SOUTHWESTERN NEWS

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UT SOUTHWESTERN EYE RESEARCHERS TEST ORAL VACCINE THAT PREVENTS CORNEAL-TRANSPLANT REJECTION

DALLAS — September 20, 1997 — Ophthalmologists at UT Southwestern Medical Center at Dallas have developed an oral vaccine that may prevent rejection of corneal transplants, the most common type of tissue transplant.

About 40,000 corneal transplants are performed in the United States each year with a success rate approaching 90 percent; however, UT Southwestern ophthalmologists are conducting research to help the 10 percent who continually reject corneal transplants. The ophthalmologists are perfecting a novel oral vaccine that slowly trains the recipient's immune system to accept donated corneas.

"Even in the face of powerful immunosuppressive drugs that are used to downgrade the immune system, some people still reject their first corneal transplant. For these patients, rejection of subsequent corneal transplants skyrockets," said Dr. Jerry Niederkorn, professor of ophthalmology and microbiology. "This is why we are trying to find out if we can induce a tolerance in cornea recipients without having to indiscriminately use drugs to turn off the entire immune system."

Niederkorn published results of his ongoing laboratory study in this month's issue of the *British Journal of Ophthalmology* and is presenting his research findings at the national meeting of Research to Prevent Blindness in Los Angeles Sept. 20-24.

Although the premise of oral vaccination seems simple, the immune system and the specific immunological mechanism Niederkorn's team is targeting are complex. The oral-vaccination method involves feeding processed corneal cells from donor corneas over a period of time to the recipients, which at this point are laboratory mice. The study subjects are fed the processed cells via a liquid, which contains alloantigens (special proteins made on the surface of cells) from a donor cornea. Alloantigens normally provoke robust immune

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responses that lead to quick and complete rejection of many types of transplants.

Niederkorn's work showed that in the absence of immunosuppressive drugs, like those normally given to tissue- and organ-transplant recipients, unvaccinated study subjects rejected 100 percent of the corneal transplants. "However, subjects fed either corneal cells or blood cells from prospective donors prior to receiving corneal transplants had a remarkable reduction in corneal-graft rejection," Niederkorn said.

Study subjects that were fed the processed cells, but not given immunosuppressive drugs, rejected the transplants only 55 percent of the time. This proved that the slow buildup of the foreign alloantigens apparently trains the body to accept the transplanted cells as its own.

"Only the immune response to the donor-tissue antigens is turned off. The recipient's capacity to respond to pathogens and other environmental agents is preserved," said Niederkorn, who is the George A. and Nancy P. Shutt Professor in Medical Science.

Niederkorn and his team next chemically modified the cells in the oral vaccine and were able to reduce the rejection rate to 9 percent. They also found that skin cells could be used to promote corneal graft survival, which is beneficial because skin can be cultured and precious donor corneas don't have to be broken apart by researchers.

One obstacle Niederkorn had to overcome was that nutrients passing through the gastrointestinal tract are sometimes excreted from the body without being absorbed. Niederkorn and his colleagues solved this dilemma by attaching the alloantigens to neutralized cholera toxins. These harmless toxins contain receptor molecules that help them bind to specialized intestinal cells, which helps the alloantigens get transferred into the bloodstream.

The next step is to test the vaccine in humans, and Niederkorn believes it will be successful.

"That would be good news for corneal-transplant recipients who continually reject corneas," he said.

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