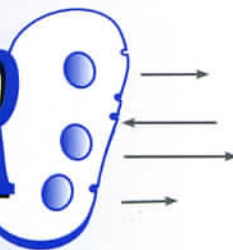


NEURO

MESSENGER



Newsletter of the LSU Neuroscience Center of Excellence

Issue No. 2

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*New Science for a New Century:
Health Through Discovery*



Monday, October 15, 2001
2020 Gravier Street, New Orleans, LA 70112



Message from the Director

Nicolas G. Bazan

In the inaugural issue of *Neuromessenger* (November 1999), it was my pleasure to share with you the excitement of the initial growth of the Neuroscience Center: our new, state-of-art facilities, the expansion of our faculty to include several talented young neuroscientists, and some of our successes in attracting research grants. This first year of the new millennium is also the beginning of a new period of the life of the Center, and in many ways the beginning of a Phase II. Therefore, a new science for a new century will evolve with the purpose of contributing to health through discovery.

Initially, the Neuroscience Center's development was about building academic excellence, consolidation of our interdisciplinary PhD program, and establishing faculty development programs and a fully interactive research facility.

Our Interdisciplinary PhD Program in the Neurosciences (established in 1992, and co-directed by Dr. Ranney Mize, Chairman of the Department of Cell Biology and Anatomy, and myself) has provided research training for many young scientists. Up to now, eleven doctoral diplomas have been awarded to talented young investigators who have gone on to outstanding research institutions or to continuing medical education.

Two new community outreach programs have enjoyed success as well. Each summer, top undergraduate students are given an opportunity to participate in an intensive curriculum of lectures and research called the Summer Undergraduate Neuroscience (SUN) Program. We also

offer yearly activities to both children and adults as part of our participation in Brain Awareness Week, a nationwide effort to educate the public about the importance of neuroscience research and the impact of brain disease.

Phase II for the Neuroscience Center will focus on strengthening and expanding our research teams and further building partnerships, as well as translating our research into benefits for the community. It is off to a very good start: The Neuroscience Center, in a collaboration with eight other universities, received the largest award ever granted to the Louisiana Board of Regents' EPSCoR program from the National Science Foundation for the project "Micro/Nano Technologies: Neural Signaling Research." Our team has a prominent role in this fundamental research, which also has great commercial potential.

This year, we have formulated a new concept through which fundamental knowledge can be translated into commercial applications: the Neurobiotechnology Program of Louisiana. A research alliance with Tulane University Health Sciences Center and other Louisiana academic institutions, this program is a statewide initiative to develop a neurobiotechnology-pharmaceutical industry in Louisiana. The benefits to our state will be enhancement of our economic competitiveness by attracting out-of-state businesses, the establishment of start-up companies within the state, and the creation of a highly trained and highly paid work force. The clinical neurosciences development alongside of this industry will enhance medical care and reveal new treatment strategies for the people of Louisiana who suffer from the devastation of neurologic disorders.

In collaboration with Professor Julio Alvarez-Builla of the Universidad de Alcala (Spain), I have obtained two patents for a new analgesic, thereby laying the foundation for the start-up company St. Charles Pharmaceuticals. The company has attracted investment capital, and has been awarded three grants from the National Institutes of Health. Preclinical studies are nearing completion, and an application for Investigational New Drug status from the Food and Drug Administration will be submitted in November. Phase I and Phase II clinical trials will begin in 2002. In addition we have built a multidisciplinary team of scientists from LSUHSC and UNO. It is so rewarding to me to witness the completion of this cycle of discovery and application of new knowledge for the benefit of all! This new analgesic will provide relief from pain without the devastating consequences of liver damage caused by some existing analgesics.

I am particularly pleased to introduce the new faculty of the Neuroscience Center, Drs. Anthony Ricci, Gudiseva

Chandrasekher, Chu Chen and Walter Lukiw, who are featured in the following pages. Their expertise is a wonderful asset to the Center. They are conducting several truly exciting, cutting-edge research projects on hearing, vision, memory and learning, and Alzheimer's disease.

What else do I see for Phase II of the Neuroscience Center? Growth and accelerated pace of research. I am very excited about the future of the Neurobiotechnology Program of Louisiana and its important role in the economic growth of our region. We all know the importance of economic diversity, for New Orleans as well as for Louisiana. I envision a "ripple effect" from the establishment of a neurobiotechnology-pharmaceutical industry that will strengthen our tax base, provide employment opportunities and retention to our best and brightest, and provide for the improvement of regional schools as a result of the demand for a well-educated workforce.

In Phase II, we will actively pursue the resources to expand our physical facility to accommodate our rapid growth, to house highly specialized research instrumentation, and to make room for the consolidation and expansion of our research programs.

I believe that now the Neuroscience Center has approached the "critical mass" of research expertise that will attract the finest researchers in the neurosciences. For Phase II, we have identified several specialized areas of research, complementary to our present faculty, into which I hope we can recruit outstanding candidates. We already know that when scientists come together from many disciplines, the research rewards are huge!

In particular, the Neuroscience Center will increase the number of clinician-neuroscientists, who, like our Dr. Larry Carver, will provide a strong link between our laboratories and our patients, and who will design and direct clinical trials for the treatment of Alzheimer's and Parkinson's disease, stroke, brain trauma, pain, and epilepsy. We are integrating our expertise, as well as cutting-edge knowledge evolving from biochemistry, molecular biology, cell biology, physiology, pharmacology, behavior, and disease models, to intensify our concerted effort to discover the inner workings of brain function and diseases that affect the brain.

In conjunction with the LSU Eye Center and the University of New Orleans, a major effort is underway involving retinal degenerative diseases, particularly retinitis pigmentosa. This program, supported by the Villere Chair, has provided a tremendous opportunity to tackle this blinding eye disease. I have recently filed a patent application on a new compound that may be useful to slow down the loss of photoreceptors in retinitis pigmentosa.

I see the five-year, Phase II development of the LSU Neuroscience Center as the time when our region becomes renowned for excellence in research in the neurosciences through insightful collaborations and cooperative efforts. Our ultimate goal is to establish a regional identity in neuroscience that is comparable to that of Houston in cardiovascular science and cancer.

I welcome you to today's ceremonies and to the future of neuroscience!



Mr. Ernest Villere (1904-1986) and Mrs. Yvette Villere (1908-1991) established the Ernest C. and Yvette C. Villere Chair for the Study of Retinal Degeneration in 1981. The program was founded to support the study of retinitis pigmentosa, a degenerative disease of the retina from which their son, George, has suffered. Dr. Bazan cites this Chair as a strong influencing factor in his decision to join the Department of Ophthalmology led by Dr. Herbert E. Kaufman twenty years ago.

It is only through studies such as those funded by the Chair that discoveries about the mechanisms of blinding disease are made. Mr. Villere recognized the fact that retinal degenerations are a leading cause of blindness, and that the only way to prevent and treat these blinding diseases is through research. The findings from this research may eventually lead to the development of effective treatments, and perhaps even preventive regimens and cures, for these devastating diseases.

Dr. Donald L. Price, M.D.

*Professor of Pathology, Neurology, and Neuroscience
at The Johns Hopkins University School of Medicine,*

*Vice Chairman for Research in the Department of Pathology,
Director of the Division of Neuropathology,
Director of the Alzheimer's Disease Research Center,
Co-Director the Parkinson's Disease Research Center, and
Co-Director Amyotrophic Lateral Sclerosis Research Center at
The Johns Hopkins Hospital and The Johns Hopkins University School of Medicine*

Dr. Price received a B.A. in English Literature from Wesleyan University in 1956 and an M.D. from Albany Medical School, Union University in 1961. After an Internship and Residency in Internal Medicine, he completed a Residency in Neurology (including one year of Neuropathology) at the Massachusetts General Hospital (MGH), where he was Chief Resident in Neurology (1966). During the Viet Nam War, he was a Lieutenant Commander in the U.S. Navy serving as a Senior Staff Neurologist at Bethesda Naval Hospital (1966-68), where he cared for patients, including those from armed forces and government referred for complex neurological disorders. After finishing specialty training as Chief Resident in Neuropathology at the MGH (1968-69), Dr. Price completed his postdoctoral basic research training as a Research Fellow in Cellular/Molecular Neurobiology at Harvard University (1969-1970). Prior to his appointments at Johns Hopkins Medical Institutions (JHMI), he joined the Departments of Neurology and Pathology as an Assistant Professor of Neurology and Pathology at Harvard Medical School. Board-qualified in Internal Medicine and Board-certified in both Neurology and Neuropathology, Dr Price practiced neurology and neuropathology while an Assistant Professor in Boston.

Dr. Price has served as the Director of the Division of Neuropathology since 1971 and Director of the Alzheimer's Disease Research Center at JHMI since 1985. He is a Professor in the Departments of Pathology and Neurology (since 1971) and a Professor in the Department of Neuroscience (since 1983). More recently, he has served as Co-Director of the Parkinson's Disease Research Center and the Amyotrophic Lateral Sclerosis Research Center at JHMI.

A neurologist-neuropathologist-neurobiologist, Dr. Price has made important contributions to the understanding of a variety of diseases, particularly peripheral neuropathies, disorders caused by toxins (tetanus toxin, botulinum toxin), and, most significantly over the past two decades, neurodegenerative disorders like Alzheimer's disease (AD) and amyotrophic lateral sclerosis (ALS). Dr Price's major research interest is the analysis of animal models that can be used to examine pathogenic mechanisms to identify possible therapeutic targets and test novel therapies. These approaches have become particularly important with the recent progress in genomes of several species, the progress in identifying genes linked to disease, and the power of transgenic and knockout approaches to clarify biology of normal and abnormal gene products in vivo.

Dr. Price is the Principal Investigator of Centers, Program Projects, and R01 funded programs (all supported by NIH), as well as Director of two NIH-funded Neurobiology of Disease Training Programs. His research has received support from a number of private foundations and from the pharmaceutical and biotechnology industries. Under Dr. Price's mentorship, the Neuropathology Laboratory has produced many investigators who are now leaders in their fields. He is an author of over 400 publications in scientific journals and over 200 book chapters/reviews. According to *Science Watch* (12: 1-2, 2001), he was ranked in the top ten neuroscientists as Authors of High Impact Papers in Neuroscience during the "Decade of the Brain" (1990-2000).

LSU Neuroscience Center Welcomes Four New Faculty Members



Spotlight Interview with Anthony Ricci, Ph.D.

Dr. Anthony Ricci's area of specialty is single-cell electrophysiology and imaging. "I am interested in signal processing," says Dr.

Ricci, "primarily calcium regulation of signal processing in auditory sensory cells, called hair cells."

Dr. Ricci received his Ph.D. in Neuroscience from Tulane in 1992. Before returning to New Orleans as Assistant Professor for the LSUHSC Neuroscience Center and Kresge Hearing Labs in 1999, he was a post-doctorate fellow at the University of Texas Medical Branch at Galveston, and later at the University of Wisconsin.

It was in the University of Wisconsin's Department of Physiology where his research in calcium regulation in auditory hair cells began. At LSUHSC, Dr. Ricci's lab primarily focuses on signal processing at the hair bundle and the afferent synapse.

Dr. Ricci comments on why he selected the LSUHSC Neuroscience Center as the basis from which to continue this research: "The Neuroscience Center is a growing, vibrant environment with new investigators all at the cutting edge of their respective fields. It offered a chance to interact with both established investigators and new investigators."

He continues, "the Neuroscience Center is a growing resource with state-of-the-art laboratory space and all of the modern technologies available." This year Dr. Ricci, along with Dr. Jeff Magee, is developing a multi-photon imaging system that will be the first for both LSU and the state of Louisiana. "This was made possible by the leadership of Dr. Nicolas Bazan, whose unusual scientific insight led him to predict how the brain responds to sleep deprivation. Based on this new concept, he assembled a team of neuroscientists, and competed for and obtained a large grant from DARPA to tackle this fundamental problem. One by-product of all these efforts is the funding necessary to purchase the components of this powerful tool. In addition, these funds allowed us to visit the elite laboratories where this technology was developed, and have

provided the space and equipment for us to put this system together."

Of his joint appointment in Otorhinolaryngology and the Kresge Hearing Labs, he says that it "has made me a part of the long tradition of strong basic research in auditory physiology, and allows me to interact with some of the established investigators at the Kresge Hearing Labs."

One of Dr. Ricci's significant recent accomplishments has been to develop an isolated cochlear preparation for hair cell imaging in the intact epithelium. This preparation allows for the stimulation of the hair cells at the nanometer level, the recording of the hair cell's response, and for more quantitative investigations of these sensory cells.

Another of Dr. Ricci's achievements has been the characterization of a calcium-dependent tuning mechanism, located in the sensory hair bundle, that is responsible for hearing sensitivity. Any disturbance of this mechanism may lead to maladies such as temporary threshold shifts, noise-induced hearing loss, and tinnitus.

Several of Dr. Ricci's publications have received special recognition, including a cover for the *Journal of Neuroscience* and a perspective article in the *Journal of Physiology*. In 1999 he received a Young Investigator Award from the Deafness Research Foundation for a proposal to investigate mechanical tuning properties of sensory hair cells.

Future projects for Dr. Ricci's lab will include developing a cochlear culture system to investigate hair cell properties at the molecular level using viral transfection and gene gun technology. This technology will also allow for the investigation of ototoxic drugs and mechanisms of cell damage due to noise exposure.

Dr. Ricci is proud to be a part of an organization that is growing physically and financially, and also in reputation: "It is important to me to play a role in establishing this reputation, not just in the city or state, but across the country and internationally. As the center grows, we are the example that research of the highest quality can and does exist in Louisiana and at LSU."



Walter Lukiw, Ph.D.

Dr. Walter Lukiw has been jointly appointed as a Research Assistant Professor in the Neuroscience Center and Department of Ophthalmology since 1998. Prior to this appointment, he was an Instructor and Post-Doctoral Fellow from 1993 through 1998 for LSU Medical Center. He received his Ph.D. in Neuroscience and Human Physiology from the University of Toronto in 1992. Dr. Lukiw's experience spans molecular biology, biochemistry, basic neurosciences, and physiology. His main focus of attention is gene

regulation and its impairments in Alzheimer's Disease. Dr. Lukiw has successfully competed for an investigator-initiated competitive grant from the National Institute of Health on how genes are affected in Alzheimer's Disease. He has begun applying novel gene exploration technologies on brains from patients affected with Alzheimer's. He has discovered unique alterations during this disease that may become targets for the development of new drugs. Dr. Lukiw has been invited to speak at several national and international meetings in recognition for his contributions to the understanding of Alzheimer Disease's.



Gudiseva Chandrasekher, Ph.D.

Dr. Gudiseva Chandrasekher has over 15 years of experience in biochemical research. After receiving his Ph.D. in Biochemistry from the University of Mysore, India, in 1983, he completed a senior research fellowship on cataract formation for the Indian Council of Medical Research. A second fellowship with the Department of Biochemistry at the University of Melbourne, Australia, provided him with the opportunity to conduct research on lens crystallins and proteases.

Dr. Chandrasekher's career at LSUHSC began in 1996 as a research scientist in the Department of Ophthalmology.

Here he completed his post-doctoral training under Dr. Haydee Bazan in 1999. He is now jointly appointed as an Assistant Professor in the Department of Ophthalmology and in the Center.

His present research interest is the mechanics and cell formation of the ocular lens. Last year, he was awarded a 4-year NIH grant for the project, "Growth factor receptor-mediated signaling mechanisms in the lens." Dr. Chandrasekher explains that the goal of this research is to "unravel the basic mechanisms involved in the differentiation of lens epithelial cells during lens development, and to determine the molecular basis of human cataract formation."



Chu Chen, Ph.D.

Dr. Chu Chen is an Assistant Professor of Neuroscience and Otorhinolaryngology. He came to the Department of Otorhinolaryngology at LSUHSC as a post-doctoral fellow after earning his Ph.D. in physiology from Tulane University in 1993. He was then appointed to the position of instructor in 1995. In 1998, he joined the Neuroscience Center as an assistant professor.

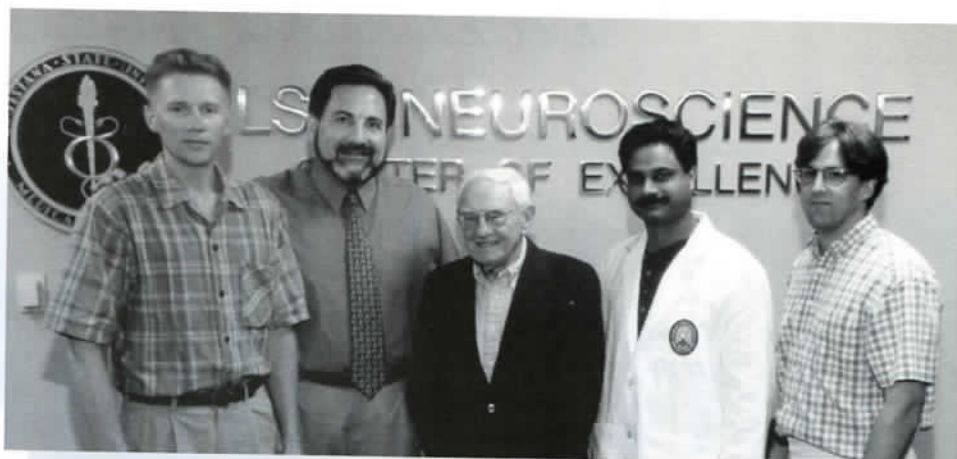
His current research interest is the study of the role of the enzyme cyclooxygenase-2 (COX-2) in long-term synaptic

plasticity in the hippocampus. "In the brain, COX-2 is thought to play an important role in inflammatory response," says Dr. Chen. "Growing evidence, however, suggests that the functional significance of COX-2 is far beyond that which was initially revealed, and that COX-2 may be involved in several neurological disorders, including stroke, seizures, and Alzheimer's disease."

Dr. Chen expects this research to further the understanding of physiological and pathological events mediated by COX-2, as well as the significance of prostaglandins in memory storage and neurological diseases.

Visitors

Jeffrey Erickson, Ph.D., Nicolas G. Bazan, M.D., Ph.D., Julius Axelrod, Ph.D. (National Institutes of Mental Health, Nobel Laureate in Medicine or Physiology, 1970), Rene Anand, Ph.D., and Jeffery Magee, Ph.D.



R. Ranney Mize, Ph.D., (Professor and Head of Cell Biology and Anatomy, Professor in Neuroscience), Iris Lindberg, Ph.D. (Professor of Biochemistry and Molecular Biology and Professor in Neuroscience), Edmond Fischer, Ph.D., (University of Washington, Seattle, Department of Biochemistry, Nobel Laureate in Physiology or Medicine, 1992).



Azucena Kakazu, Ph.D., Stanley B. Prusiner, M.D. (University of California, San Francisco, Nobel Laureate in Physiology or Medicine, 1997), Haydee E.P. Bazan, Ph.D., Austin J. Sumner, M.D. (Professor and Head of Neurology and Professor of Neuroscience), Paolo Ottino, Ph.D., Gudiseva Chandrasekher, P.D., and Faramarz Taheri, graduate student.

Dr. Eric Kandel (Nobel Laureate, 2000), Dr. Nicolas Bazan, and Dr. Paul Greengard (Nobel Laureate in Physiology or Medicine, 2000) during the Society for Neuroscience meeting in New Orleans.



Selected Recent Publications
of Neuroscience Faculty
located at the headquarters of the Neuroscience Center

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Current Grants

H. Bazan

Corneal Lipid Metabolism & Response to Inflammation, NEI, 1998-2003, \$966,512 (\$191,428 current year)
Cell Signal Transduction in Corneal Wound Healing, NEI, 1997-2002, \$1,060,623 (\$216,772 current year)
Signaling to genes: matrix metalloproteinases, Novartis, 2001, \$58,000

N. Bazan

Phospholipids & Arachidonic Acid in Epilepsy, NINDS, 1996-2002, \$1,231,402 (\$265,361 current year)
RPE Messengers, Transcription & Photoreceptor Renewal, NEI, 2001-2005, \$1,001,000 (\$250,250 current year)
Automotive Highway Research Initiative, Dept. of Transportation, 1999-2004, \$700,000 (\$174,200 current year)
Synaptic Plasticity Modifications, Gene Expression..., DARPA, 2001-2002, \$498,517
Micro/Nano Technologies in Neural Signaling, ..., EPSCOR - NSF, 2001-2004, \$2,775,000 (\$925,000 current year)

G. Chandrasekher

Growth Factor Receptor Mediated Signal Mechanisms, NEI, 2000-2004, \$705,669 (\$174,794 current year)

E. de Turco

Rhodopsin Trafficking & Photoreceptor Membrane Renewal, NEI (subcontract), 1999-2003, \$63,774 (\$12,744 current year)
 Novartis, 2001-2002, \$58,000

J. Erickson

Vesicular Transporter Specificity, NINDS, 1998-2001, \$810,972 (\$207,749 current year)
Vesicular Transporter Specificity, NINDS – Supp, 2000-2001, \$50,000

W. Lukiw

Gene Expression in Alzheimer's Disease, NIA, 2001-2006, \$1,188,690 (\$237,738 current year)
 Novartis, 2001-2002, \$58,000

J. Magee

Dendritic K⁺ & IH Channels in Hippocampal Neurons, NINDS, 1997-2001, \$362,125 (\$106,678 current year)
Dendritic K⁺ & IH Channels in Hippocampal Neurons, NINDS – Supp, 1999-2001, \$40,000
Dendritic Integration in Hippocampal Pyramidal Neurons, NINDS, 1999-2004, \$817,909 (\$142,062 current year)
 Sloan Fellowship, 1999-2001, \$35,000 (\$17,500 current year)

A. Ricci

Endogenous Factors Regulating Transducer Adaptation, NIDCD, 2000-2002, \$506,390
Endogenous Factors Regulating Transducer Adaptation, NIDCD – Supp, 2000-2002, \$19,770

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