SOUTHWESTERN NEWS

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RESEARCHERS TO STUDY GENE COMMUNICATION

DALLAS — August 22, 1997 — Researchers at UT Southwestern Medical Center at Dallas received a grant from the National Institutes of Health (NIH) to develop technology that will uncover networks of gene interactions. Technology that shows how genes are interconnected will lead to a better understanding of disease processes, which will enable the development of new diagnostic methods and new therapies.

The NIH awarded a three-year grant of nearly $1 million to Dr. Ronald Butow, professor of molecular biology and oncology, and colleagues Drs. Glen Evans, H. "Skip" Garner, and Kenneth Kupfer of the UT Southwestern Eugene McDermott Center for Human Growth and Development to work on the project.

They are using the yeast *Saccharomyces cerevisiae* as a model system because, as a result of a recently completed international effort, the sequences of the entire genome containing 6,200 genes are known.

The project can be broken down into three general parts: the microdisplay of representatives of all 6,200 yeast genes arrayed on a "chip"; the biological experiment itself in which yeast cells with an altered gene are grown under different physiological conditions and the messenger RNAs from these cells collected, copied and tagged; and the analyses of these tagged copies by "reading" their interaction with the gene sequences on the microdisplay. The results will show which genes the altered gene communicates with.

"Then we can ask the question: 'If you modify the expression of one gene, how does this impact on all the rest of the genes?'" said Butow, holder of the Beatrice and Miguel Elias Distinguished Chair in Biomedical Science.

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Evans, head of the genome project at UT Southwestern and director of the McDermott Center, will synthesize representatives of all the yeast genes. Garner, professor of biochemistry and holder of the Philip O'Bryan Montgomery Jr., M.D., Distinguished Chair in Developmental Biology, is developing robotic technology to put the genes on chips and a high-resolution laser scanning device that will allow the analysis of chip results; at present the technology exists for only one variable. Butow will do the biological experiments and label the resulting messenger RNA copies with fluorescent tags. Kupfer, assistant professor of molecular biology and oncology, is in charge of data acquisition and analysis. He will develop the computer algorithms necessary to analyze the data and output it in a manageable form.

These complex experiments, which are large in scope, will be done on a microscope slide, and the results will be available a short time later. Previously, these types of experiments were impossible.

Although these experiments will be done in yeast, the technology may eventually be directly applicable to humans, who have 100,000 genes — 16 times that of yeast. Instead of looking at all 100,000 human genes, investigators may examine smaller gene groups to decipher specific networks to uncover, for example, which gene alterations precede the onset of a specific disease.

"The functional analysis of entire genomes, rather than single genes, is the logical sequel to the human genome project. Being able to rapidly access 100,000 genes on a DNA microchip will have an enormous impact on the medical practice of the 21st century," said Evans, who holds the Eugene McDermott Distinguished Chair for the Study of Human Growth and Development.

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