Bankhead-Coley Cancer Research Program

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Biological Science — *2009 Program*
Florida State University — *Bridge (1-year project)*

Project Title: Cyclosporine, Cyclophilins, and HCV Replication

Project Summary: The long-term goal of our research program is to advance the knowledge of virus' host cell interactions that are relevant for liver cancer. Hepatitis C virus (HCV) infects 3 percent of the world's population and causes fibrosis, liver cirrhosis, and hepatocellular carcinoma (HCC), which is a malignant liver cancer that kills most patients within a year. There is no vaccine to prevent HCV infection, and the only FDA-approved treatment, interferon combined with ribavirin, faces serious drug-resistance issues. New classes of anti-HCV drugs are urgently needed. Cyclosporine A (CsA) and its derivatives represent promising candidates of such drugs and can be combined with the current interferon-based therapy. Despite the potent antiviral effects, exactly how CsA functions to inhibit HCV replication remains unknown. In addition, drug resistance to CsA has not been studied systematically. Both of these issues need to be addressed for CsA or any of its derivatives to be developed into a successful drug. The experimental goals are to illustrate the mechanisms that determine the antiviral effect of CsA and the related drug resistance using comprehensive virology and structural biology techniques. Our results may reveal additional targets for therapeutic intervention. Given the medical importance of HCV infection and HCC, knowledge that can be gained from the grant will also have direct implications for both antiviral and anticancer drug development.