

# Hepatitis B Foundation

## Annual Progress Report: 2009 Formula Grant

### Reporting Period

January 1, 2010 – June 30, 2010

### Formula Grant Overview

The Hepatitis B Foundation received \$1,073 in formula funds for the grant award period January 1, 2010 through December 31, 2010. Accomplishments for the reporting period are described below.

### Research Project 1: Project Title and Purpose

*Identifying Novel Antiviral Agents against Hepatitis B Virus* - The purpose of this project is to identify new viral targets for development of antiviral agents against hepatitis B virus. Identified targets will be tested for antiviral activity. This will lead to potential future antiviral development, necessary to augment the short-comings of existing antiviral therapies, including the development of resistance.

### Anticipated Duration of Project

1/1/2010 – 12/31/2010

### Project Overview

Objective 1: To reduce the burden of chronic hepatitis B and its associated liver disease, including liver cancer, through the identification and development of successful treatment methods.

*Specific Aim 1A:* To screen compounds regulating HBV replication from the Library of Pharmacologically Active Compounds-1280.

Objective 2: To expand and diversify the future pool of biomedical researchers in Pennsylvania.

*Specific Aim 2A:* To train and encourage young investigators, with an intensive 10-week summer internship, to pursue careers in biomedical research focusing on the prevention and treatment of viral hepatitis and liver cancer.

There is currently no cure for chronic hepatitis B, and 15-40% of the 2 million Americans infected with chronic hepatitis B will develop cirrhosis or liver cancer. The currently available therapies have varying levels of long-term response and multiple side-effects, which can affect a favorable outcome for the patient. Thus, it is necessary to find new and improved therapeutic methods for treatment of chronic HBV. The Library of Pharmacologically Active Compounds-1280 (LOPAC) includes 1280 drug-like compounds that have been developed against all major

target classes. This library will be screened for anti-HBV activities via a series of assays, with the goal of identifying novel virus targets for antiviral agents. Through this research project, student summer interns who are recruited from Pennsylvania colleges and universities will work to characterize the antiviral activities of small interferon-stimulated genes against hepatitis B virus. Student recruitment will focus on minority students of Asian and Pacific Islander or African American descent, the two ethnicities in Pennsylvania that are disproportionately affected by both chronic hepatitis B and liver cancer. The results of this project will give new insight into the mechanisms by which interferon alpha modulates an immune response against HBV, and can offer a new direction for future hepatitis B therapy. It will also expand and diversify the future pool of biomedical researchers in Pennsylvania.

### **Principal Investigator**

Chari A. Cohen, MPH  
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### **Other Participating Researchers**

Pamela Norton, PhD – employed by Hepatitis B Foundation

### **Expected Research Outcomes and Benefits**

There are approximately 2 million Americans living with chronic HBV, and research indicates that 15-40% of them will develop cirrhosis or liver cancer, which are both associated with high rates of mortality. It is expected that the results of this research project will result in the identification of new viral targets for development of antiviral agents, and may reveal new chemical leads for future antiviral development. Augmenting existing antivirals, which suffer from the frequent emergence of resistant viruses, can ultimately translate to reduced rates of cirrhosis, liver failure and liver cancer for the 2 million Americans living with chronic hepatitis B.

### **Summary of Research Completed**

Objective 1: To reduce the burden of chronic hepatitis B and its associated liver disease, including liver cancer, through the identification and development of successful treatment methods.

*Specific Aim 1A:* To screen compounds regulating HBV replication from the Library of Pharmacologically Active Compounds-1280.

The summer project goal was to screen compounds from the Library of Pharmacologically Active Compounds-1280 (LOPAC) for potential in regulating HBV replication. A total of 29 compounds are currently being screened. These compounds all showed promise in preliminary

studies via simple dot blot measurement of total HBV DNA present in infected cells that had been treated with the LOPAC compounds, followed by Southern blot analysis measuring HBV DNA that had been packaged into the viral capsid (representing true replication intermediates).

The 29 compounds are now being screened by a designated summer college intern. Ms. Daniella Hess, working under the tutelage of Dr. Haitao Gou, is currently performing dose response analysis of the 29 compounds, across the range 0.3-30 uM. The ultimate goal of the study is to determine which of the 29 compounds result in a 50% reduction in viral replication, and to determine if at least one of the compounds will result in a 90% reduction in HBV DNA. Results will be ready for presentation by the last day of her internship, which is August 6, 2010.

Objective 2: To expand and diversify the future pool of biomedical researchers in Pennsylvania.

*Specific Aim 2A:* To train and encourage young investigators, with an intensive 10-week summer internship, to pursue careers in biomedical research focusing on the prevention and treatment of viral hepatitis and liver cancer.

The 2010 Hepatitis B Foundation (HBF) summer research internship program is currently underway. A total of 13 undergraduate students have completed 40% of their summer 2010 internship (4 out of 10 weeks), which will end mid-August. The student representation is 50% female; 75% are Pennsylvania residents and 75% attend Pennsylvania colleges or universities.

All thirteen summer interns have spent 70% of their time conducting laboratory research with their appointed laboratory mentors. Each student has also attended and presented at weekly journal clubs, laboratory “lunch and learn” seminars, and weekly seminars by visiting scientists and biotechnology experts. Special Seminar topics included “Choosing Biotechnology as a Career Path,” “Introduction to Public Health and Health Disparities,” “Patenting Biotechnology Inventions,” and “Building for a Cure.” The students have attended weekly educational seminars given by Hepatitis B Foundation public health and outreach staff, to enhance their understanding of the public health impact of hepatitis B on a local, national, and global level. The students have also learned about the Pennsylvania Keystone Innovation Zone program, and an emphasis has been on informing the students about the many biotechnology opportunities there are in Pennsylvania.

Upon completion of their summer research projects, students will present their findings to over 100 scientists and entrepreneurs at a special seminar, held at the Pennsylvania Biotechnology Center of Bucks County (PABIO).