

Applicant's Name: Isamu Z. Hartman, B.S.

Applicant's Division: Immunology

“A Cell-Free Recapitulation of Antigen Processing For Class II MHC: HLA-DM is a Key Player in the Selection of Immunodominant Epitopes”

Isamu Z. Hartman¹, Wendell P. Griffith², Dongxia Wang², Suzanne Kalb², Kimberly M. Walter³, Robert J. Cotter², and Scheherazade Sadegh-Nasseri^{1,3}

¹ Graduate Program in Immunology, ² Department of Pharmacology and Molecular Sciences, ³ Department of Pathology, Johns Hopkins University School of Medicine, Baltimore, MD 21205

Background and Design: Rational design of immunotherapeutics relies on clear knowledge of the immunodominant epitopes of antigens. Predicting immunodominant epitopes solely through identifying kinetically stable peptide-MHC complexes yields false positives. Computational approaches for class II MHC epitope prediction have not been effective. We report the establishment of a reductionistic system incorporating known participants of MHC class II antigen processing including protein antigens, the human class II MHC molecule HLA-DR1, a selection of proteases, and HLA-DM. The ability to form an HLA-DM-resistant complex with class II MHC may be a characteristic that is crucial for a peptide to emerge as an immunodominant epitope. Bovine type II collagen and influenza hemagglutinin were used as model antigens.

Results and Conclusion: Peptides eluted from HLA-DR1 after these components were allowed to react with each other were highly enriched for proteolytic fragments of the model antigens containing their known DR1-restricted immunodominant epitopes. In the absence of HLA-DM, however, additional epitopes were co-isolated with HLA-DR1. This establishes HLA-DM-mediated editing as a significant contributor to immunodominance. This assay may be effective for the *de novo* identification of immunodominant epitopes from novel antigens.