



Recent Developments in Human Leukocyte Antigen Testing and Kidney Transplantation

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There is a new “minor antigen” gaining attention in the field of human leukocyte antigen (HLA) testing and kidney transplantation: the major-histocompatibility-complex (MHC) class I-related chain A, or MICA antigen. It is classified as a “minor antigen” because it is not an HLA antigen (ie, HLA-A, HLA-B, etc.). The major reason MICA has become a molecule of interest is related to the natural history of renal allograft survival.

While the one-year graft survival rates for living and/or deceased donor kidney transplants are approximately 90%, graft survival rates drop to about 80% at five years and to 50% or less at 10 years. Advances in both immunosuppression and HLA matching, particularly of HLA-A, HLA-B, and HLA-DR antigens, have contributed to improved graft survival and patient survival, especially within the first year. ABO blood group antigen matching has also improved graft survival. However, the long-term graft failure rates still remain a major problem in kidney (and other solid organ) transplantation. Some believe that antibodies to MICA antigens may play a significant role in acute and/or chronic graft rejection and therefore offer a new target for improving graft survival.

MICA antigens are encoded by a genetic locus located adjacent to HLA class I loci. The MICA locus encodes diverse antigens, which are similar in structure to HLA antigens. The function of MICA antigens, however, is believed to be much different from that of HLA antigens. MICA antigens are expressed on the cell surfaces of many types of cells (epithelial, endothelial, fibroblasts, and monocytes) and act as ligands for natural killer (NK) cells. However, while graft HLA antigens cause graft rejection through interaction with recipient alloantibodies or by presentation of peptides to recipient T-cells, graft MICA antigens are thought to cause NK cell activation. Studies have also shown that recipients with alloantibodies against MICA have sera, which are cytotoxic to cells expressing MICA.¹ Therefore, MICA antigens themselves may also be the targets of recipient alloantibodies. MICA antigens could thereby result in direct damage to the graft due to these anti-MICA antibodies.

Two recent studies have investigated the role of MICA antibodies in graft survival in kidney transplantation.^{2,3} Both have demonstrated poorer graft survival rates at one year post-transplant and also after longer follow-up (four to five years). Some laboratories have begun testing for anti-MICA antibodies and proficiency testing will be available soon through the College of American Pathologists (CAP). MICA antibody testing may show promise in improving graft survival, but the exact amount of clinical benefit it will provide is still unknown.⁴

References:

1. Stastny, P. Polymorphism and antigenicity of HLA-MICA. *ASHI Quarterly.* Second Quarter 2002:64–65.(Would author provide volume # and page #s?)
2. Terasaki PI, Ozawa M, Castro R. Four-year follow-up of a prospective trial of HLA and MICA antibodies on kidney graft survival. *Am J Transplantation.* 2007;7:408–15.
3. Zou Y, Stastny P, Susal C, Dohler B, Opelz G. Antibodies against MICA antigens and kidney transplant rejection. *N Engl J Med.* 2007;357:1293–300.
4. Flegel, WA. Will MICA glitter for recipients of kidney transplants? *N Engl J Med.* 2007;357:1337–9.