SOUTHWESTERN NEWS

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UT SOUTHWESTERN NOBEL LAUREATE LEADS BOLD PROJECT CHANGING WAY SCIENTISTS CONDUCT RESEARCH

DALLAS – Sept. 5, 2000 – Nobel laureate Dr. Alfred Gilman, chairman of pharmacology at UT Southwestern Medical Center at Dallas, will lead a $10 million-per-year project allowing researchers around the world to pool their efforts in studying one of the biggest unsolved problems in biomedicine -- how cells interact with, or signal, each other.

Work of these Alliance for Cellular Signaling (AFCS) researchers in the post-genome era ultimately could lead to the development of a "virtual cell" that could be used to test new drugs.

The 10-year project has these unique features:

- It breaks new ground in medical research by teaming up large numbers of scientists via the Internet, where new discoveries will be posted as they are made;
- AFCS participants will relinquish intellectual property rights on scientific discoveries. Universities and researchers normally claim those rights in hopes that the research will quickly have practical applications.

The AFCS involves 20 universities and 50 participating investigators: 48 in the United States, one in Canada and one in the United Kingdom. In addition, more than 250 scientists worldwide have joined the Alliance as members, hosting Web sites called "molecule pages" that will be important components of the Alliance's public database. The National Institute of General Medical Sciences (NIGMS), part of the National Institutes of Health, anticipates spending a projected $25 million over the first five years to the AFCS. The federal government, pharmaceutical companies, private donors and several academic institutions are involved in the partnership and will provide additional funding during the first five years. Gilman said the remaining five years of the plan would be funded by further grants.

Gilman will serve as chairman of the steering committee.

The focus of the AFCS is to study cell signaling, the way cells communicate with each

(More)

other to determine their functions and actions. Gilman was awarded the 1994 Nobel Prize in physiology or medicine for his work with G proteins, which serve as a crucial part of this "cellular switchboard."

Multicellular organisms, such as mammals, have many different types of cells whose activities have to be coordinated so the organism can function efficiently.

"If the brain needs sugar, the liver has got to put it out. If the muscles need more blood, the heart has got to beat faster," Gilman said. "Hundreds of different chemical signals flow around the body, released from one cell to influence the activities of other cells. Cells are constantly being bombarded with very large numbers of chemical signals that tell them what to do and how to perform."

Previous studies have looked at individual pathways in cells, but the interaction among the pathways and among the cells has not been researched as intensely.

"The bigger problem, and the one that is most difficult to figure out, is how all of these modules interact together," Gilman said.

The AFCS will help investigators understand the global properties of cellular signaling. The research could lead to the development of a "virtual cell," a computer program that would mimic the function of a cell, Gilman said.

"When we have a complete virtual cell, it can be used as a drug discovery engine to test drugs on the computer, rather than on cells or animals. It would be a wonderful way to understand what the optimal point would be to place a drug to achieve a specific goal in a specific patient in a specific kind of disease," Gilman said.

AFCS researchers will focus on two kinds of cells, both from mice: the cardiac myocyte, the primary contractile cell in the heart; and the B-lymphocyte, a major cell that synthesizes antibodies in the immune system.

The researchers and universities involved have relinquished intellectual property rights to findings, so information will be made public as it is discovered and verified. The results of related studies will be available on the Internet (http://afcs.swmed.edu) on molecule pages maintained and updated by AFCS investigators.

Planning for AFCS began in 1999 after the NIGMS started a series of meetings to discuss

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"new ways to do science in the post-genome era," said Gilman.

NIGMS has called the AFCS funding "glue grants – grants to glue together different sorts of people for a common goal," Gilman said. "We actually are gluing together people's brains and their ideas, but the research is not going to be done in their individual labs."

Instead, the researchers will use the Internet as their joint laboratory.

"This is all Internet-enabled, and we're going to meet by the Internet. We'll have audiovisual conferencing systems, so I'll have a computer here where I can meet with up to 36 people. We can see each other, hear each other and share any computer applications," Gilman said. "This will be on Internet 2, a whole new university-based Internet that has a lot of bandwidth and ability to transmit lots of data very quickly."

Dr. Rochell Long, a pharmacologist with the NIGMS, said, "Advances in genomics, proteomics and informatics make the timing right for this bold experiment in how science is conducted. Al Gilman's vision is to transform the way cell signaling research is done, and he's dedicating his career from this point forward to making this work."

The researchers will do most of the experimental work in six or seven laboratories that will belong to the AFCS. A faculty member at each participating institution will be in charge of oversight of the lab. Three of the labs will be at UT Southwestern.

In addition to UT Southwestern, institutions hosting the main laboratories for AFCS are the California Institute of Technology, San Francisco Veterans Affairs Medical Center, Stanford University and the University of California, San Diego. Sixteen researchers from UT Southwestern are participating in AFCS.

Additional funding is coming from pharmaceutical companies and not-for-profit organizations including Eli Lilly and Co., Johnson & Johnson, Merck Genome Research Institute, Novartis Pharmaceuticals Corp., Chiron Therapeutics and Aventis, which will each provide about $500,000 per year for the first five years; and the Agouron Institute.