

Unexpected variation in immune genes poses difficulties for transplantation

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the genes that allow our immune system to tell the difference between our own cells and foreign invaders – are evolving much more rapidly than previously thought, according to an article online on August 3 in *Trends in Genetics*. The resulting degree of variation improves our ability to fight off disease, but could also present challenges to current worldwide efforts aimed at identifying potential donors for patients undergoing stem cell transplantation.

"This new work makes clear the daunting and near hopeless challenge of keeping track of the continuous output from the HLA mutational spigot," says first author William Klitz, from the University of California, Berkeley.

HLA proteins sit at the surface of human cells. Every individual has a specific HLA on the surface of their cells and these proteins effectively act as an identification card. Any other [cells](#) that have the same HLA on the outside are recognized as 'self'; foreign particles like bacteria or viruses are identified as invaders and the [immune system](#) kicks in to remove them. The same system that helps us fight off germs makes organ or stem cell transplantation difficult. Our bodies treat transplanted tissue as foreign and reject it. Unless, however, the patient and the donor share the same HLA [genes](#). As a result, worldwide efforts are underway to identify all possible HLA variants, in the hopes of more effectively matching patients with potential donors.

The difficulty is that within the human population, HLA genes are

mutating rapidly and Klitz estimates that more than a million variants exist in the current population. Trying to identify all the variants will be nearly impossible and ultimately pointless, according to Klitz, because of how quickly these genes are evolving. This rapid evolution is a boon in some ways because it means that, at the population level, our immune systems are getting better at fighting off pathogens. For transplant recipients, however, the most likely implication is that the best chance for a match will be found in first-degree relatives rather than in a worldwide search for donors.

More information: Klitz et al.: "New reservoirs of HLA alleles: Pools of rare variants enhance immune defense" *Trends in Genetics*, 2012.

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