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GENE TEST DETERMINES TRANSPLANT DRUG TOLERANCE

Test Could Affect Dosing and Raise Benefits, Lower Side Effects

Washington, DC (May 19, 2009) — A simple genetic test can determine a kidney transplant patient's tolerance for a potent anti-rejection medication, according to an upcoming study in the *Journal of the American Society Nephrology* (JASN). The test could allow doctors to individualize each patient's dose, optimizing the drug's benefits and minimizing its side effects.

Cyclosporine A is an important immunosuppressant therapy for individuals who receive kidney transplants—without it, many patients would experience organ rejection and would not survive. Unfortunately, cyclosporine A can cause serious side effects such as elevated blood pressure, increased risk of infections and cancers, and kidney function deterioration. The frequency and severity of cyclosporine A-related side effects vary among patients, even at comparable cyclosporin A levels in the blood. Determining which patients are more sensitive than others is a challenge for physicians who prescribe the medication.

Giuseppe Remuzzi, MD, FRCP, and Piero Ruggenenti, MD (Mario Negri Institute for Pharmacological Research, Italy), and their colleagues, hypothesized that genetics may influence patients' susceptibilities to cyclosporine A's side effects. In particular, they suspected that variations in a gene called *ABCB1*, which creates a protein that transports drugs out of cells, may play a role. In individuals who have certain genetic changes in the *ABCB1* gene, the transporting protein is sluggish so that when a drug is present, it lingers within cells and tissues. This can amplify the drug's effects.

After studying the genetics of 147 kidney transplant recipients, the researchers found that patients with these genetic changes in the *ABCB1* gene were more likely to experience side effects after receiving cyclosporine A than patients without the variants. These effects included delayed functioning of the transplanted kidney, increased need for anti-hypertensive medications, and the development of diabetes, infections, and cancers.

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"The identification of particular genetic variants performed before transplantation, while patients are on the waiting list, could provide useful information to tailor cyclosporine A dose as early as possible after transplantation, with the ultimate goal to decrease toxicity, improve efficacy, and increase long-term graft survival," said Dr. Remuzzi.

The authors report no financial disclosures.

The article, entitled "ABCB1 Genotypes Predict Cyclosporine-Related Adverse Events and Kidney Allograft Outcome," will appear online at http://jasn.asnjournals.org/ on May 21, 2009, doi 10.1681/ASN.2008080819.

ASN is a not-for-profit organization of 11,000 physicians and scientists dedicated to the study of nephrology and committed to providing a forum for the promulgation of information regarding the latest research and clinical findings on kidney diseases. ASN publishes JASN, the *Clinical Journal of the American Society of Nephrology* (CJASN), and the *Nephrology Self-Assessment Program* (NephSAP). In January 2009, the Society will launch *ASN Kidney News*, a newsmagazine for nephrologists, scientists, allied health professionals, and staff.

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