



Brain Aging Bulletin

University of California, Irvine

SUMMER 2003

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Brain Aging is the newsletter of the Institute for Brain Aging & Dementia, a non-profit Institute dedicated to improving the lives of those afflicted with Alzheimer's disease through research and education.

2003 Regional Alzheimer's Disease Conference Research and Caregiving: The Best of Both Worlds

The UCI Institute for Brain Aging and Dementia and the Alzheimer's Association of Orange County held its first collaborative two-day Regional Alzheimer's Disease Research Conference on May 8-9, 2003 at the Newport Beach Marriott. The exciting two-day conference combined UCI's spring "Beckman" Conference and the Alzheimer's Association of Orange County's "Facing the Challenge" Conference. An outstanding roster of distinguished speakers and researchers presented new research information, state-of-the-art caregiver issues, and the most current findings in the race to find the cause, treatment, and cure of this disease. Attendance for this conference was outstanding, with over 470 participants and a large number of sponsors and exhibitors. The Conference received extensive local news coverage and very enthusiastic compliments from those in attendance. When the attendees were polled, many of the responses were very positive, "Great conference! Good balance of scientific and practical information!"

This year's theme for the conference was "Behavior: Measurement, Intervention, and Consequences". The goal of the conference was to examine new behavioral and pharmacological strategies for maintaining high cognitive



Dr. Carl Cotman and Dr. Guy McKhann discuss ways to "Keep Your Brain Young"

function during aging and to assist those with dementia to have a high quality of life. The emphasis was placed on behavioral strategies, as this is an area where basic research is increasingly demonstrating that such strategies can stimulate the benefits and optimization of drug effectiveness.

Exercise can help maintain cognitive function and decrease brain atrophy



Keynote speaker, Arthur Kramer, M.D.

The conference was kicked off by keynote speaker Arthur Kramer, Ph.D., from the University of Illinois. Dr. Kramer spoke on "Cognitive Vitality and Aging" and how exercise can help maintain cognitive function and decrease brain atrophy that can occur with normal aging. He presented brain imaging data

"Conference" Continued on Page 3

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UCI Institute for Brain Aging & Dementia

What's New at the Institute?

Community Partners: Adult Day Services of Orange County

Recently the UCI Institute for Brain Aging and Dementia teamed up with Adult Day Services of Orange County to create a partnership and provide clinical assessment services at the Huntington Beach site. The program opened its doors to its first participants in July of last year.



The new satellite clinic proves to be a success, drawing in persons of different ethnic backgrounds, particularly those of Hispanic and Vietnamese descent. Neurological and Neuropsychological testing is available in English, Spanish, and Vietnamese. Appointments can be scheduled by calling the main clinic appointment line at (949) 824-2382.

New Clinic for Aging Research and Education Opens Its Doors in Laguna Woods

The Clinic for Aging Research and Education (C.A.R.E.) hosted an Open House on November 8, 2002. Along with munchies and drinks, handouts and sample apparatus tests were administered to visitors along with guided tours of the new facility. Door prizes for free meals at the newly opened Home Town Buffet located in the same complex were given away to two lucky winners that rainy day. The C.A.R.E. office is

Calendar of Upcoming Events...

2003 Family Educational Series

Co-Sponsored by the UCI Institute for Brain Aging & Dementia, Alzheimer's Association, and Adult Day Services of Orange County. All Sessions meet from 4:30-6:30pm at the University Club, UCI Campus. Call (949) 824-2382 for reservations and details.



September 9- Research Advances: Are We Almost There Yet?

December 9- Coping with Grief and Loss During the Holidays



"Coping at Home: A Survival Guide For Alzheimer's Families"

Co-Sponsored by the UCI Institute for Brain Aging & Dementia, and the Alzheimer's Association. All Sessions meet from 2:00-4:00pm at the University Club, UCI Campus. Call (949) 824-2382 for reservations and details.

August 7- Compassionate Communication With The Memory Impaired

August 14- Behavioral Challenges Associated with Alzheimer's Disease

August 21- In Times of Crisis: What You Should Know

August 28- Body Mechanics: Don't Break Your Back

the newest addition to the Institute for Brain Aging and Dementia at UCI.

ways to maximize the potential of the oldest-old as they age.

The researchers at the C.A.R.E. office are currently enrolling participants into the 90+ Study, a new study for people who are 90 years of age and older. These researchers, under the direction of Claudia Kawas M.D., plan to study

To learn more about the 90+ Study, call 949-824-9121 to have a free informational brochure sent to you.



Dr. John Ringman interviewing a 90+ Study Participant

**New UCI
Institute for
Brain Aging
and Dementia
Website!**



[http:// www.alz.uci.edu](http://www.alz.uci.edu)

*Sections of the new website may still be under construction.

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“Conference” Continued from Page 1

(MRI, magnetic resonance imaging) that demonstrated those who exercise and are fit have less age-related brain atrophy.

Elizabeth Head, Ph.D., from UC Irvine, expanded on Dr. Kramer’s talk, discussing “Antioxidants, Cognitive Enhancement, and Successful Aging”. Research from longitudinal studies with aged dogs suggests that modifications of diet and environmental variables can help to promote successful aging. Dr. Head shared that through modifications of the environment (i.e., diet, exercise, and education), and changing lifestyle choices, a person can promote successful brain aging.



David Troxel, M.P.H. shares his expertise with conference attendees

David Troxel, M.P.H., from the California Central Coast Alzheimer’s Association argued that behavioral interventions are an essential part in the management of dementia patients, activities, games, socialization, and exercise.

Behavioral interventions and pharmacological approaches continue to be one of the gold standards

In parallel with behavioral interventions, pharmacological approaches continue to be one of the gold standards. Murray Raskind, M.D., from the Seattle VA Medical Center, spoke about the management of agitation and dementia and outlined several strategies for the selection and utilization of various new second-generation antipsychotic medications. He noted these drugs should be started at low dosages, increased very slowly, and the dosing should be stopped when there is an improvement or if a side effect develops. If ineffective over the dose range, another should be tried as there are subtle but real response differences among the second-generation antipsychotics. He emphasized the

importance of the proper use of these drugs since they are the mainstay of treatment for agitation and psychosis and usually effective.

Linda Teri, Ph.D., from the University of Washington outlined strategies to recognize and understand the behavioral problems of dementia, learn how to problem-solve associated patient problems, enhance social skills, maximize cognitive functions, and finally, how to learn to admit to get help.



Dr. Linda Teri and Dr. Carl Cotman

Laura Mosqueda, M.D., from UC Irvine, discussed medical facts about behavioral problems and what we should and should not believe. She suggests that we, as medical consumers, families, and caregivers should try to learn as much medical information as possible, especially when it pertains directly to a current situation. She also suggests that as we are given information through various channels



Dr. Laura Mosqueda takes a moment to listen and talk to several caregivers at the conference

(news, media, hypes, etc.), we should put the next promise of a miracle cure/treatment into perspective. Think critically about any information that you hear or read.

One of the dementias that has shown various behavioral

“Conference” Continued on Page 4

UCI Institute for Brain Aging & Dementia

“Conference” Continued from Page 3

problems is that of Frontal Temporal Dementia (FTD), discussed by J. Patrick Kesslak, Ph.D., of UC Irvine. Dr. Kesslak went into depth about FTD, the course of the disease, and some of the behavioral problems that occur amongst individuals who have been diagnosed with FTD.



Dr. Kesslak talks to a conference attendee

A series of several informal roundtable sessions were held in separate rooms for the audience to get an update on a range of topics. These were presented by members of the Alzheimer’s Association of Orange County’s Medical Scientific Advisory Board, bringing to the audience information on various dementia subtypes, medication management, as well as clinical/legal issues involved with dementia. The informal sessions provided a great forum for attendees to interact with the speakers in a smaller setting. A Panel discussion, made up from the roundtable session presenters, was then led by Dr. Raskind who helped to summarize the findings and reports of each session. Several Caregiver roundtables were arranged for the second day of the conference and also provided the audience with an opportunity to interact with those speakers, who discussed topics such as Elder Abuse, Health Insurance, Benefits of Structured Activities, and other very helpful topics.

New training methods for healthcare workers

Beverly Sanborn, L.C.S.W. Sanborn presented some alarming facts about the need for an increase in the number of health care workers in the near future. She stated that in the next five years, there will be a need for a 25% increase in nursing assistance and a need for a 74% increase in home health aides! She predicted that by 2020, there would be a need for 1.1 million more people in the nursing field! One of the biggest limitations, however, in this area is the recruiting, training, and maintenance of good staff. Sanborn suggested training through observation by creative use of videos and

she demonstrated the use of specially developed robots that are placed in assisted living facilities! She mentioned that these tools have tremendous potential for large companies and multi-campus facilities, allowing them to save time and money by having higher-level staff coach front-line staff in an efficient and effective manner.

Living with Dementia: An Early-Stage Panel

One of the most engaging sessions of the conference, was the “Insights into Early Dementia Panel”, that was moderated by Cordula Dick-Muehlke, Ph.D., of Adult Day Services of Orange County. Within the panel, there were three individuals, who had been diagnosed with Mild Cognitive Impairment, accompanied by their spouses, who had graciously agreed to participate in a live panel discussion at the conference. They discussed real-life situations and the changes they have had to make to adapt to their current life problem. The panel put the practical issues into perspective from a standpoint that is often not heard and at the time of closing the audience gave them a standing ovation.

Keeping your brain young

The closing keynote speaker Guy McKhann, M.D., from Johns Hopkins University summed up the conference. Dr. McKhann is most recently recognized for the best seller book that he co-authored with Marilyn Albert, Ph.D., **“Keeping Your Brain Young: The Complete**



Linda Scheck, of the Alzheimer’s Association, with members of the Medical Scientific Advisory Board

Guide to Physical and Emotional Health and Longevity”. Dr. McKhann summarized the current state of research to improve health and how it is increasingly integrated with basic science. He discussed how to keep your mind active and stimulated in order to enhance cognitive

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“Conference” Continued from Page 4

function, stressing the “If you don’t use it, you lose it!” theory. Dr. McKhann also gave tips on what you can do to “Keep Your Brain Young”, such as physical activities, mental activities, the role of nutrition, and things that one can do to help stimulate the mind. He also gave some pointers on genetic risks, therapies (past, present, and future), and what can be expected in the area of brain aging research. He also led a discussion with the conference co-chair and director of the UCI Institute for Brain Aging and Dementia, Dr. Carl Cotman. This discussion allowed the audience an opportunity to ask questions and provided them a chance to learn from one of the U.S.’s leading neurologists!

This year’s conference was a tremendous success and the UCI Institute for Brain Aging and Dementia and the Alzheimer’s Association of Orange County look forward to coordinating another exciting and informative conference next Spring. If you would like more information or would like to be added to the mailing list to receive information on upcoming educational events and the Regional Alzheimer’s Disease Research Conference in 2004,



Conference attendees showed great enthusiasm and interest for the various speakers and topics for the 2003 Conference

please call (949) 824-2382 and ask to be added to the mailing list. We hope that you will be able to join us at next year’s conference, May 6-7th, 2004!



A special thank you to all of the 2003 Regional Alzheimer’s Disease Research and Education Conference sponsors and exhibitors who helped to make the conference a success!

Sponsor/Exhibitor Opportunities for the 2004 Regional Alzheimer’s Disease Research and Education Conference available! Reserve your table today! For more information, call (949) 824-8135

Alzheimer’s Disease Research Center of California

at the
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For information and appointments please call: (949) 824-2382

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Faculty Spotlight: Frank M. LaFerla, Ph.D.

The Making of the Transgenic Mouse

Alzheimer's disease is the most common form of dementia worldwide, with the vast majority of Alzheimer's disease cases occurring sporadically in elderly individuals over 65-70 years of age. Some Alzheimer's disease cases, however, are familial and transmitted from one generation to another. These familial Alzheimer's disease cases generally develop at a much earlier age of onset compared to the sporadic version. For instance, some familial Alzheimer's disease cases begin as early as 16 years of age! Other than the age of onset, both forms are quite similar pathologically and clinically. At the neuropathological level, the Alzheimer's disease brain is characterized by two hallmark lesions: amyloid plaques and neurofibrillary tangles. These two lesions occur in selective brain regions such as the temporal lobe. Plaques are comprised of small proteins called β -amyloid, whereas tangles are comprised of biochemically modified form of the tau protein. It is currently not clear what the relationship of these two lesions are to the disease phenotype, although converging evidence from multiple fields suggests that β -amyloid may be the trigger for all cases of Alzheimer's disease.

To study the pathogenesis of Alzheimer's disease, researchers turn to animal models such as the mice. These mouse models are useful because they are relatively cheap, easy to breed and maintain, and more importantly, because human genes are biologically functional even when expressed in common laboratory animals such as the mouse. These genetically modified mice are referred to as transgenic mice, because they contain foreign transferred genes.

The LaFerla lab has recently two important transgenic mouse models. The first is an animal model of Alzheimer's disease and the second is of a muscle disorder that is related to Alzheimer's disease called inclusion body myositis.

Transgenic model of Alzheimer's disease Although the field has been able to model either plaques or tangles in transgenic mice, recapitulating both lesions in the same mouse model in Alzheimer's relevant brain regions has proven to be a difficult challenge. The LaFerla lab utilized a novel strategy for developing a transgenic mouse that harbors three mutant Alzheimer's related genes. Because of the strategy that they

employed, all three transgenes are inherited in every generation, which means that the mice breed as easily as any single transgenic mouse. In addition, all of their mice are on the same genetic background, thereby eliminating a critical confounding variable that typically is difficult to avoid.

LaFerla's triple transgenic mice develop both plaques and tangles in a progressive and age-related manner (see picture below). The accumulation of these lesions also parallels the distribution pattern that has been observed in the human Alzheimer's disease brain. Notably, the β -amyloid plaques develop several months prior to the development of the tangle pathology. This finding is consistent with the genetic evidence in human studies that show that β -amyloid lies upstream of tangles in the neuropathological cascade. These triple transgenic mice are particularly useful for testing potential therapeutic compounds and will allow investigators to determine if clearing β -amyloid deposits is sufficient to prevent or reverse the tangle pathology.



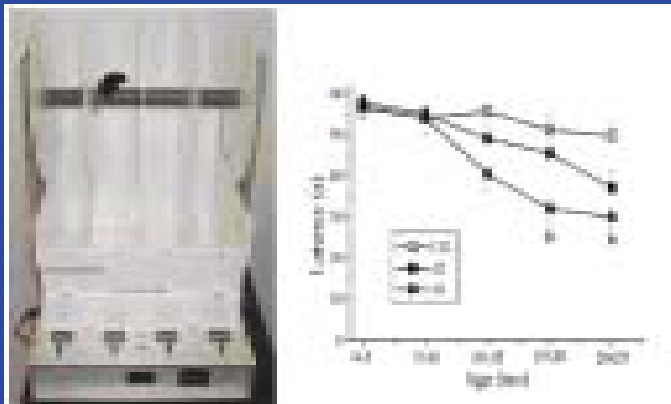
High magnification view of the hippocampus of a triple transgenic mouse showing β -amyloid staining in brown and tangles in blue. The arrows point to extracellular β -amyloid deposits. Note that many cells manifest both pathologies (arrowheads).

Transgenic model of inclusion body myositis Inclusion body myositis is the most common muscle disease in individuals over the age of 55. It is an incurable disorder that

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leads to severe disability. Like Alzheimer's disease, inclusion body myositis occurs sporadically or can be inherited. Most cases of inclusion body myositis are sporadic, with an unknown etiology. Surprisingly, this muscle disorder has much in common with Alzheimer's disease. Although inclusion body myositis patients are not demented, their muscle fibers are characterized by the accumulation of many "dementia"-related proteins, most notably the β -amyloid peptide. Eventually the accumulation of these proteins in the muscle fibers of these patients leads to their paralysis.

The role of β -amyloid in the pathogenesis of inclusion body myositis is still unresolved. To develop a transgenic mouse model of this common, age-related muscle disorder, we selectively targeted overexpression of the β -amyloid precursor protein to skeletal muscle through use of the muscle-specific gene promoter. We showed that the overexpression of this Alzheimer's related protein in transgenic mice led to the development of histopathological and clinical features characteristic of human inclusion body myositis, including motor deficits in aged-mice. One method of studying the motor ability of mice is to place them on a motorized rotating well that is called the rotarod (see picture below). Healthy mice can remain on the rod for longer periods of time than transgenic mice.



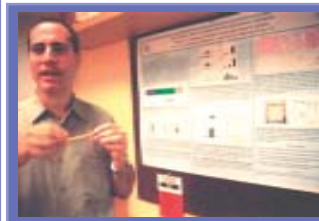
This figure compares the motor performance of normal mice and two transgenic lines: A2 and A6, which express the transgene to the low and high levels respectively, on the accelerating rotarod. Note that the controls show no substantial age-related deficit but that both the A2 and A6 transgenic lines exhibit an age-related deficit beginning around 10 months.

Biography of Frank M. LaFerla, Ph.D.

Frank M. LaFerla obtained his undergraduate degree from St. Joseph's University (Philadelphia) in 1985 and his doctorate from the University of Minnesota (1990). He subsequently completed his postdoctoral training at the Holland Laboratory of the American Red Cross. There he



became interested in the development and characterization of genetically-modified animal models of complex human neurologic disorders such as Alzheimer's disease. In late 1995, he was appointed as an assistant professor in the Department of Neurobiology and Behavior at the University of California, Irvine. He became a tenured associate professor in 2000 and also serves as the associate director for brain science for the Institute for Brain Aging and Dementia. At UC Irvine, his laboratory remains focused on dissecting the



neuropathogenesis of Alzheimer's disease. He has been well recognized for his research accomplishments and has received several awards

including the Ruth Salta Investigator Award for Alzheimer's Disease Research by the American Health Assistance Foundation (2000) and serves on the Brain Disorders and Clinical Neurosciences Grant Review Panel for the National Institutes of Health.



You can learn more about Professor LaFerla's research on his webpage:

<http://neurobiology.bio.uci.edu/faculty/laferla/>

or by visiting the Institute for Brain Aging & Dementia website at: <http://www.alz.uci.edu>

UCI Institute for Brain Aging & Dementia

Memory Walk 2002: Another Year to Remember

The UCI Institute for Brain Aging and Dementia Memory Walk Team wins the "Largest Team" for the 7th consecutive year



"Orange" We the Largest Team?!

The 2002 UCI Institute for Brain Aging and Dementia Memory Walk Team

Children and adults of all ages attended last year's Robinson's May Alzheimer's Association Memory Walk at the Irvine Spectrum on October 5, 2002. Hosting the largest Memory Walk in the nation, with almost 5,000 participants, Orange County raised over \$550,000 for the Alzheimer's Association of Orange County.

For the seventh consecutive year, the UCI Institute for Brain Aging and Dementia won the "Largest Memory Walk Team", thanks to the hundreds of walkers and "forget-me-nots" who participated with the UCI Memory Walk Team 2002! The UCI team recruited over 300 walkers and raised over \$10,000 in funds that will go towards helping a countless number of families and patients through the Alzheimer's Association.

A special thanks goes to Dr. Diane Edwards (Professor at the Saddleback College Emeritus Institute), Milly Polash, and Maurice Labovich, who helped to recruit over 200 Leisure World Exercisers! Great Job!



We could not have done it without all of the participants and dedicated efforts to help in the fight against this devastating disease! A huge "thank you" to everyone who has made last year's Memory Walk a success!

THANK YOU!



Come Join the Fun in 2003!

Mark your calendars for the 2003 Alzheimer's Association Memory Walk!

When: Saturday, October 4th, 2003

Where: Irvine Spectrum

To receive information about the walk or joining the UCI Memory Walk Team, call (949) 824-2382.

On the Forefront: An Update on Clinical Trials Current and Upcoming Clinical Study Options



For more information, please call Beatriz Yanez or Aleece Noujaim at (949) 824-5733 or visit our website at: <http://www.alz.uci.edu/clinicaltrials/>

Homocysteine Treatment Study for AD

- ◆ Double-blind 18-month study of B-6, B-12, and Folic acid for delay of progression in Alzheimer's disease (AD)
- ◆ For men and women over the age of 55 who have been diagnosed with AD
- ◆ Cannot currently be taking B-6, B-12, or Folic Acid supplements

Statin Treatment Study for AD

- ◆ Double-blind 21-month study of simvastatin for delay of progression in Alzheimer's disease (AD)
- ◆ For men and women over the age of 55 who have been diagnosed with AD
- ◆ Cannot currently be taking cholesterol lowering medication

Depression and Alzheimer's Disease

- ◆ Follow-up study for individuals with Alzheimer's disease with and without depression; not a treatment study
- ◆ For men and women who have AD; limited to patients seen at our assessment center; informant needed
- ◆ A small fee is paid at each visit for participation in this study

Valproate Study for Alzheimer's Disease

- ◆ Double-blind 26-month study to test the ability of Valproate to prevent the occurrence of behavior problems in individuals with Alzheimer's disease
- ◆ For men and women 50 years of age or older who have been diagnosed with Alzheimer's disease, and who have not experienced agitation and/or psychosis since the onset of their illness

Aricept Treatment Study for Mild Cognitive Impairment

- ◆ Double-blind 1-year study of donepezil (Aricept) to treat mild cognitive impairment
- ◆ Objective is to test the ability of Aricept to improve memory and/or delay the progression of the memory problem
- ◆ For men and women 45 years of age or older who have a memory complaint recognized by an informant



Specialized Educational Support Groups for FTD & Lewy Body Dementia Caregivers

We welcome all caregivers of patients with Frontal Temporal Dementia (e.g., Pick's Disease and Primary Progressive Aphasia) and caregivers of those with Lewy Body Dementia to our monthly support groups.

When? Meetings are held the first Wednesday of each month from 9:30am-11:30am

Where? Meetings are held in the 1st floor conference room of the Gillespie Neuroscience Research Facility on the UCI Campus

Co-Facilitators are Lynne Conger of the Alzheimer's Association and Shirley Sriyordsa of the UCI Institute for Brain Aging & Dementia. For more information about the group, please call (949) 824-8135.

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A special thank you for all of the donors who have contributed to the UCI Institute for Brain Aging and Dementia. Your generous and thoughtful gifts will help to promote advances in Brain Aging Research at the University of California, Irvine.

All artwork for this Donor section is from the 2002 Alzheimer's Association Memories in the Making[®] program.

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There are many ways to support the clinical and basic science research activities at the UCI Institute for Brain Aging and Dementia. If you would like to receive more information on giving, please contact Shirley Sriyordsa at (949) 824-8135.

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Circus in Town- by Eugene

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- 1.) Checks should be made payable to:
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section please write: **Alzheimer's
Research**
- 2.) If the donation is being made in
memory/honor of someone, please
include a note with information as to
where the acknowledgements should
be sent to.
- 3.) Please mail the donations to:
Institute for Brain Aging & Dementia
1113 Gillespie Neuroscience Research Facility
Irvine, CA 92697-4540

To make a donation to the UCI Institute
for Brain Aging, log on to:
<http://www.alz.uci.edu/donate.html>
or call (949) 824-8135.

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CALENDAR 2003

August

“Coping at Home: A Survival Guide for Alzheimer Families”, A 4-Part Series
Thursday Afternoons
University Club, UC Irvine

September 9

Family Educational Series Workshop
Research Advances: Are We Almost There Yet?

October 4

2003 Alzheimer's Association Memory Walk
Irvine Spectrum



November 8

What is Memory Loss?
Offered in Spanish
Adult Day Services of
Orange County

December 9

Family Educational Series Workshop
Coping with Grief and Loss During the Holidays

May 6-7, 2004

2003 Regional Alzheimer's Disease Research and Education Conference
More information coming soon!

“The Old Bridge in the Fall” by Beth

Artwork borrowed from 2002 Orange County Alzheimer's Association

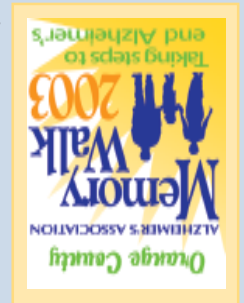
Memories in the Making ©Calendar. The Calendar may be purchased by calling (714) 283-1111.

To join the UCI team or for more information, please call (949) 824-2382

Irvine Spectrum, Irvine

Saturday, October 4th, 2003

Sign-Up with the UCI Institute for Brain Aging Team by September 12th and receive a free T-Shirt! Come and join the fun!



Memory Walk

2003 Alzheimer's Association

University of California, Irvine
Institute for Brain Aging & Dementia
1113 Gillespie Neuroscience Research Facility
Irvine, CA 92697-4540



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