	Fractal 2-Back (F2B)	Attention and working memory	Dorsolateral prefrontal Cortex, Cingulate, Hippocampus	1.93
	Abstract Matching Task (AMT)	Abstraction and mental flexibility	Prefrontal Cortex	2.33
	Line Orientation (LOT)	Spacial orientation	Right Temporo-Parietal Cortex, Visual Cortex	2.07
	Emotion Recognition (ERT)	Emotion recognition	Cingulate Cortex, Amygdala, Hippocampus, Fusiform Face Area	2.03
	Matrix Reasoning (MRT)	Abstract reasoning	Prefrontal Cortex, Parietal Cortex, Temporal Cortex	2.09
	Digit Symbol Substitution (DSST)	Complex scanning, visual tracking, attention	Temporal Cortex, Prefrontal Cortex, Motor Cortex	1.60
	Balloon Analog Risk (BART)	Risk decision making	Orbital frontal Cortex, Amygdala, Hippocampus, Anterior Cingulate Cortex	2.39
	Psychomotor Vigilance (PVT)	Vigilant attention and psychomotor speed	Prefrontal Cortex, Motor Cortex, Visual Cortex	3.17

The Cognition Test Battery

Cognition was specifically designed for astronauts and is currently used during 6-month ISS missions and in multiple space analog environments (including Antarctica, HI-SEAS, and HERA).



The Bacteriome in the Gastrointestinal Tract

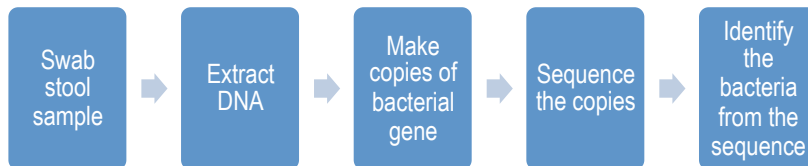


Fred Turek, Ph.D.

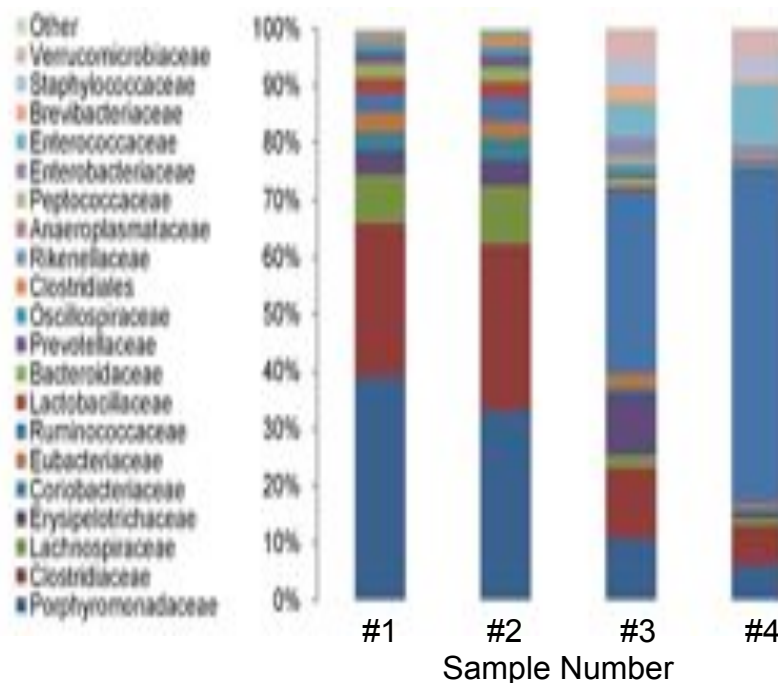
Specific Aims

The GI tract of humans is populated by a diverse “ecosystem” of micro organisms, mostly bacteria: the bacteriome. The bacteriome can help-- contributing to digestion and immune system function-- or harm-- overgrowth of some types accompanies illness or stress.

This project will examine what changes occur to the bacterial populations over a year in space, that are different from the changes over time on Earth. Are particular types of bacteria susceptible to the space environment, and if so, which types?



Classify bacteria from each sample



Relative abundance of different families of bacteria. Will there be systematic changes in the twin in space not seen in the twin on Earth?

Implications of the Research for Space & Earth



Space: Knowing how the bacteriome changes over time in space can help us make plans to protect astronauts’ health for longer-term space flights. For example, adjustments to diet could help maintain beneficial bacterial types.



Earth: Observing how the bacteriome changes in relation to health and environmental changes, (such as those studied in other Twin Projects) can provide insights into how the bacteriome may respond to challenges and contribute to the human host’s health.

Integrated Omics: Mike Snyder, Ph.D.



Michael Snyder, Ph.D.



Juliane Winkelmann, M.D.

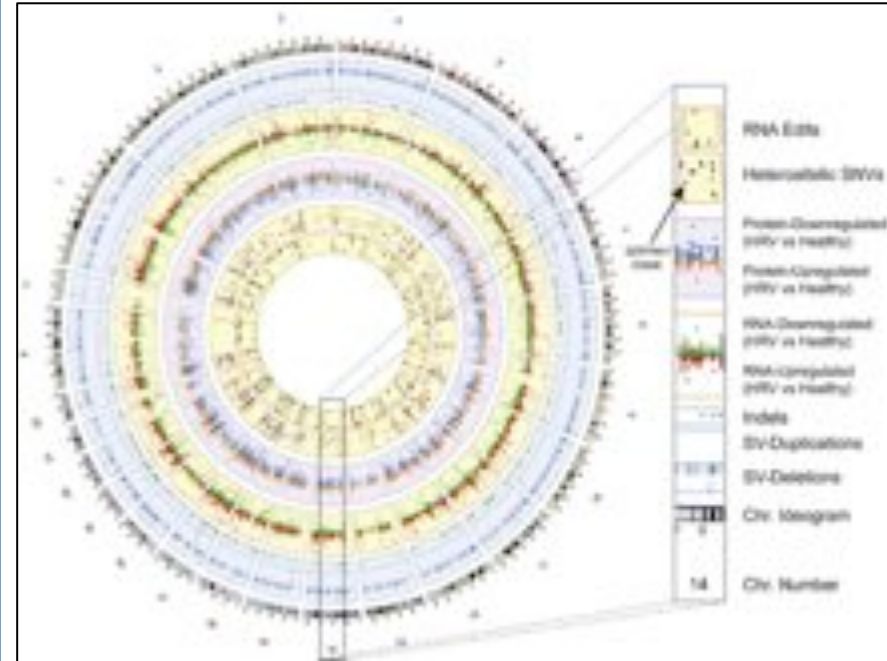
Specific Aims

Our main objective in the twin study is to perform a complete analysis of all biomedical and molecular data collected during the mission to produce the singular most comprehensive portrait of the human biophysical response to the rigors of spaceflight. We are at an unprecedented era in genomic medicine, allowing for the sensitive and precise measurement of billions of biochemical molecules, which will allow us to detect the subtlest of changes in Scott and Mark's physiology over time. By integrating these data, we can follow alterations in their cellular systems to both better understand the effects of space travel on human health, and how an astronaut's genome may contribute to his/her own unique physiologic response to microgravity.

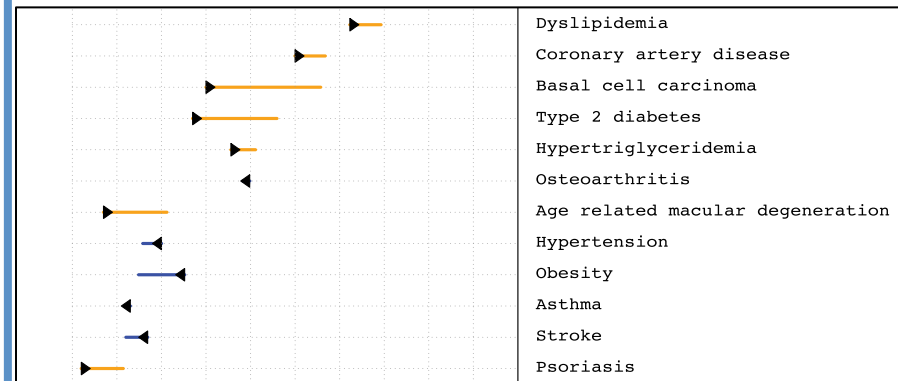
Implications of the Research for Space & Earth

Space: We will generate a detailed benchmark for how human physiology changes in space in great molecular detail. This wealth of data will be essential for any future planning of long duration space exploration missions, and provide a proof-of-principle for better monitoring and managing astronaut health.

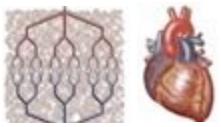
Earth: With this study, Scott and Mark Kelly will be the most thoroughly profiled twins in history, and the resultant data will offer new insights into how two siblings with nearly-identical genomes respond to different conditions.



Integrative multi-omic model



Risk-o-gram



Vasculature
Lee



Cognition
Basner



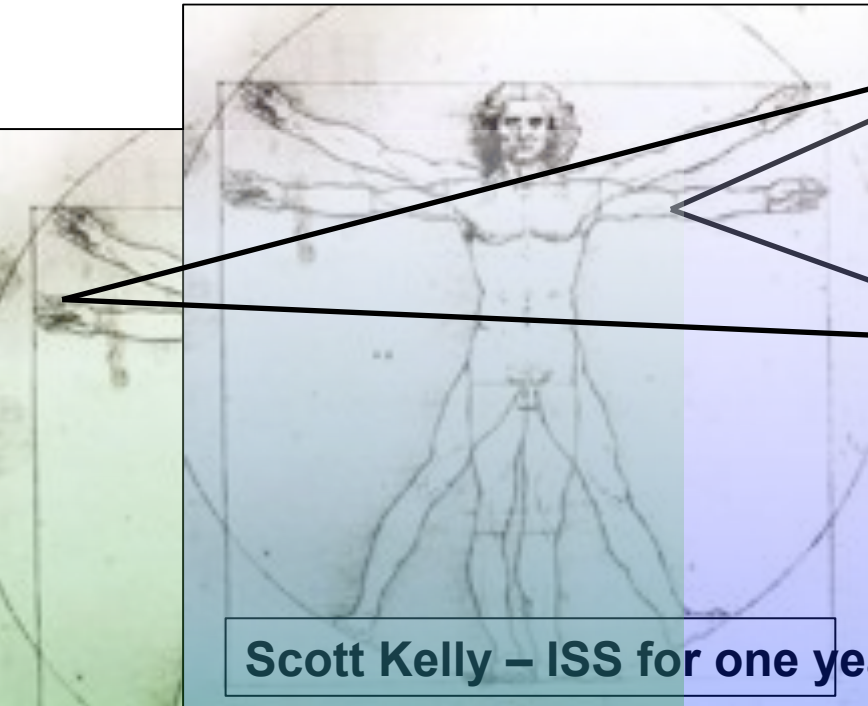
Microbiome
Turek



Targeted and Global Metabolomics
Lee/Rana, Mignot/Snyder & Smith

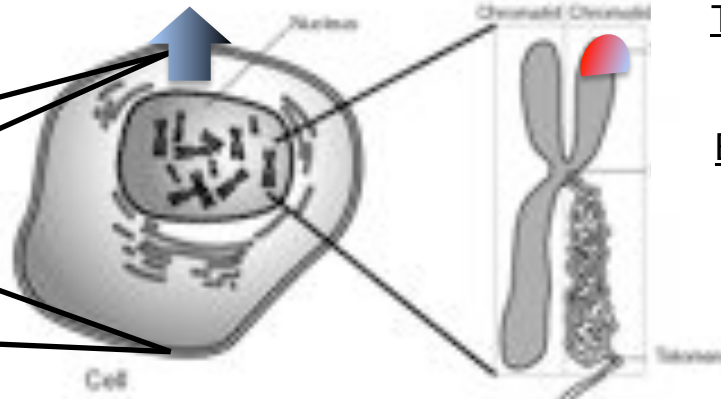


Cytokines
Mignot



Scott Kelly – ISS for one year

Mark Kelly – Earth control

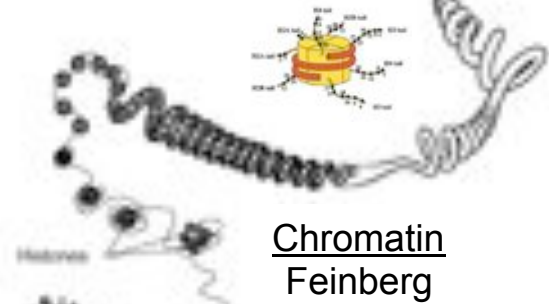


Telomere Length
Bailey

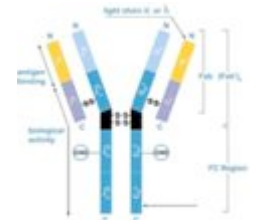
B-cells / T-cells
Mignot



Antibodies
Mignot/Snyder

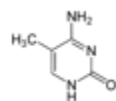
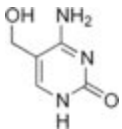


Chromatin
Feinberg



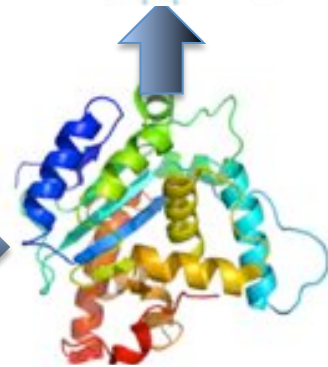
DNA Mutations
Feinberg

DNA Hydroxy-methylation
Mason



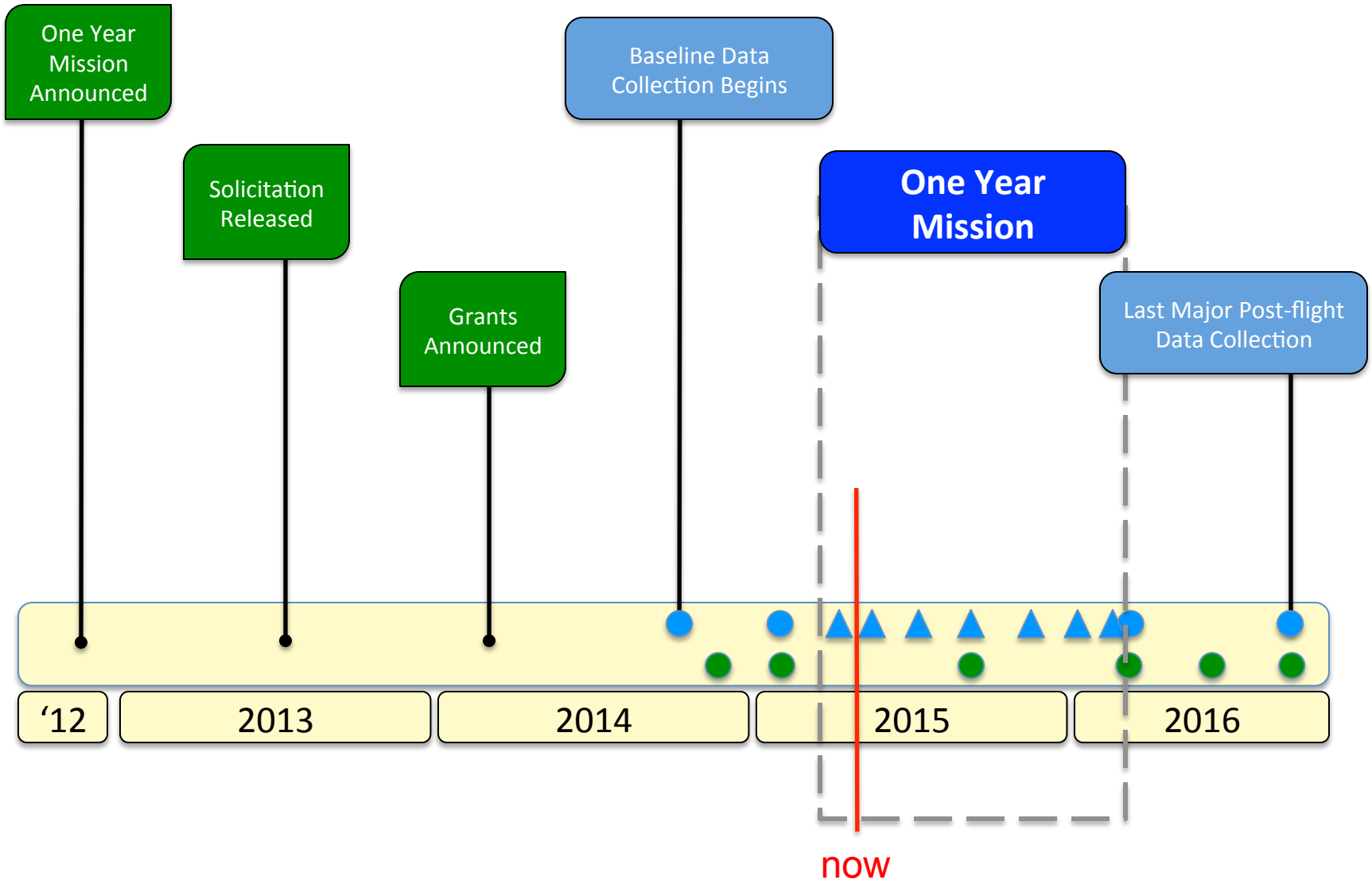
DNA Methylation
Feinberg & Mason

large/small RNA & RNA Methylation
Mason



Proteomics
Lee/Rana

Timeline



Progress to Date

- Pre-flight, baseline data collections complete
 - Most protocols already established
 - New protocols developed for Cell Preparation Tubes (CPTs)
 - To sort or not to sort?

- In-flight collections have begun
 - CPTs processed and frozen
 - CPTs processed and en route to Houston right now!



Issues Associated with Omic Research

- Research ethics
 - The **primary risks** involved in genetic research are risks of **social and psychological harm**, rather than risks of physical injury
 - Could provoke anxiety and confusion about disease risk
 - Uncover unwanted information about heritage, ancestry, and family relationships
 - **De-identification** of genomic information is **difficult**
 - Astronauts are **public figures**
 - **Information given to subjects**
 - Individual genome sequence data?
 - Interpretation of the genome sequence and/or **genetic counseling**?
 - Option to decline to receive all or part of the results (Right Not to Know)?
 - **Research community's access** to genomic information
 - Interim policy on genetic research **JID 1800.4**
 - **NASA-wide** policy under **development**

- **Medical care**
- **Occupational health**
- **Insurance (health, disability, life)**
- **Employment activity**



Conclusion

- The Twins Study (Scott and Mark Kelly) is NASA's first foray into 21st-century omics research
 - Built around Scott Kelly's one year mission
- The Twins Study will examine
 - Genome, telomeres, epigenome
 - Transcriptome and epitranscriptome
 - Proteome
 - Metabolome
 - Physiology
 - Cognition
 - Microbiome
- NASA is addressing
 - Protections for research participants
 - Use of data in medical care, occupational medicine, mission planning



Acknowledgements



The Twins Study Investigator Team



***John
Charles***



***Mike
Barratt***



***Bill
Paloski***



***Graham
Scott***



***Jeff
Sutton***



***Mark
Shelhamer***



time.com/meet-the-twins-unlocking-the-secrets-of-space/



www.nasa.gov/content/twins-study