



Medical Education and Research Grant Outcome Report

Name: Optimizing Immunosuppressant Therapy Based on Viral Genetics to Improve Hepatitis C Infected Transplant patient Outcomes

Principal Investigator: Robert Striker, MD, PhD, Assistant Professor

Phone/Email: 608-263-2994/rtstricker@wisc.edu

Department: Medicine – Infectious Disease

Program: New Investigator Program

Grant Duration: 02-01-06 to 02-29-08 (Completed 6-30-07) (17 months)

Expenditures: \$100,000 (100%)

Use of Funds (Taxonomy): Type 1 translational research

Research Keywords: Hepatitis C Virus, transplantation, immunosuppression, resistance, antiviral

► **Description:** Hepatitis C Virus (HCV) is a major cause of liver disease worldwide, and the most common reason for liver transplant and re-transplant in the United States. Clinical studies have shown that some immunosuppressant drugs can improve the outcomes for HCV infected patients, but there is no consensus about the optimal drug therapy. This project will allow development of molecular diagnostics to tailor immunosuppressant therapy to the specific HCV strain infecting a patient.

► **Contributions/Results:** Hepatitis C Virus is the single largest reason why liver cancer rates in Wisconsin are increasing. The virus also plays a minor role in the increasing incidence of nonhodgkins lymphoma in Wisconsin. The goal of this study was to tailor therapy for Hepatitis C virus (HCV) patients using a detailed understanding of viral genetics. The study mapped how mutations in HCV altered the susceptibility to a drug already used in HCV infected transplant patients, Cyclosporine. The results provide an independent supportive piece of evidence to controversial clinical data that cyclosporine does benefit certain HCV patients. The study accomplished two aims: Mapped the Cyclosporine resistant mutants (AIM1) and found no relationship between cyclosporine resistance and susceptibility to a second immunosuppressant azathioprine that we have discovered or interferon (AIM2)

► **Met Objectives:** Completed

► **Timeline for Application of Results:** 3-5 years

► **New partnerships or collaborations:** The study laid the foundation for a collaboration with UW transplant clinicians to look for cyclosporine resistance mutations in HCV infected transplant patients treated with Cyclosporine. The project developed a direct collaboration with the Infectious Disease Section in the Department of Medicine.

► **Contributions to the Transformation:** This project continues a long-standing tradition in the transplant program of translating basic science to the clinic.

► **Matched Dollars (cash or in-kind):** \$0

► **Dissemination:** Publication: Sensitivity of hepatitis C virus to cyclosporine A depends on nonstructural proteins NS5A and NS5B Fiona Fernandes 1, Daniel S. Poole 1, Spencer Hoover 1, Rannveig Middleton 1, Adin-Cristian Andrei 2, Justin Gerstner 1, Rob Striker 1, Hepatology Volume 46 Issue 4, Pages 1026 – 1033 Published Online: 28 Jun 2007

► **Additional Funding:** American Cancer Society 4 year grant for \$670,000.