SOUTHWESTERN NEWS

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FASTER METHOD FOR CREATING ANTIBODIES IN MICE DISCOVERED BY UT SOUTHWESTERN RESEARCHERS

DALLAS – Aug. 11, 2003 – Researchers at UT Southwestern Medical Center at Dallas have discovered a system to create antibodies in mice up to 10 times faster than previous laboratory techniques allowed.

Their findings, to be published in the September issue of *Nature Biotechnology* and available online today, describe a new high-speed throughput system for making antibodies, which bind to proteins. Antibodies help scientists better identify and measure human proteins, the workhorses of cells that also serve as markers for disease, by causing measurable chemical reactions, said Dr. Ross Chambers, assistant professor of internal medicine and an investigator in UT Southwestern's Center for Biomedical Inventions (CBI).

"Antibodies are the most commonly used reagents to measure proteins in humans, but antibodies, up to now, have been very complicated and expensive to create," said Dr. Chambers, co-author of the *Nature Biotechnology* study. "Because of that, antibodies on the market today target only about 4,000 proteins, which is only a small fraction of the hundreds of thousands of proteins in the human body."

Many of the antibodies that scientists currently create are of poor quality, Dr. Chambers added. Ineffective antibodies are the hold-up in many areas of research, he said.

"We wanted to develop a system that could use all the sequence data being produced by the genomic revolution to produce antibodies for the proteomic revolution," said Dr. Stephen Albert Johnston, director of the Center for Biomedical Inventions and co-author of the paper. "Dr. Chambers and his group combined several inventions we had made earlier and added some more bells and whistles to make antibody production systematic."

In 1992, CBI researchers led by Dr. Johnston invented genetic immunization that now allows scientists to inject genes rather than proteins into animals to produce an immune response to a particular protein. They also developed a technique called "linear expression elements" in

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1999 that allows them to avoid cloning, a multi-step and time-consuming process.

"To produce antibodies, we can go directly from sequence on a computer screen to a robot and then to an animal," said Dr. Johnston, professor of internal medicine and microbiology.

The standard method to make antibodies is to clone a gene, produce and purify the protein corresponding to the gene and then inject the protein into an animal. The process takes weeks to complete. The method the CBI scientists developed consists of chemically synthesizing the gene and then injecting this directly into the animal. The process takes a few days, and many genes can be done at once.

"We have also found elements to put into these gene vaccines that make the immune response much more potent and high quality," Dr. Johnston said. "A surprising result was that we could even make mice make antibodies to their own proteins.

"We think this system could be used to make antibodies to all the proteins in the genome."

Scientists also believe this type of antibody production could play an important role in a new approach to diagnostics called biosignatures, whereby hundreds of proteins in a small amount of blood are analyzed so that doctors can detect a disease even before symptoms manifest themselves. The facile production of antibodies could make this type of diagnostic strategy practical.

"Our focus in CBI is on using this technology to advance biosignatures diagnostics," Dr. Johnston said. "We also hope these antibodies will contribute to discoveries that drive new advances in disease treatment."

The National Heart, Lung and Blood Institute's Program in Genomic Applications is supporting this high-speed throughput system as a resource for researchers needing antibodies. Researchers can go to the CBI's Web page, http://pga.swmed.edu/, and order a free pre-existing or new antibody.

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