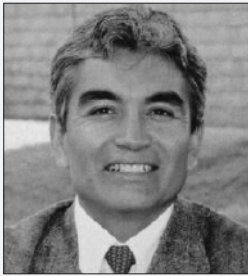




FREE PUBLIC LECTURE

### Can Snoring Affect Your Health?



Dr. Jose S. Loredo  
Department of Medicine

Wednesday  
November 16, 2005, 7:00 PM  
Garren Auditorium  
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### NEXT MONTH

#### DNA Mismatch Repair: From Basic Mechanisms to the Genetics of Cancer Susceptibility

Dr. Richard Kolodner  
Department of Medicine

Wednesday  
December 7, 2005, 7:00 PM  
Garren Auditorium  
Basic Science Building  
University of California, San Diego

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Healthwise is available online at [sira.ucsd.edu](http://sira.ucsd.edu).

## A Fond Farewell: Adam Milgram's Retirement

Dilip V. Jeste, M.D., SIRA Director

As many of you may know, Adam Milgram, the executive director of the Stein Institute for Research on Aging (SIRA) and editor of the *Healthwise* newsletter, has retired. He retired from his position here at UCSD this past August to pursue other interests and enjoy the next chapter of his life. Adam will certainly be missed by his colleagues and staff and the general community impacted by his work. His dedication to the SIRA and its many activities was greatly valued and appreciated. He was, in many ways, the "face" of SIRA over the last several years.

Adam has had an eventful career that expanded outside of his years here at SIRA. His educational background was in psychology, with a focus in clinical psychology and group processes and organizational development. He was active as a

psychotherapist for twenty years and taught courses at the community college and college level. Previous jobs also included working as the chief psychologist at a maximum-security state correctional institution and serving as the executive director of the Hemophilia Association of San Diego County. Throughout his career, he has honed his skills as a public speaker and a writer focused on the many aspects of daily living. We know he will continue to develop his many skills and influence others and we wish him much success in his future endeavors.

Following Adam's leave, Jennifer Reichstadt, M.S., assumed the role of program director of SIRA and is the primary contact for all general SIRA matters. Previously, Jennifer was the research

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<b>UC SD TV</b> <b>PUBLIC LECTURE SERIES UCSD-TV SCHEDULE</b> Lectures air on Cox Communications San Diego, channel 66; Cox North County, channel 69; Time Warner Cable, channel 18; Del Mar TV 66, or UHF (without cable), channel 35.	<b>Success of Gene Transplant</b>	11/10 8:00 PM
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	11/22 6:00 PM

For clinical trials at UCSD: <http://health.ucsd.edu/ntrials/>

## SIRA Receives NIH-Funding to Conduct Summer Research Training for Medical Students

The SIRA was recently awarded a five-year grant from the National Institute on Aging (NIA) to conduct summer research training of medical students, with a focus on healthy aging. The American Federation for Aging Research (AFAR) and the John A. Hartford Foundation are co-sponsors of this initiative.

The SIRA Medical student Aging Research Training (SMART) program provides a unique opportunity for medical students from across the nation to work with some of the best molecular, translational, and clinical scientists working on aging-related research during an 8–12 week period over the summer. Students receive an opportunity to gain hands-on research experience in aging and form a valuable mentoring relationship with a UCSD faculty member. (Students may also work with the faculty from the Salk, Burnham, and Scripps Institutes as a result of the SIRA's collaboration with these institutions.) Additionally, a combination of didactics and workshops reinforces the skills learned during the direct research experience.

The SIRA was ranked at the top of all institutions in the nation to receive this grant, above fellow recipients, such as Harvard, Michigan, Hopkins, and UCLA. The SMART program was started this summer (2005) with a group of 19 incoming second-year medical students, all from UCSD. Each of these students will present a poster summarizing their research both on the UCSD campus this November and at the annual American Geriatrics Society conference in May 2006. SIRA will maintain contact with student participants over time to track their career progress and accomplishments.

During this past summer, SIRA formed a collaboration with the National Institutes on Health (NIH)-funded summer research program lead by Dr. Maria Savoia here at UCSD. Both groups of grant recipients attended common didactic sessions and a one-day retreat. The collaboration of these two programs has ensured that an unprecedented number of medical students not only gains valuable experience in research, but also receives exposure on the critical topic of aging and geriatrics.

Although student recruitment was focused only on UCSD medical students for the first year of the program, recruitment will occur on a national level in the years to come. To continue the interest in aging research by UCSD medical students, additional funds will be sought for local student support.

The SIRA was very pleased with the students selected to participate in the 2005 program and received positive feedback from them regarding the quality of the research they conducted alongside their mentors and the value of the complementary didactic sessions and workshops. A lot of planning and time went into providing them with a worthwhile summer experience, which could not have been accomplished without the generous support of the UCSD School of Medicine's administration and SIRA faculty members and staff.

The research accomplishments of the 2005 SMART program participants will be highlighted in SIRA's next issue of *Healthwise*.

## RECENT DONORS TO THE SIRA

*We would like to express our deep appreciation for all those listed, as well as the anonymous donors, who chose to support the research, education, and patient care at the Sam and Rose Stein Institute for Research on Aging.*

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## Prevention in Late Life: The Role of SIRA

Barry D. Lebowitz, Ph.D., SIRA Deputy Director

In its influential 1994 report, *Reducing Risks for Mental Disorders: Frontiers for Preventive Intervention Research*, the Institute of Medicine (IoM) of the U.S. National Academy of Sciences (Mrazek and Haggerty, 1994) assessed the state of knowledge in prevention research. The index of this substantial volume contains no entries for "aging," "aged," "elderly," "geriatric," or "gerontological." In a section on illustrative preventive intervention research programs, two examples are given: a program for caregivers of people with Alzheimer's disease and a program for widows. The authors could identify no randomized controlled preventive trials in the area of aging.

Prevention has been seen, traditionally, as an area restricted to issues in childhood and adolescence. Our first thoughts are to vaccines for common childhood illnesses and to the long-term benefits of active and healthful lifestyles. Prevention and aging just did not belong together. Very simply, prevention was taken to mean youth. Theory and research in prevention were restricted to issues of child development and intervention early in the life course.

Why be concerned with prevention in late life? For one thing there is the demographic imperative brought about by the overall aging of the world population and in particular by the aging of the older population itself. The average life expectancy in the U.S. has increased from 47 years in 1900 to 77 years today. The next 25 years will witness the largest-ever increase in numbers of older people. With the aging of the "baby boom" generation, the number of Americans over 65 will double to more than 70 million in the year 2030. Projections of population growth raise concerns about pandemic

levels of disability (Gruenberg, 1977; Kramer, 1980). As a result, prevention of the onset of illness or of excessive degrees of dependency and disability have emerged as major concerns for research. These concerns form the core of SIRA's program planning and development.

The traditional public health view of prevention derives from infectious disease and is divided into primary, secondary, and tertiary prevention. Primary prevention is directed toward maintaining health by isolating the causes of disease and eliminating or counteracting them. Secondary prevention is directed toward enhancing recovery by case identification and prompt intervention early in the course of illness. Tertiary prevention is directed toward those already ill and emphasizes treatment and rehabilitation (Caplan, 1964; Commission on Chronic Illness, 1957).

There is a growing expert consensus that this traditional public health view is not optimal. The components of this approach including, for example, concepts such as pathogens, risk factors, disease vectors, and definitions of caseness do not translate easily into pathology and disability typical of chronic disease. The 1994 IoM report adapts a scheme developed by Gordon (1983) to characterize preventive interventions as universal (targeted to a general population), selective (targeted at individuals at increased risk), or indicated (targeted to individuals with minimal levels of signs or symptoms).

Universal interventions are broad public health measures intended for an entire population or for significant geographic, socioeconomic, or categorical subgroups within it (e.g. rural residents, low income older persons, or pregnant women). Universal interventions (e.g. iodizing

salt or putting infants to sleep on their backs) may reduce risk for a large seg-



ment of a population. In all likelihood these do not have impact on those already at high risk, for whom more selective approaches would be necessary. Cost-benefit is a clear decision criterion for the development and implementation of universal interventions since they would, by necessity, involve exposure of many individuals not at risk for development of that illness at all.

Selective interventions are targeted toward those individuals at significantly increased risk of developing the particular illness or condition. Brain structure or function, genetic factors, other illnesses, stress and other psychosocial or environmental factors are all examples of the means by which selectively focused preventive interventions could be developed. The main themes of the SIRA research program are included in this general area.

SIRA has launched comprehensive, longitudinal, bio-psycho-social studies of successful aging. During the past year, SIRA has developed partnerships with a number of local retirement communities, a low-income senior housing complex, an educational venue for retired people, the local Area Agency on Aging, and collaborations with other UCSD-affiliated studies funded by the NIH, including the Women's Health Initiative, the largest and longest, nationwide study of postmenopausal women in history; the Selenium and Vitamin E Cancer Prevention Trial (SELECT), a large, national study of prostate cancer prevention; the Alzheimer's Disease Research Center; and the San Diego Aging Twin

*continued on page 4*

## Prevention in Late Life *continued from page 3*

Project. We have collected data on self-rated successful aging as well as medical history, physical disability, family history, quality of life, health behaviors, resilience, coping styles, cognitive functioning, and various other measures in over 1,500 community-dwelling individuals between the ages of 60 and 100. Preliminary analyses of our data suggest that a large proportion of the respondents feel that they are aging successfully, often despite having physical illnesses and some disability. Significant predictors of successful aging in our sample include overall level of activities, social contacts, resilience, absence of smoking and of depression, better cognitive functioning, and a positive attitude toward aging. Our results suggest that successful aging can and does co-exist with physical disease and disability. We anticipate that our subject cohort will increase to about 5,000 within the next year.

The next step in this research program will be to understand the mechanisms underlying successful or healthy aging. In this type of research, we will build upon UCSD's world-renowned expertise in brain imaging, molecular genetics, and experimental medicine to identify "biomarkers" of successful or healthy aging. The establishment of biomarkers is the critical step in the discovery and development of selective interventions to increase the likelihood of success.

Although selective interventions may seem easy, careful efforts are needed to assure proper identification and to avoid discrimination, stigmatization, or unnecessary fear that may be associated with biomarkers, particularly those that involve

genetic factors. UCSD bioethicists have led the field in considerations of these issues. This area of research is very much a part of the overall vision for SIRA's program development efforts.

Indicated interventions are targeted on those individuals who are already symptomatic and in whom early or sustained intervention may alter the longitudinal course or optimize the outcome of the illness. There are few conditions in all medicine in which benefit is associated with delay in diagnosis and treatment. Continuation with treatment is an essential part of approaches to long-term disease management and reducing the risk of relapse or recurrence. Scientists associated with SIRA and the UCSD School of Medicine are exploring approaches to achieve full adherence to complex disease management even in individuals whose overall cognitive and intellectual functioning may be compromised.

I have presented the broad outlines of SIRA's programmatic approach to prevention in late life. This is new territory for the field of aging. There is no established approach to prevention research that could be easily adapted to meet the needs of the aging field. Our program is built upon improved understanding of etiology, pathophysiology, and risk. This understanding derives from the fundamental discoveries in basic science and translational research for which UCSD is acclaimed. SIRA's new approach to prevention holds the promise to be a significant development for the field. We know that the mission we have crafted is not a simple one. At the same time, we have no doubt that success is achievable.

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## A Fond Farewell

*continued from page 1*

coordinator for SIRA. She can be reached at (858) 534-1226 or jreichst@ucsd.edu. Dr. Barry Lebowitz, deputy director, is the new editor of the *Healthwise* newsletter. With our talented staff, the year ahead promises to be tremendously eventful and productive. We look forward to providing you with continuous updates on our research, research training, and educational activities in future issues of *Healthwise* and on our Web site, <http://sira.ucsd.edu>. Please contact us if you have any questions and your comments are always welcome.



## Active at Any Age

Jacqueline Kerr, Ph.D., Postdoctoral Fellow, PACE Projects,  
Department of Family and Preventive Medicine, UCSD

Kevin Patrick, M.D., Professor, Department of Family and Preventive Medicine,  
Editor-in-Chief, *American Journal of Preventive Medicine*, UCSD

There is a common misperception that as you get older you need to “slow down.” Family, friends, and even some medical professionals might warn “you’re not as young as you used to be.” Yet research increasingly demonstrates that engaging in regular physical activity has benefits late into life, both preventive and therapeutic. At almost any age, decline in physical function can be reversed by starting an exercise program, and function can be maintained by continuing to be active. Several medical conditions can be mitigated by physical activity, the onset of some diseases can be delayed through regular physical activity, and participation in regular physical activity following a disease event may improve rehabilitation and prevent further occurrences.

There is growing evidence of a causal relationship between insufficient physical activity and the onset of cardiovascular disease, cancer, musculoskeletal disorders, some measures of poor psycho-social health, loss of independent living and poor health related quality of life (Taylor, 2004; Surgeon General’s Report, 1996). Approximately 350,000 deaths (15 percent) per year in the United States are premature due to physical inactivity and poor diet (Mokdad, 2004). Epidemiological data have established that physical inactivity increases the incidence of at least 17 unhealthy conditions, almost all of which are chronic diseases or considered risk factors for chronic diseases (Booth, 2000). Regular physical activity greatly reduces a person’s risk from dying of heart disease, and decreases the risk for colon cancer, diabetes, and high blood pressure. Physical activity also helps to control weight;

contributes to healthy bones, muscles, and joints; helps to relieve the pain of arthritis; reduces symptoms of anxiety and depression; and can decrease the need for hospitalizations, physician visits, and medications (CDC Web site). In addition to epidemiological data, there is evidence that exercise programs can positively modify independent risk factors for disease, even if the evidence is currently lacking for the disease outcomes themselves (Taylor, 2004). Importantly there appears to be a dose response relationship, such that even small amounts of activity can have meaningful effects on health outcomes in older adults (Manson, 2002; Hakim, 1998). Moving the lowest quintile to the next quintile is associated with the greatest reduction in all cause mortality (Blair, 1989).

Research on the benefits of physical activity in older adults, who previously may have been excluded from studies due to their age or disease status, is increasing. In part, this is because fears about injury or cardiac events in elderly populations are decreasing as the incidence of these events appears low. The need for this research is pressing as older adults make up an increasingly large part of the population, yet they are the least active group. Less than 40 percent of over 65 year olds are meeting the physical activity recommendations (BRFSS, 2003). There is often a sharp decline in activity from the age of 75 onwards. Although there is an age related decline in physical activity in all cultures, populations, and species (Ingram, 2000), differing rates of decline and reversal of decline through training suggest that some of the decrease in function is avoidable and due to disuse (Taylor, 2004). For example,

fear or falling may result in self-imposed decline in activity and function, not necessitated by disability or injury (Hogan, 2005). Factors such as illness and isolation, which act as modifiers on the level of physical activity, can themselves be affected by the level of physical activity, indicating the presence of complex interactions and feedback mechanisms between disease, disability, and physical activity (Health Canada, 2002). For example, depression and physical functioning may be mutually reinforcing (Biddle & Faulkner, 2002).

Two promising new areas of research in physical activity and health include the impact of physical activity on cognitive function in older adults and the influence of the built and natural environments on the amount and quality of activity people engage in. For older adults who may no longer be able to drive, access to walkable environments may be particularly important for health and independence. There is also growing evidence for the impact of the environment on mental health. It seems plausible therefore that more stimulating environments may also promote cognitive functioning. Studies are now using Functional Magnetic Resonance Imaging to assess cognitive function and SIRA is hoping to develop a program of research investigating the relationship between physical activity, the environment, and cognitive function.

Despite the benefits of a physically active lifestyle, encouraging physical activity in older adults is particularly difficult. There is little evidence on which interventions work and how they work in “real life” community settings. Offering choice and

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**Active at Any Age** *continued from page 5*

increasing confidence are key to physical activity programs for the elderly. Since in older age groups there is generally a decline in functionality over time, even interventions that achieve maintenance of function can be considered successful.

Increasing the nation’s physical activity levels is an important public health goal and a priority in the Healthy 2010 targets. In 2001, The National Blueprint was launched to increase physical activity among adults aged 50 and older. For good physical and mental health, it is recommended that all adults, including the elderly be moderately active on most days of the week for at least 30 minutes. Brisk walking, for example, in continuous or accumulated bouts, is an activity that should be integrated into daily life. Guidelines for exercise in the elderly also include recommendations for strength, flexibility, and balance training. Even if you have been sedentary, you can benefit at any age from starting to exercise gently. In sum, being currently active is key, as the benefits of an active childhood or early adulthood may not continue once activity is discontinued. In other words: “Use it or lose it!”

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## Success of Gene Therapy:

### An Overview of SIRA's September Public Lecture

Theodore Friedmann, M.D., Department of Pediatrics

Treatment of many human diseases is difficult and often ineffective, at least partly because their causes are unknown and because the existing treatments are aimed at symptoms, rather than the underlying causes. Most human diseases have complex causes that include both genetic factors as well as environmental influences. With the explosion of knowledge of human genetics during the past several decades, the genetic aspects of much of human diseases has come to be better understood and many of the genes responsible for disease have been identified, isolated, and studied.

It has become apparent that recognition of the genetic influences in many of our society's most common diseases such as cancer, Alzheimer's and Parkinson's diseases, heart disease, arthritis, infectious diseases such as AIDS, and many others, has opened doors not only to improved concepts of drug treatment, but also to completely new kinds of treatments that are aimed not at the results of the disease but rather at their causes. In the late 1960s

and early 1970s, it became apparent to some investigators that if a specific gene is recognized to be important in the development of a disorder, a uniquely new and definitive kind of therapy might be possible by replacing the defective form of the disease-causing gene with normal copies of the gene; i.e., gene therapy.

Since 1990, many hundreds of clinical studies have been carried that have slowly but surely given credibility to this concept, despite the difficulty of the science and a number of severe scientific and procedural setbacks. During the past few years, gene therapy has moved from an attractive but unproven concept to real therapy for a number of diseases. Children with at least three different kinds of genetically-caused immune deficiencies have been treated with disabled and inactivated viruses armed with normal copies of their disease-causing genes and have responded with a complete restoration of their immune systems, completely normalized childhood lives, some for as long as six years. But the price for this advance has

been high, because at least in one study, several of the children have developed leukemia as a direct result of the treatment. In that regard, gene therapy is not different from most other complex new therapies like cancer chemotherapy, organ transplantation—such important advances usually carry many dangers and risks, some even life-threatening.

The field of gene therapy has now become a clinical reality, although still a very young one—still inefficient and full of technical and conceptual problems. Fortunately, many new approaches are in the wings, some of which will make gene therapy of many more diseases and disabilities like cancer, neurological disease, some kinds of blindness and many others, feasible and more effective, but some of which will raise important and even intractable social and ethical problems of what human non-disease traits we choose to modify. The solution to these difficulties lies in both better science but also in more enlightened and vigorous public discussion.

### Dr. Barry Lebowitz to Receive UCLA Academic Geriatric Resource Center Distinguished Professorship Award

Dr. Barry Lebowitz, SIRA's deputy director, has been nominated for the UCLA Academic Geriatric Resource Center Distinguished Professorship Award for 2006.

The UCLA AGRC is an interdisciplinary consortium representing the Schools of Medicine, Nursing, Dentistry, Public Health, Department of Social Welfare, and the College of Letters and Sciences. The center's goal is to promote education and training related to aging and geriatrics across university and community sites. David Reuben

is program director. Each year, since 1990, the Executive Committee selects an outstanding individual, who has made considerable contributions in the field of aging for the distinguished professorship. Past recipients include James Birren, Robert Kane, James Jackson, Alexander Capron, Joseph Newhouse, Richard Besdine, Cornelia Beck, Tom Prohaska, David Satcher, and Robert Butler.

This is quite an honor and SIRA congratulates Dr. Lebowitz on this achievement.



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Thank you for your generous support. (Make checks payable to UC San Diego Foundation—SIRA and mail to Stein Institute for Research on Aging, 9500 Gilman Drive, La Jolla, CA 92093-0664.) All membership contributions are tax deductible.

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# Successful Aging

**T**he 95-year-old physician who still works 12-hour days...

The 89-year-old machinist still stamping out auto parts...The 93-year-old secretary who's taking computer classes to expand her skill set...the 85-year-old teacher who's looking forward to many more years in the classroom.

In every corner of the United States, Americans are not only living longer, they're maintaining such excellent physical and mental health that they're able to remain remarkably active well into their eighties and nineties. So well in fact, they have the option of continuing to work or to simply enjoy many more years of retirement, often undertaking new types of exciting activities they did not have time to engage in earlier in life. Importantly, some of the successfully aging seniors have physical illnesses and disabilities, yet are productive and happy in their golden years.

The question on the minds of many people now in their sixties and seventies, not to mention tens of millions of "Baby Boomers" waiting in the wings, is why these seniors are aging so well and what can they do to ensure their own graceful entry into the upper reaches of human longevity.

UCSD, and specifically, the Sam and Rose Stein Institute for Research on Aging (SIRA), is working to seek answers to those and many more questions in the near future. Founded in 1983 as the first aging-focused center of its kind in the University of California system, SIRA has supported general geriatric research and served as a resource for information to the community. In recent years, SIRA, under the direction of Dilip V. Jeste, M.D., has become one of the nation's most active and innovative centers for the study of healthy aging.

In fact, SIRA and Jeste's other geriatric programs at UCSD are now seeking and winning major research grants traditionally awarded only to the traditional powerhouses in aging such as Harvard, Johns Hopkins, and University of Michigan. Two most recent examples: The John A. Hartford Foundation in March gave \$450,000 to SIRA, the UCSD School of Medicine, and the VA San Diego Healthcare System, to create the Center of Excellence in Geriatric Psychiatry that will train a new generation of psychiatrists to address the growing problem of mental illness—ranging from depression to dementia—among seniors. And in May, SIRA was named as one of only five national centers to be funded by the National Institute on Aging, the American Federation for Aging Research, and the John A. Hartford Foundation for offering summer research training in aging for medical students from across the country for the next five years.

