



Forum in Focus

WINTER 2010

President's Letter

Happy 40th Anniversary!
(1970 - 2010)

Dear Forum Members,

At each of the Forum's board meetings, we hear updates about what is going on at the Foundation. In October, it was reported that 2009 was a record year for new competitive grants awarded to SFBR, exceeding the previous record by more than \$10 million. This record has been achieved at a time in which competition for grant awards from the National Institutes of Health and other national funders is fierce. Each grant award is a victory and indicative of the sheer brilliance and preparation of our scientists.

The great part of this story is that the Forum plays a key role in this success. Here's how we fit in – each time an SFBR scientist writes a proposal for new research, he or she must support their ideas with scientific data and proof of concept. Gifts from the Forum fund pilot grants, which are exactly this aspect of SFBR's endeavors – science at the idea stage. These grants give SFBR scientists – armed with the supporting data – a chance to rise above others in their field.

As the Forum moves into our big, fundraising push, I ask each of you to consider what a \$1 gift can do

The purpose of the Southwest Foundation Forum is to support the Southwest Foundation for Biomedical Research through community relations, volunteer service and fundraising.



Terry Gouger

for these scientists that we support. I cannot stress enough that no gift is too small. There is much leveraging power in donations. Over the past ten years, each dollar donated by the Forum has generated \$26 in additional grant monies. Contributions can be made by attending our annual Gala, purchasing raffle tickets,

giving a 100% tax deductible gift to Forum Grants, attending our lecture luncheons or simply becoming a member. Each of these options can be seen and accessed at www.swff.org.

I am very grateful to every Board member for their continued support throughout the year. I would especially like to thank **Josie Flesher** and **Christy Meador** for their timely completion of the Forum's updated directories, **Dana Hamilton** and **Mary Potts** for revamping the Insider's Tour and making it so personal and informative, **Courtney Percy** and **Michele Stevens** for organizing the fun-filled and profitable Ladies Night Out at Julian Gold, **Karen Lee Zachry** and **Julie Zacher** for all their hard work on our Fall Lecture Luncheon, and finally, **Julie Dudley** who sees to it that all of our events get publicized.

Together let's make our 40th year the best one yet!

Warmly,

A handwritten signature in black ink, appearing to read 'Terry', with a horizontal line underneath.

Terry Gouger
President

THE FALL LECTURE LUNCHEON

SWFF MEMBERS LEARN SECRETS TO STAYING YOUNG

The SWFF fall lecture luncheon was a tremendous success, with 160 members and their guests attending to hear Dr. Clint Baisden explain how lifestyle choice contributes to a person's "Real Age." Real Age, a concept developed by Dr. Michael Roizen, calculates how biologically old or young your body feels in comparison to your chronological age.



Dr. Baisden, a cardio-thoracic surgeon and professor at UTHSCSA, and his wife Rena, a registered dietician, became interested in the science behind why some people look and feel either older or younger than their chronological age. Furthermore they also became interested in Dr. Roizen's research, which identifies hundreds of contributing factors to a person's relative youth. Not surprisingly, a healthy diet and exercise can add years to a person's life, and smoking and excessive drinking can take years off a person's life.



However, Dr. Baisden's talk revealed that a glass of red wine, a small piece of dark chocolate, a cup or more of coffee, and an aspirin a day can all make a person years younger! Also beneficial are getting eight hours of sleep a night, driving the speed limit, eating breakfast every morning and having a dog as a pet (sorry, cats don't seem to help!). Perhaps the most interesting statistics were that stress and anxiety can take away 8-25 years of a person's life, while flossing your teeth daily can make you 7-8 years younger! For more information or to calculate your "real age," Dr. Baisden referred members to the website www.realage.com.



Thank you to all the members and guests to came to enjoy the lecture and luncheon.

MORE FALL LECTURE LUNCHEON PHOTOS



Bienvenidos to the “Esplendores de la Cultura Mexicana” . . . Welcome to the Splendors of Mexico!

On September 16th, the 2010 Gala Committee began their journey into the beautiful and elegant culture of Mexico with a kick-off meeting and breakfast at The Argyle. The committee members are enthused and ready to make this the best gala yet. Committee chairs have been hard at work for the past several months organizing many of the details that will make this such an amazing evening!

This year’s gala will be held at The Argyle on Saturday, May 1, 2010 from 6:00 p.m. until midnight and will celebrate the splendors of the culture of Mexico. Chairman, Paola Lloyd, Co-Chairman, Mary Beth Mosbacker, and Assistant, Kathleen LeFlore, are grateful to the many volunteers who are working tirelessly to organize this spectacular evening benefitting the Southwest Foundation for Biomedical Research.

This year promises to be a truly unique and authentic celebration of our inspiration country – Mexico. It will be meaningful for many of us who enjoy close ties with the history and culture of our nearest neighbor! With the Argyle’s marvelous food, fabulous party favors, artistic floral design, dancing to the sounds of Third Language, and a few other exciting “sorpresas,” this will be a cultural experience you won’t want to miss.

Letters for corporate table sales and Forum Grants have already gone out. If you know of a company that is interested in purchasing a table and has not yet received a letter, please contact the Table Sales Committee Chairs, Melissa Barnett and Kimberly Archer. As always, the Gala sells out quickly, but it’s not too early to begin organizing your table. Eleven tables sold within the first two weeks of receiving the table sales letters. Additionally, we have already received over \$10,000 in Forum Grant donations!



The After Party Chairs, Amy White and Chaney Stuart, are organizing a fun, inviting post-dinner celebration. We have lowered the ticket price this year to \$50 per person, so come to dance, visit with friends, and enter one of our fantastic raffles.

Raffle Chairs, Whitney Solcher-Miller, Courtney Percy, Christy Meador, and Tricia Dilling have already secured not one, but TWO amazing \$100 ticket prize packages. These are both once-in-a-life-time trips which have never been offered before, and each is for multiple couples! Our team is also working on five to six \$50 ticket prize packages which will include trips, special experiences, and unique merchandise items.

For more information on ticket/table reservations, or to make a Forum Grant, please visit our website at www.sfbr.org.

Paola, Mary Beth, and Kathleen are grateful to each and every committee member for their hard work and dedication. We look forward to a memorable evening with friends and hope to be able to make a significant contribution to the scientists who are working so hard every day to make our world a better, healthier place.

SFBR SCIENTIST DR. JOHN BLANGERO FEATURED AT SPRING LECTURE LUNCHEON

Mark your calendars and plan to join us on Wednesday, March 31st at 11:00 a.m. for the Southwest Foundation Forum's Spring lecture luncheon. We are pleased to have Dr. John Blangero, a scientist at SFBR, speak to us on the topic of "***What Our Genes Tell Us.***" Individual tickets will be \$45, or \$360 for a table of eight guests, and your payment is your reservation.

Dr. Blangero is not a conventional research scientist – a fact immediately apparent by his rock musician look. He also challenges the ordinary, the accepted, the status quo – and this has served him well as his innovation has "rocked" the conservative world of biomedical research. He led an SFBR team in developing the software used by more than 3,000 researchers worldwide to identify genes that influence the risk of disease. Dr. Blangero, world renowned for his work as a statistical geneticist, is the director of the AT&T Genomics Computing Center at SFBR. Established just seven years ago, this powerful center contains more than 4,000 computer servers – the largest cluster in the world dedicated to genomics. This computational resource allows analyses, that once took months to complete, to be finished in only minutes – dramatically accelerating the speed of gene discovery for complex diseases. In the last five years, the specialized facilities of the AT&T Genomics Computing Center have allowed SFBR geneticists to make dramatic progress in localizing and identifying genes which influence heart disease, diabetes, obesity, epilepsy, behavioral and psychiatric dis-

orders, cancer and osteoporosis. Dr. Blangero's group has also tackled a heart-breaking rare genetic disease, cystinosis.

Dr. Blangero has parlayed this unique competitive edge into exceptionally strong funding levels and research productivity from the U.S. National Institutes of Health. Dr. Blangero is currently an investigator, or co-investigator, on 16 research projects sponsored by the National Institutes of Health. He is also the holder of a coveted MERIT award from the NIH – awarded to less than one of every thousand applicants – to continue his development in theory of genomics.



After receiving his PhD from Case Western Reserve University in Population Genetics, Dr. Blangero began his research career at SFBR in 1986 as a postdoctoral fellow. He has been honored as a Health Care Innovator and locally is a member of the San Antonio Science and Technology Hall of Fame. Dr. Blangero is an enthusiastic and energetic explorer in his field who is blessed with an amazing ability to communicate the impact of his work.

If you have any questions, please call or email Karen Lee Zachry at 829-8585 or zychryk@swbell.net. We look forward to seeing you in the Spring for another exciting presentation!

There is nothing more hip than supporting a good cause . . .

For the seventh year in a row, the Southwest Foundation Forum teamed up with Julian Gold to host Ladies Night Out. The event was held on Thursday, September 24th and featured catering by La Fonda Alamo Heights, a trunk showing by South Texas native Dian Malouf, and, of course, all of the latest trends in fall fashion. Brilliant Magazine, San Antonio Woman magazine, and other local media were on hand to cover the event that was well attended by Forum members, family, and friends. As in years past, Julian Gold generously donated 10% of all sales from the evening's event to the Forum. This year, a donation was made in the amount of \$2,500.00. Food, drinks, and shopping! What a wonderful way to support a great cause and create awareness about Southwest Foundation Forum and the Southwest Foundation for Biomedical Research.



SWFF Science Education Awards Update

Each year, the Science Education Awards are given jointly by the Southwest Foundation Forum and the V. H. McNutt Memorial Foundation. This year marks the 17th anniversary of these awards!

High school science teachers in and around San Antonio may submit grant applications. Teachers submit a proposal requesting, in detail, the purchases they would like to make to help develop their science programs. Proposals are judged and awards given to those teachers who demonstrate the strongest commitment to furthering the development of innovative and progressive science education programs.

\$20,000 will be awarded:

First Place	\$7000
Second Place	\$4500
Third Place	\$3500
Forth Place	\$2500
Fifth Place	\$1500
Honorable Mention	\$1000

Additionally, thanks to the L. D. Ormsby Charitable Foundation, the first ten applicants who submit qualified proposals will receive \$50 for the teacher's personal use and \$200 for that school's science program. It PAYS to apply early this year!

Applications are due on March 1, 2010. Winners will be announced at the April 14, 2010 SWFF board meeting followed by a special luncheon at The Argyle in their honor.

To view past winners or for more details about these awards, please visit our website: www.swff.org and click on Science Education Awards.

We look forward to rewarding many dedicated and deserving teachers and their schools this year!

INSIDERS TOUR

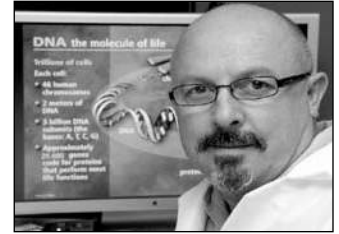
On October 14, 2009, SWFF members and their guests were treated to an exciting tour at the Southwest Foundation for Bio-medical Research. Participants experienced the rare opportunity to tour the Primate Research Center. Guests learned about the interesting data gained from years of monitoring the pedigreed baboon colony, as well as advances and changes in research conducted with chimpanzees. Visitors were also admitted to the BSL4 laboratory and learned about the many complicated viral pathogens currently under investigation by SFBR scientists.

Following the tour, SWFF President Terry Gouger and SFBR President Kenneth P. Trevett welcomed everyone to the event and began the luncheon catered by Page Barteau. SFBR scientists were seated at each luncheon table and provided stimulating conversation. Participants were able to discuss in depth the research that is supported by SWFF.

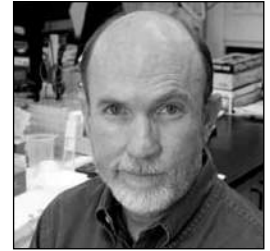
The SWFF would like to thank Corbett Christie and Amy Abdalla of the SFBR for their support and organization of this event, and to all the SFBR scientists who participated in educating and inspiring the guests. We look forward to offering this event again in the future and hope that many more members will take advantage of this special offering.

SFBR Foundation Updates

- **Eric Moses, Ph.D.**, of SFBR's Department of Genetics, is honing in on the genetic risk factors for preeclampsia. With the help of SFBR's AT&T Genomics Computing Center, Moses has found the region on chromosome 2 that he believes contains a genetic variant involved with risk for preeclampsia, which he has also found on chromosomes 5 and 13. His work is supported by grants from the National Institutes of Health and the Southwest Foundation Forum.



- **Robert Lanford, Ph.D.**, of SFBR's Department of Virology & Immunology, leads the effort to develop a vaccine for hepatitis C, which affects approximately 3.2 million people in the United States and 170 million worldwide. A recent evaluation in chimpanzees of a new antiviral therapy for hepatitis C has yielded promising results, while at the same time seems to lower blood cholesterol levels. The technology itself may be used to target genes involved in cancer, HIV, and inflammatory diseases. Lanford's research was published in early December by the journal *Science*.



- SFBR scientists are developing and expanding new collaborations in the fields of spinal injury and brain development with colleagues around the world. The aim is to better understand how the spinal cord repairs itself following injury when it occurs at very early stages of development. This self-healing ability is associated with differences in the expression of genes involved in the inflammatory response to injury of the opossum *Monodelphis domestica* and seems to be lost by the age of four weeks old.
- SFBR President Kenneth P. Trevett has announced the membership of a new national advisory committee. It is comprised of individuals with excellent credentials and will meet annually to advise the SFBR Board of Trustees and management on strategic issues. Members include:

Claude Bouchard, Ph.D., executive director of the Pennington Biomedical Research Center and holder of the George Bray Chair in Nutrition at Louisiana State University in Baton Rouge.

Richard Doughty, MS, CMA, associate director of administration at the Oregon Health Sciences University and Oregon National Primate Research Center.

James LeDuc, Ph.D., professor of microbiology and immunology and holder of Shope-Dunn Chair in Global Health, and associate director of the Galveston National Laboratory at the University of Texas Medical Branch.

Margaret Kripke, Ph.D., professor of immunology and, until recently, executive vice president and chief academic officer at the M.D. Anderson Cancer Center in Houston.

Robert Mahley, M.D., Ph.D., president of the J. David Gladstone Institutes and professor of medicine and pathology at the University of California at San Francisco.

Kenneth Shine, M.D., executive vice chancellor for health affairs for the University of Texas System and professor emeritus and former dean of medicine as well as provost for health sciences there, at the University of California at Los Angeles.

2009 Forum Grant Awards

The year 2009 is a record year in competitive grant awards to SFBR researchers – at this time more than \$65 million in awards. Each of the grants awarded is a story to itself – but many of these awards have one thing in common – a Forum Pilot Study Grant was previously made to the researcher. Forum Grants make our scientists much more competitive because they have developed supporting data or conducted proof of concept work. Forum Grants do make a difference and give us an important edge.

NEW GRANTS AND CONTRACTS AWARDED TO SFBR DURING 2009

Sponsor (1st/2nd/3rd)	Date of Award	Title	Principal Investigator	Duration	Total Amount	SFBR	
						All Years	First Year
PHILANTHROPIC RESEARCH GRANTS							
Genetics (15 PIs)							
1 SW Fdn. Forum	9/29/2009	Measuring the Mutation Rate	Anderson	1 Yr.	\$35,000	\$35,000	\$35,000
2 SW Fdn. Forum	9/29/2009	Characterization of the Neurite Outgrowth Gene SLITRK6, and its Role in Human Brain Structure	Carless	1 Yr.	\$34,871	\$34,871	\$34,871
3 SW Fdn. Forum	9/29/2009	Identification and Characterization of Micro RNAs Influencing Dyslipidemia in Baboons	Karere	1 Yr.	\$28,993	\$28,993	\$28,993
4 SW Fdn. Forum	9/29/2009	A Pilot Assessment for a CVD Genetic Study in Parsi Zoroastrians in Texas	Voruganti	1 Yr.	\$27,260	\$27,260	\$27,260
5 SW Fdn. Forum	9/29/2009	A Baboon Model for Genetic Mechanisms of Reduced Bone Formation in Space	Haviill	1 Yr.	\$24,690	\$24,690	\$24,690
Total for Genetics					\$150,814	\$150,814	\$150,814
Virology & Immunology (10 PIs)							
6 SW Fdn. Forum	9/29/2009	Are “gamma delta tau” Cells HIV/SIV Reservoirs and Targets for HIV Treatment Strategies?	Hodara	1 Yr.	\$35,000	\$35,000	\$35,000
Total for Virology & Immunology					\$35,000	\$35,000	\$35,000
Total for Philanthropic Donations					\$185,814	\$185,814	\$185,814
GRAND TOTAL OF NEW GRANTS AND CONTRACTS AWARDED					\$185,814	\$185,814	\$185,814

MEASURING MUTATION RATE

AWARD 1

Malaria parasites are mosquito transmitted protozoans and the most important of the human parasitic diseases. Every year over 500 million people in 90 countries contract malaria and 1.5-2.7 million die following infection with this disease. Aside from the human health burden, malaria infection is estimated to slow the economic growth of the affected countries in sub-Saharan Africa by 1.3% per annum. Transmission of malaria was halted in the USA in the 1950s – however this disease remains a significant problem for the armed forces fighting in endemic countries. There are five species of malaria parasite that infect humans: this project focuses on the most pathogenic of these – *Plasmodium falciparum*.

This project aims to address a fundamental gap in our knowledge of malaria parasite biology by measuring the rate and pattern of mutation in the malaria parasite

genome. Accurate estimates of mutation are essential for better understanding of drug resistance evolution and antigenic variation. Mutation in the parasite genome has allowed malaria population to evolve resistance to all available classes of antimalarial drugs. Furthermore, extensive mutation in major antigen genes of malaria has precluded development of effective vaccines: despite 20 years of effort to design a malaria vaccine, there has been very little progress towards this goal. Finally, “switching” of surface antigen genes on the parasite cell surface occurs by a mutational process, and prevents the human immune system from clearing parasites from the blood stream. Despite the central importance of mutation in malaria parasite biology, there are no good estimates of the mutation rate in this parasite.

2009 Award Grants

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2009 Forum Award Grants
AWARD 1 – Continued from Page 9

The project design is very simple. We will maintain a series of parasite cultures all derived from a single parasite cell in culture for just under one year. Every two days, parasites pass through a single cycle in which they enter red cells, and pass through 5 cell divisions before daughter cells burst out of the red blood cell and infect new cells. Hence, by following 40 cultures for 150 cycles we can effectively examine mutational changes occurring over 30,000 cell divisions. We will then compare the genome of the original parasite used to start the experiment, with the genomes of the parasite lines after 150 cycles to see what changes have occurred. This project is now possible because we now have efficient tools, such as next generation sequencing and microarrays that allow us to measure variation across the malaria parasite genome. In this pilot project we will focus on genome rearrangements, involv-

ing either loss or duplication of segments of chromosomes, which we will detect using DNA microarrays. In further work we will investigate other forms of variation such as mutations in single base pairs (single nucleotide polymorphisms or SNPs), or changes in number of repeats in repetitive DNA (microsatellite and minisatellites).

There is currently a renewed interest in tackling diseases such as malaria, TB, and HIV that predominantly afflict people in developing countries. There is also an increased awareness that we need a better understanding of the basic biology of pathogens if we are to effectively design tools for their control. To this end, the National Institutes of Allergy and Infectious Diseases now has a grant review panel entitled “Genetics, Variation and Evolution.” With preliminary data in hand from this pilot project, we believe that we will be well placed to obtain a 5-year NIH RO1 grant focusing on understanding malaria parasite mutation through this review panel.

NEURITE OUTGROWTH GENE *SLITRK6*

AWARD 2

Mental illness disorders such as schizophrenia, bipolar disorder, depression, autism and Alzheimer’s disease represent a major burden on society. In fact about 26.2% of adults, or 57.7 million people, in the United States are affected with a diagnosable mental disorder. Mental disorders are accompanied by detectable physical and cognitive traits including differences in region-specific brain volumes. By studying traits, such as brain volume, we can identify genes that contribute to the development of mental disorders and by uncovering such genes, we will identify new target areas for novel treatments for mental illnesses.

We have recently performed large scale studies to identify genetic variation throughout the genome that might be associated with differences in brain volume. Through this, we identified one particular genetic variation that was strongly associated with gray matter thickness in about 11 different brain regions. The *SLITRK6* gene is located within close proximity of this variation and is known to be involved in brain development. Due to these characteristics, we believe that variation within this gene is likely to play a role in determining brain volume in our identified regions and is therefore likely to also be involved in the development of mental illnesses.

This project will undertake a comprehensive analysis of the *SLITRK6* gene. This will include sequencing to determine all genetic variation within the entire gene as well as regions surrounding the gene in a small population of Mexican American individuals that represent a founder population. After we have identified all potential variation, we will continue to determine the nature of this variation in a larger population of Mexican Americans that are predominantly descended from these founder individuals. We will perform statistical analyses to determine what particular variants contribute most strongly to differential volumes within a number of brain regions. Finally, we will choose one specific variant that is most likely to influence brain volumes for further analysis that will assess its role in neural development. By performing such a comprehensive analysis, we hope to show involvement of a specific gene in region-specific brain volumes, which will indicate its likely involvement in the development of mental disorders. Future analysis of this gene, and variation within the gene, in populations affected with mental disorders may aid in the development of diagnostic protocols and new treatments for these disorders.

MICRO RNAs INFLUENCING DYSLIPIDEMIA IN BABOONS

AWARD 3

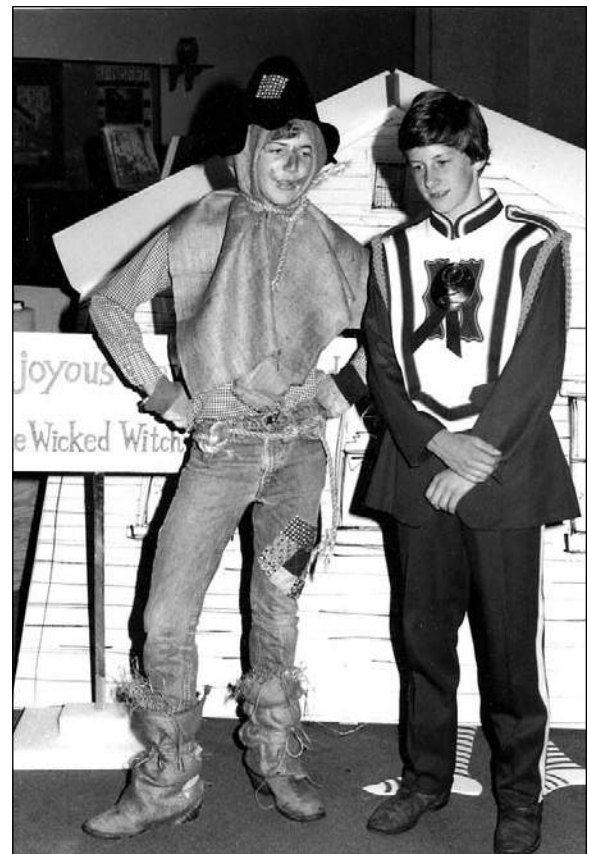
In the United States, heart disease is the leading cause of death, with 2,500 people dying every day due to cardiac dysfunction. Atherosclerosis (coronary artery disease) is the primary cause of heart disease and is influenced by gene-gene and gene-environment (diet) interactions. As part of the NIH program project “Diet and Genotype in

Primate Atherosclerosis,” our laboratory is involved in identifying genes that influence quantitative traits related to dyslipidemia (aberrant levels of cholesterol in the serum), a risk factor for atherosclerosis. To achieve

2009 Award Grants
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Memories from past Galas



2009 Forum Award Grants
AWARD 3 – Continued from Page 10

this goal, we have used genotype and phenotype information of baboons selectively bred for specific traits to identify quantitative trait loci (QTL) influencing phenotypes related to dyslipidemia. We have identified a QTL localized on baboon chromosome 11 that may be influencing serum LDL-cholesterol (LDL-C) levels in baboons. In an effort to identify candidate gene(s) that encodes this QTL, we have employed a systems biology approach by performing whole genome transcriptome profiling using liver RNA isolates from baboons phenotyped as high or low LDLC responders, on chow and an atherogenic diet containing high fat high cho-

A CVD GENETIC STUDY IN PARSİ ZOROASTRIANS IN TEXAS
AWARD 4

The Parsi Zoroastrians form a very interesting, genetically isolated group which migrated to India from Iran in the 8th century. They are distinct in their religious, social and cultural aspects. It is a fairly closed community, with preferred marriages occurring within their community. They have high incidences of breast cancer and mental illness as compared to other populations. They have observed an increase in diabetes and heart problems in the past decade. In recent years, there has been an increase in Parsis migrating to the United States, with a sizable population now residing in Texas. Currently, we are in the process of exploring a genetic study in India with the help of an organization, PARZOR, which is assisted by the United Nations Educational, Scientific and Cultural Organization (UNESCO), and is committed to preservation and promotion of Parsi culture and heritage and scientific investigations into health and genetic problems.

Concurrently, we intend to setup a genetic study in the Parsi community in Texas, to be able to identify the genetic influences on the prevalent health problems, particularly

lesterol (HFHC). In the proposed study, we will complement the current effort of prioritizing candidate genes in the QTL of interest by performing profiling of small RNA molecules, micro RNAs, which regulate gene expression and are responsive to environmental changes. We will integrate gene expression for the entire genome with micro RNA expression to identify dietary fat responsive gene networks that are regulated by micro RNAs. The identification of these networks will reveal genetic mechanisms that influence atherosclerosis risk and provide therapeutic targets for dyslipidemia. Because baboons closely resemble humans in both genetic and physiological aspects, our findings will be directly relevant to human atherosclerosis.

heart disease. In this pilot study, we propose to recruit Parsi families from the state of Texas and collect information related to basic demographics and histories, along with simple anthropometrics and blood pressure measures.

With this pilot study, we expect to find answers to following questions:

1. What heart disease risk factors are prevalent in this population?
2. What type of family structures do they have?
3. Is there evidence for differences in lifestyle and risk factors between older and younger members of the populations?

This pilot study in Texas will provide the preliminary data required to understand the family structure and patterns in this community. It will also provide valuable information on the medical history and health habits of this population and will provide critical data to support the development of a larger proposal for a genetic study in the Parsi Zoroastrians in the US to be submitted to the NIH.

REDUCED BONE FORMATION IN SPACE
AWARD 5

Throughout life, bone strength is maintained through a balance of bone formation and resorption in response to the body's nutritional health and physical requirements. Maintenance of bone strength depends on physical forces, such as walking or exercising, that are transmitted throughout the bone. There are two primary types of bone cells that play a role in this maintenance. Osteoblasts deposit bone where it is needed and osteoclasts remove bone where it is not.

Bone loss due to the absence of gravity in space is a serious health consequence for astronauts who are unable to properly exercise and stimulate the physical forces necessary to maintain bone strength. Even with an exercise

program designed to maintain bone strength, astronauts on the MIR spacecraft and International Space Station (ISS) quickly experienced bone loss. This bone loss is seen the most in areas that bear the majority of the body's weight, and this makes these areas most susceptible to fracture. Recovery of bone mass upon return to Earth does not fully restore bone strength to pre-flight levels. The bone loss the astronauts experience can put them at risk for bone fracture both in the short term and in the long term as it may accelerate their risk for osteoporosis ("fragile bone disease").

2009 Award Grants
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More Galas
from the past

2009 Forum Award Grants
AWARD 4 – Continued from Page 12

It is difficult to determine the exact cause of this bone loss and how to slow or reverse it due to the complexity of conducting a controlled experiment in space. In order to study the bone loss here on Earth, NASA developed a machine that simulates the microgravity conditions that the astronauts experience in space.

We propose to use this machine to investigate differences in baboon and human bone cells and genetics when subjected to a microgravity environment similar

to that in space. To do this, we will obtain osteoblasts from both healthy and osteoporotic baboons. We will subject the normal osteoblasts to the microgravity environment and determine to what degree these cells are a good model for what happens to the osteoblasts in space. Our goal is to determine and characterize the differences shown by these bone cells in microgravity to better understand the underlying cause of this bone loss experienced by astronauts so that we may develop ways to prevent or treat this phenomenon and to develop an animal and cell culture model in which to test such new therapies.

ARE GAMMA DELTA TAU CELLS HIV/SIV RESERVOIRS

AWARD 6

HIV/AIDS is an infectious disease that kills about 2 million people worldwide each year. Only 31% of the 40 million adults and children living with HIV/AIDS have access to therapy. Combination drug therapy, known as highly active anti-retroviral treatments (HAART), helps to prevent disease progression, but side effects are significant, resistant mutations may overcome the therapy, it is not affordable in the third world, and virus reemerges when treatment stops. No matter how successful HAART can be in limiting disease progression, the virus is still hidden in cell reservoirs at certain sites. A new approach is necessary to develop a treatment that can completely eliminate HIV after infection.

CD4+ T lymphocytes and monocytes have been suspected to be HIV reservoirs for rebounding virus. They are easily infected because they both have the main receptor for HIV (CD4+) and they live long with no or very low replication of the virus. The immune system does not attack them, and anti-HIV drugs do not affect them. Other cells, such as the $\gamma\delta$ T cells, may be important reservoirs. $\gamma\delta$ T cells have been experimentally infected with HIV in vivo and in vitro, and after infected cells are activated, they proliferate and express the HIV co-receptor CCR5. We proposed to investigate whether $\gamma\delta$ T lymphocytes are HIV reservoirs that, once activated, can be targeted with anti-HIV drugs or the host immune response. Interestingly, in healthy people there are two main subpopulations of $\gamma\delta$ T cells: the V δ 1 predominant in mucosal tissues (e.g., intestine mucosa), and the V δ 2, predominant in blood. HIV-infected people have an inverted expression profile: decreased V δ 2 in blood and increased V δ 1 in the intestine mucosa.

We will study blood and intestine biopsies from chimpanzees that have been infected with HIV for long

periods of time, but show undetectable or very low virus in plasma (similar to long-term survivors or patients on HAART). We will isolate V δ T lymphocytes from these chimpanzees and activate the V δ 1 and V δ 2 cells in vitro to see whether they are infected; viral replication will be assessed by testing the supernatant of the cultures for the appearance of the core protein p24 at multiple timepoints; TaqMan RT-PCR will be used to amplify and detect HIV RNA. We will study 3 HIV-infected chimpanzees, 3 HIV-infected chimpanzees co-infected with hepatitis C virus (a very common infection in HIV-infected individuals), 3 chimpanzees infected with HCV but not with HIV (HCV control), and 3 chimpanzees that are naïve for both infectious agents (uninfected control). We will also obtain lymphocytes from healthy naïve chimpanzees, separate the V δ T cells, activate them, and infect them in vitro to determine whether there is any preferential infection tropism for one of the two subsets of V δ T cells. Lymphocytes will be isolated from blood, lymph nodes, and gut mucosal tissue. Functional assays will be done with the activated and infected cells to determine whether V δ T cells have the potential to kill HIV infected cells.

These studies will determine whether V δ T cells are infected in vivo, if there is a preferred subset or residence site that can be isolated, and whether it would impact reactivation when drug treatment is stopped. Different levels of virus reactivation after culture of cells from the different sites may also explain their importance in viral transmission. Data obtained from these experiments on the role of V δ T cells in HIV infection, disease progression, and latency may be beneficial in the design of new vaccines and development of new therapies or new treatment strategies to completely eliminate virus from infected individuals.



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2009-2010**

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