

# Transplant success tied to naturally high levels of powerful immune molecule package

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This is 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. Credit: Phil Jones

Patients with highest levels of the most powerful version of the immune molecule HLA-G appear to have the lowest risk of rejecting their transplanted kidney, researchers report.

A study of 67 transplant patients – 50 with no evidence of rejection and 17 with chronic rejection – showed those most tolerant of their kidney

had naturally high levels of HLA-G dimer, where two of the immune molecules bind together, said Dr. Anatolij Horuzsko, immunologist at the Medical College of Georgia at Georgia Regents University.

Knowing which form of HLA-G correlates with optimal transplant success could enable physicians to further tailor the delicate balance of prescribing patients sufficient immune-suppressive drugs to keep a donated organ without significantly increasing the risk of infection and cancer, said Dr. Laura L. Mulloy, Chief of the MCG Section of Nephrology, Hypertension and Transplantation Medicine.

"If we know a patient has naturally [higher levels](#) of HLA-G dimer they might need less immunosuppression which means less toxicity, less drug complications, and less cost," said Mulloy, a co-author of the study in the *Journal of Immunology Research*. Conversely patients with low levels might benefit from higher drug doses. "With this information, you can better customize and tailor-make your immunosuppressive cocktail."

High levels of HLA-G dimer also correlated with lower levels of inflammation, an immune response that can lead to rejection. The most successful transplants also had higher levels of HLA-G receptors, noted Horuzsko, the study's corresponding author.

While larger patient numbers are needed, the researchers' findings have continued to hold true in more than 150 [kidney transplant patients](#) at Georgia Regents Medical Center to date.

High HLA-G levels are known to correlate with successful pregnancy, HIV infection, and some cancers; low levels correlate with chronic miscarriages. Higher HLA-G levels also have been found in the blood of successful transplant patients, but the specific type was unknown, Horuzsko said.

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.

Healthy individuals likely have very low levels of HLA-G dimer, which is part of the checks and balances of the immune response.

And, much as some fortunate people have naturally high levels of the good cholesterol, researchers now know that some [transplant patients](#) generate higher levels of this powerful HLA-G package, he said.

The tradeoff is 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.

Transplant patients are typically prescribed a standard immunosuppressive cocktail to avoid rejecting a new kidney and it's often unclear why some transplants fail and others succeed, Mulloy said. While necessary, the drugs increase the risk of other diseases and can even be toxic to a new kidney. A drug that worked more naturally and locally, "would be perfect," Mulloy said.

Horuzsko envisions HLA-G dimer eventually being delivered directly to dendritic cells, which make decisions about what to attack and ignore. He's already successfully delivered HLA-G carrying, degradable microparticles to mice with skin grafts to enhance tolerance. Ideally, patients would need such therapy only for a few weeks until dendritic cells learn to ignore the new organ. Drugs also are available to boost expression of HLA-G receptors.

Physicians already 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.

Provided by Medical College of Georgia

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