RESEARCHERS & PHYSICIANS RECEIVE $9.1 MILLION
To Study Vascular Disease

LA JOLLA, CALIFORNIA Nov. 23, 1992 -- Investigators at The Scripps Research Institute (TSRI) in La Jolla, California have been awarded $9.1 million by the National Heart, Lung and Blood Institute of the National Institutes of Health (NIH) to develop new approaches to the diagnosis and treatment of vascular diseases such as stroke and heart attack.

The project, which is funded for a seven-year period, will be a collaborative effort of scientists at TSRI and physicians at Scripps Clinic and Research Foundation and the VA Hospital in La Jolla.

"The project will include everything from fundamental research into the basic mechanisms of cell growth and adhesion, to studies in mice, and eventually to the patient’s bedside," said the study’s principal investigator Mark Ginsberg, M.D., a member of TSRI’s Committee on Vascular Biology.

Carol H. Letendre, Ph.D., associate director for scientific programs at the NIH Division of Blood Diseases and Resources, says the Scripps program was chosen for funding "because of the excellent science proposed and the quality of investigators."
She said the Scripps award is part of a national seven-year, $56.9 million project to fund programs that combine basic research and clinical medicine to improve vascular health.

Additional research/medical centers to receive grants were the Center for Blood Research and Brigham and Women's Hospital, both affiliated with Harvard University; Stanford University; the University of Alabama; and Emory University in Georgia.

According to Ginsberg, the Scripps researchers will investigate the molecular mechanisms of cell adhesion, the process by which cells assemble to form tissue. In addition to basic studies in such areas as structural analysis, gene expression and intracellular signaling, the researchers will conduct clinical studies.

David J. Loskutoff, Ph.D., of the TSRI Committee on Vascular Biology says he will head a group that will "measure the expression of adhesion molecule genes in diseased human tissue and in the tissue of mice that have been bred to inappropriately express these genes."

"The inappropriate expression of these genes in man may contribute to the pathogenesis of human vascular disease. Thus, we are trying to determine when and where these genes are normally expressed," Loskutoff said. "We will then attempt to relate changes in the level of expression of these genes to the disease process."
TSRI researchers will also continue on-going research of anti-thrombotic agents. Since 1985, Zaverio M. Ruggeri, M.D., of the TSRI Committee on Vascular Biology, has been interested in the mechanisms and processes that normally lead to the arrest of bleeding but may underlie thrombosis -- the dangerous formation of blood clots.

"Over the years, we’ve identified one of the specific pathways that may lead to arterial occlusion and we’ve designed an inhibitor that would prevent an acute problem," Ruggeri said.

Although most people past the age of 40 have arterial atherosclerotic plaques, they have no problems unless an "acute event involving blood platelets occurs," according to Ruggeri. "The molecular inhibitor that we’ve designed will block aspects of platelet function that are involved in acute events. Within the next few months, we expect approval from the Federal Drug Administration for clinical trials at Scripps Clinic."

Another member of the project team for the NIH grant will be Eugene Bernstein, M.D., Ph.D., a member of Scripps Clinic’s Division of Vascular and Thoracic Surgery. He said the role of clinicians in the project will be "to help the basic scientist orient the current and future applications of their work towards clinical problems in diagnosis and management."

In addition to helping with clinical trials of new diagnostic techniques or therapies, Scripps Clinic physicians will obtain samples of both healthy and diseased vascular tissue from patients "to build a library of human vascular tissue so researchers can better understand the mechanisms of the disease process," Bernstein said.

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Another phase of the clinical studies involves restenosis in angioplasty patients. Restenosis is the gradual narrowing of blood vessels that occurs over three to six months in 30-40 percent of patients who have had a balloon angioplasty procedure to open a blood vessel blocked by plaque.

Allen D. Johnson, M.D., head of Scripps Clinic’s Division of Cardiovascular Diseases, noted that "understanding the mechanism of restenosis is of overwhelming importance to the cardiologist. Solving this problem is one of our highest priorities."

Also working on the restenosis problem will be William Penny, M.D., director of the cardiac catherization laboratory at the VA Hospital in La Jolla and an assistant professor of medicine at UCSD.

"By determining how restenosis happens, we hope to design new strategies or medications to prevent it," Penny said.

Additional project participants will include TSRI researchers Dario Altieri, M.D.; Joseph Loftus, Ph.D.; Nora Sarvetnick, Ph.D.; and Martin Schwartz, Ph.D.

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