News
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****Neuroscience research gains momemtum at UT Southwestern

Modern rehabilitation techniques, plus individual determination, can help stroke and paralysis victims overcome many obstacles. But they can only take people so far. The rest of the road to recovery will require new knowledge that can only be gained through basic scientific research.

That's why A. James Hudspeth, Ph.D., M.D., chairman of the Department of Cell Biology and Neuroscience at The University of Texas Southwestern Medical Center at Dallas, is eager to launch a major research effort on neural regeneration.

"We're already doing some top-notch research here," said Hudspeth, "but that's not to say we couldn't do more."

The $5 million being raised by the Kent Waldrep National Paralysis Foundation promises to help Hudspeth and his colleagues do much more. Already, more than $1 million has been raised. The Foundation's Texas Tycoon Gala, held Jan. 13 this year, raised more than $500,000 for neuroscience research. That amount is being matched by an anonymous donor. The funds will endow several new research positions in the area of neural development and regeneration and help

(More)

attract research leaders in those fields to the UT Southwestern faculty.

"Basic research into the activities of nerve cells, their interactions and internal circuitry is where breakthroughs are going to come from," Hudspeth said. "Currently, we're studying some exciting things, such as the pathways by which neurochemical signals travel from one nerve cell to the next or traverse the length of a single nerve cell. By studying the cellular agents involved in these processes, we are developing a better picture of what happens when the signals don't make it and how the systems are created and might be reconnected once severed."

UT Southwestern Medical School was established less than 50 years ago. In that short time, UT Southwestern has built a solid reputation for basic scientific research in areas such as arthritis, genetics, immunology, cardiology, mineral metabolism, nutrition, biochemistry, pharmacology, cell biology and reproductive endocrinology. The institution also is widely recognized for clinical advances in organ transplantation, heart surgery, neurological surgery, ophthalmology, orthopaedic surgery, head and neck surgery, burn and trauma care, plastic surgery and psychiatry. Wherever the faculty members at UT Southwestern have focused their energies, they have made significant progress. Hudspeth foresees similar success for the school's new neuroscience program.

He has assembled a team of scientists from various departments within the medical school to form the nucleus of the neuroscience program. Working together, these researchers hope to achieve

a greater understanding of how nerve cells develop and grow, how they connect with one another, how the biochemical exchanges that occur within and between cells keep nerves functioning normally, and how to repair and reconnect damaged nerve cells.

The basic research in neuroscience at UT Southwestern will complement the clinical work of UT Southwestern doctors in the centers for neurological diseases and neuromuscular disorders at the medical school and the following clinical settings: the stroke unit at Parkland Memorial Hospital, the Pauline Gill Sullivan Diagnostic and Treatment Center in Neurological Disorders at Zale Lipshy University Hospital, a newly established mobility research laboratory at the Dallas Rehabilitation Institute, and a 60-bed center for spinal cord injury that will be established at the Dallas Veterans Administration Medical Center during the early 1990s.

By 1995 two of six planned research towers will have been built on UT Southwestern's new North Campus. The neuroscience research group, by then doubled in size, will be housed in those buildings.

In addition to its involvement with the regeneration of the nervous system, UT Southwestern's neuroscience program will be a center for research in cellular biophysics, neurogenetics, and intracellular signaling.

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NOTE: The University of Texas Southwestern Medical Center at Dallas comprises Southwestern Medical School, Southwestern Graduate School of Biomedical Sciences and Southwestern Allied Health Sciences School.

A. James Hudspeth, Ph.D., M.D.
Chairman, Department of Cell Biology and Neuroscience
The University of Texas Southwestern Medical Center at Dallas

Hudspeth, co-editor and co-founder of the scientific journal **Neuron**, has been working in the field of neuroscience since his high-school days in Houston, when he served as a lab assistant for a neuroscience researcher. He came to UT Southwestern after having spent the last six years in San Francisco at the University of California School of Medicine as a researcher, professor and director of the Cell Biology program and vice chairman of the Physiology Department.

The primary emphasis of Hudspeth's research in recent years has been on the mechanism of hearing. He is an expert on the neurological activities that occur when hearing takes place. He hopes to find ways to prevent and treat the nerve damage that results in hearing loss.

A graduate of Harvard Medical School and of Harvard Graduate School and Arts and Sciences Department of Neurobiology, Hudspeth also received his bachelor's degree from Harvard. In 1975 he was awarded the W. Alden Spencer Award by the Center for Neurobiology and Behavior at the College of Physicians and Surgeons of Columbia University. The same year, he received the Dr. Harold Lamport Award for Young Investigators in Physiology or Biophysics from the New York Academy of Sciences.

NEUROSCIENCE RESEARCH AT UT SOUTHWESTERN

Summaries of neuroscience work being conducted at The University of Texas Southwestern Medical at Dallas:

Joseph P. Albanesi, Ph.D., Pharmacology Department

Nerves communicate with each other by producing biochemical signals that are secreted by one nerve and received by another. Dr. Albanesi and his research team are studying key steps and molecular components of the secretory process, in which the biochemical signals--commonly called neurotransmitters--are secreted into packets of membrane material within the cell, transported to the cell's outer membrane and released outside the cell. Return of the membrane packet to the cell's interior completes the process. Currently, the scientists are focusing particularly on

* kinesin, a protein that changes shape and thereby acts as a "motor" to move the membrane packets (called vesicles), using a biochemical called ATP as fuel.
* myosin I, another motor protein studied in micro-organisms and recently discovered by Albanesi and co-workers in cells from the brain and adrenal gland. The adrenal gland is stimulated by the nervous system and secretes hormones and neurotransmitters such as adrenaline (epinephrine) and norepinephrine.
* the central role of calcium ions in triggering secretion of neurotransmitters from the vesicles of the adrenal gland's chromaffin cells.

Francesco Belardetti, M.D., Pharmacology Department

Nerve cells have three types of ion channels in their membranes. One generates the electric signal that travels along a nerve when it is activated, one responds to neurotransmitters, and the third and more recently discovered type of channel responds to neurotransmitters indirectly and alters the electric signal as well as other general properties of the nerve cell. Dr. Belardetti and his co-workers are studying an example of the third type, a potassium ion channel called the S channel. The indirect action of neurotransmitters on this type comes through so-called "second messengers," biochemicals such as cyclic AMP that are produced inside a cell as a direct result of the action of a neurotransmitter with its receptor in the cell's membrane. The scientists' research deals with a number of second messengers that alter and regulate the S channel in different ways, thereby altering the nerve cell's activity and structure as well. Because neurotransmitters are signals from one nerve cell to another, this research may yield a better understanding of how the connections between nerve cells are controlled and altered.

Andrew L. Blatz, Ph.D., Physiology Department

Dr. Blatz and his colleagues are investigating the mechanisms responsible for activating nerve cells and their associated muscle cells. They are focusing on potassium ion channels whose activity is altered by calcium ions within the nerve cell. This type of ion channel is important because of its role in regulating repetitive firing and pacemaker activities in a wide variety of cells. Some of these potassium channels are also altered by interactions with the muscle cells that the nerves activate, a cell-to-cell interaction that may be of broad significance.

George S. Bloom, Ph.D., Cell Biology & Neuroscience Department
Dr. Bloom and his group are studying kinesin and other proteins responsible for the movement of vesicles and other organelles within nerve cells. The proteins are essential for movement along microtubules, with kinesin providing energy as a "motor." The scientists are particularly interested in learning how the action of kinesin is controlled and in further understanding the detailed structure of the microtubule system, the cell's "freeway system."

Scott Thomas Brady, Ph.D., Cell Biology & Neuroscience Department
Dr. Brady is also investigating kinesin and microtubules, working with Dr. Bloom in some of the research. Dr. Brady is focusing on the molecular mechanisms of the action of kinesin in the transport process. This process can be considered "fast," in contrast with a process of "slow" transport that is important for nerve cell growth and regeneration. Dr. Brady and his co-workers also are studying specialized microtubules and other components of the nerve cell's "cytoskeleton" involved in slow transport.

Alfred G. Gilman, M.D., Ph.D., Chairman, Pharmacology Department
In a series of fundamental studies for which he received Lasker and Horwitz awards for basic research in 1989, Dr. Gilman has produced an increasingly detailed understanding of the three-protein communications system by which cells respond to external signals such as neurotransmitters and hormones. The system regulates levels of cyclic AMP, calcium ions and other "second messengers" within nerve cells, which in turn influence ion channels and determine nerve cell activity in general.

A. James Hudspeth, M.D., Ph.D., Chairman, Cell Biology & Neuroscience
Hair cells in the inner ear convert mechanical stimulation by sound

vibrations or the head's movement into nerve signals to the brain. Dr. Hudspeth and his colleagues are studying the special opportunities hair cells offer for understanding nerve cell function at the molecular level, as well as how hair cell damage can be responsible for loss of hearing with age or exposure to loud sounds or certain drugs. Hair cells exhibit the same types of neurotransmitter and ion channel interactions and electrical responses as other nerve cells, plus special ion channels that open and close in direct response to movement of hair-like "stereocilia" that project from the cells' surfaces.

Flora Katz, Ph.D., Howard Hughes Medical Institute and Biochemistry Department

Dr. Katz and her colleagues are studying the gene-directed mechanisms that underlie nerve cell interactions to form the neural networks of the nervous system. Growth cones extending from immature nerve cells are a focal point for the development of connections between nerve cells in networks. One target of the scientists' research is a molecule on the surface of growth cones that seems to play a key role in guiding nerve cell growth. The group has found a mutant fruit fly that lacks the molecule and has distortions in its eye and central nervous system. The group is using other fruit fly mutants to identify additional genes and gene products responsible for nervous system connections.

Gregory A. Mihailoff, Ph.D., Cell Biology & Neuroscience Department

The basilar pontine nuclei, a large group of nerve cells in the brain, is a focal point for transfer of nerve impulses to the cerebellum, the part of the brain that controls muscle activity for the body's

movement. Dr. Mihailoff and his research team are investigating the molecular functions and circuit linkages of nerve cells in the basilar pontine nuclei. These studies are based in part on important differences among these cells in the neurotransmitters they produce and respond to. The scientists also are exploring how the cells develop, mature, and change their linkages.

Elliott M. Ross, Ph.D., Pharmacology Department

Dr. Ross and his co-workers are studying the protein receptors for neurotransmitters. These receptors are large molecules that bind with neurotransmitters at a nerve cell's outer surface, extend through the cell membrane, and activate other specialized proteins inside the cell to start a chain of reactions triggered by the neurotransmitter. The receptors are one of the three components of the communications system revealed in Dr. Gilman's research.

Martin H. Schaffer, M.D., Psychiatry Department

Dr. Schaffer and his co-workers are studying the synthesis of neurotransmitters in nerve cells. Their research includes identifying the genes that carry the information for the amino acid structure of several neurotransmitters. Based on their detailed understanding of the steps in the synthetic process, they intend to study how the synthesis is regulated and altered and to relate this to corresponding changes in nerve cells produced by the neurotransmitters.

Paul C. Sternweis, Ph.D., Pharmacology Department

G proteins, so-called because they are activated by guanosine triphosphate (GTP), are the second component of the three-component

cellular communications system identified by Dr. Gilman. Dr. Sternweis and his co-workers are investigating the central role G proteins play in transmitting external signals and regulating internal functions of nerve and other types of cells. They have isolated several new G proteins and subunits of these proteins, and are proceeding to look for the enzymes or other kinds of proteins on which these G proteins act. The proteins regulated by G proteins are the third component of the communications system. As new components are identified and isolated, the scientists plan to study the system by reassembling its components in test-tube experiments.

Thomas C. Sudhof, M.D., Molecular Genetics Department

Dr. Sudhof and colleagues are studying the molecular biology and gene-directed synthesis of the vesicles that transport neurotransmitters within nerve cells to be released through the cell membrane as signals to other nerves. Proteins in a vesicle's membrane play important and specific roles in neurotransmitter synthesis, uptake and storage; movement of the vesicle along a nerve cell's microtubules and other transport network components; fusion of the vesicle with the nerve cell's outer membrane and release of the vesicle's contents; and recycling within the cell to be filled and used again. The scientists expect that understanding these proteins will in turn yield a detailed understanding of the two known pathways for neurotransmitter secretion: a slow cycle (taking up to six months), in which vesicles return to and are refilled by the subcellular organelles where protein neurotransmitters are manufactured, and a fast cycle, in which vesicles at the nerve cell membrane are immediately refilled with amino acid neurotransmitters that the nerve cell does not have to

synthesize. The scientists will also study what happens if a neurotransmitter-filled vesicle is blocked or misdirected.

Gabriel H. Travis, M.D., Psychiatry Department

Alzheimer's disease, Huntington's disease and retinitis pigmentosa are among diseases in which nerve cells degenerate. In at least some instances, an inherited risk of developing the disease indicates that the patients' genes somehow functioned abnormally or failed to protect nerve cells from the underlying causes of degeneration. Dr. Travis and his research team are using the tools of molecular biology and genetics to identify and clone genes responsible for certain nerve degeneration conditions, particularly in the retinas of certain strains of mice. A defect-causing gene can then be used to identify the nerve cell molecules responsible for the degeneration and to indicate the roles they play in the functions of a nerve cell and its components. Dr. Travis intends to apply his techniques to the study of heritable human diseases as well.