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UT Southwestern researchers uncover likely source of rejection for otherwise well-matched kidney transplants

DALLAS – Sept. 26, 2007 – UT Southwestern Medical Center researchers, collaborating with colleagues in Germany, have for the first time identified antibodies associated with transplant rejection of otherwise healthy kidneys.

For years, physicians have been perplexed as to why some seemingly well-matched kidneys were still rejected. The collaborative effort has turned up a likely culprit – antibodies that aren't targeted by current testing methods.

The research appears in the Sept 27 edition of the *New England Journal of Medicine*, along with an accompanying editorial.

The antibodies in question attack a naturally occurring antigen called MICA, which is found in endothelial cells. The endothelium is the layer of cells lining the inside of the blood vessels. Each person has one or two of the more than 60 varieties of MICA antigens currently known.

“When you put a transplant in, the blood of the new host comes into contact first with the endothelium of the donor organ. That's where the host first meets the donor and where rejection starts,” said Dr. Peter Stastny, professor of internal medicine, chief of transplant immunology and an author on the study.

“The bottom line is that the data suggests that failure of otherwise well-matched kidneys may be caused by these antibodies. We are not saying that all such kidneys fail because of antibodies against MICA, but this may be part of it,” he said.

Dr. Stastny believes more research will be needed to show whether this is the direct cause, but the results offer critical direction in finding new explanations of why good transplants go bad and discovering potentially new avenues for screening to prevent rejection of transplanted kidneys.

Available kidneys remain in short supply, and more than 73,000 people await kidney transplants in the U.S., making successful transplants critical. Roughly 14,000 transplants were performed during

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the first half of 2007.

In Texas, about 600 kidney transplants have been performed this year. Between 89 percent and 95 percent of transplanted kidneys continue to function one year after the operation, according to the National Kidney Foundation.

UT Southwestern researchers became interested several years ago in the possibility that there might be some antigens in the kidney that were not present on lymphocytes, which are the cells used for typing and cross-matching for kidney transplants. Lymphocytes are white blood cells that carry out the body's immune response.

"If the antigens are not present on the lymphocytes, then the usual lymphocyte cross-match would not detect such antibodies," Dr. Stastny said.

Researchers first had to confirm that the antigens were present in the kidneys, then follow enough cases to determine whether the antibodies against MICA antigens correlated with rejection of otherwise healthy kidneys. For that, UT Southwestern investigators collaborated with researchers at the University of Heidelberg, which maintains a large depository of data and samples on transplant cases.

"They were able to provide a large number of samples – 1,910 – all taken before the transplant, so we were able to analyze them with our MICA antibody assay," Dr. Stastny said. "We found that there was a strong correlation. The presence of the antibodies against MICA was associated with earlier rejection of the kidney grafts.

"It doesn't prove that the antibody causes the rejection, but it suggests it."

In addition, researchers discovered that the patients who were considered a good risk in clinical transplantation were the ones who showed the most marked effect of these antibodies against MICA.

Dr. Yizhou Zou, assistant professor of internal medicine at UT Southwestern, was the first author on the study.

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