Breakthrough in organ rejection diagnosis examines gene behavior

November 19 2007

A new article appearing in *American Journal of Transplantation* describes a revolutionary technique for more clearly identifying the possibility of organ rejection in kidney transplants. The technique, which uses a microarray or "Gene Chip," a process of examining DNA sequences, defines how major causes of organ disease leading to rejection share similar disturbances in gene behavior.

The study is the first to show how gene sets, as opposed to single genes, can be used for diagnosis of rejection in individual patients, and offers new insight into the mechanisms of these gene changes.

"The key problem in transplantation is to diagnose rejection. This has traditionally been done with the microscope by reading the appearance of the tissue. We are showing how this can be performed by reading the changes in expression of genes, and in particular, expression of sets of genes," says Philip F. Halloran, M.D., lead author of the study and Editor-in-Chief of American Journal of Transplantation. "This is a more objective and accurate method of identifying the possibility of organ rejection."

The authors established sets of genes – transcripts sets – based on disease pathogenesis. They found a threshold for expression below which the studied biopsies did not show evidence of rejection. The findings displayed a series of major biologic indicators that occur before and during organ rejection. The results showed that previous histologic criteria, particularly relating to the cut-off between borderline organ

acceptance and rejection, are unreliable.

The gene behaviors identified showed strong correlations, indicating that disturbances leading to transplant rejection have stereotyped structures. Samples from the study that lacked these disturbances did not lead to organ rejection.

The features of this structure are also found in lower levels in many forms of organ disease and injury. “The system of reading biopsies that was developed in the study can be used with to help understand a variety of disease processes,” says Halloran.

Source: Blackwell Publishing Ltd.