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Study: Transplant Success Linked to Immune Molecule Levels

A study recently published in the Journal of Immunology Research reports that patients with highest levels of the most powerful version of the immune molecule HLA-G seem to have the lowest risk of rejecting their transplanted kidney.

Dr. Anatolij Horuzsko, immunologist at the Medical College of Georgia at Georgia Regents University and the study's corresponding author, explained that the study included 67 transplant patients, among them 17 with chronic rejection and the remaining 50 with no evidence of rejection, and pointed out that those patients who tolerated their transplant best were those with naturally high levels of HLA-G dimer, where two of the immune molecules bind together.

Dr. Laura L. Mulloy is Chief of the MCG Section of Nephrology, Hypertension and Transplantation Medicine and a co-author of the study. She said that knowing exactly which form of HLA-G associates with maximum transplant success would allow physicians to improve the fine balance of prescribing patients sufficient immune-suppressive drugs to keep a donated organ without significantly increasing the risk of cancer and infection.

Dr. Mulloy made clear treatment was improved when it is known a patients has naturally higher levels of HLA-G dimer, as they might need less immunosuppression. This is turn signified less toxicity, less drug complications and less cost she added, whereas patients with low levels might benefit from higher drug doses.
An additional correlation was seen in lower levels of inflammation, an immune response that can lead to rejection.

Acknowledging that greater patient numbers were needed, the researchers' findings have however continued to hold true in more than 150 kidney transplant patients at Georgia Regents Medical Center to date.

Horuzsko added that higher HLA-G levels also have been found in the blood of successful transplant patients, having previously been associated with successful pregnancy, HIV infection, and some cancers. Researchers now know that some transplant patients generate higher levels of this powerful HLA-G package.

In fact, HLA-G was thought to exist only as a single molecule until about five years ago, Horuzsko said. Functional assay technology has shown that if positioned just right, two molecules can connect and yield even more powerful tolerance. The tradeoff however, is that the coupling makes HLA-G dimer more fragile so Horuzsko and several biotech companies are working to develop a more stable version that could one day supplement low levels.

In the quest to avoid the body's rejection of a new kidney, a standard immunosuppressive cocktail is prescribed to transplant patients, yet the reasons why some transplants success and others fail are unknown. Mulloy highlighted that while vital, these drugs did increase the risk of other diseases, even proving to be toxic to a new kidney. A more natural and locally acting drug would be perfect according to her.

Ideally, HLA-G dimer should eventually be delivered directly to dendritic cells, which make decisions about what to attack and ignore. Horuzsko has already succeeded in delivering HLA-G carrying, degradable microparticles to mice with skin grafts to enhance tolerance.

It is hoped that this type of therapy would only be required for a few weeks until dendritic cells learn to ignore the new organ. Drugs also are available to boost expression of HLA-G receptors.

It is already customary for physicians to examine HLA, or human leukocyte antigen, when identifying the best organ donor. When a patient and donor have the same or similar antigens, which are markers for what the body identifies as self and foreign, it increases the chance of a successful transplant.

Image caption: Dr. Laura L. Mulloy, Chief of the MCG Section of Nephrology, Hypertension and Transplantation Medicine and Dr. Anatolij Horuzsko, immunologist both at the Medical College of Georgia at Georgia Regents University.
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