The National PKU Alliance is proud to announce its 2011 Research Awards! These awards are made possible by our member organizations who raise funds each year on the local level for research. Thank you for helping make these awards possible as we work towards improving treatment options for PKU and accelerating the timeline for a cure.

**Research Grants**

**Dr. Levy**, Professor of Pediatrics at Harvard Medical School and Senior Physician in Medicine/Genetics at Children's Hospital Boston, will continue a study entitled, "Maternal PKU: Offspring Follow-Up and Maternal Nutritional and Psychological Status." This is the first study to examine post-natal influences as well as prenatal predictors of offspring outcome. Preliminary findings suggest that greater attention should be given to the pre- and post-natal environment of children born to mothers with PKU, as well as to speech and language issues in these children. Ultimately, this study will change the standard of care and create a better understanding of outcomes in the children of PKU mothers. Dr. Levy's work is being funded through the Pepsi Refresh Project - a grant competition that the NPKUA won in August 2010 to support PKU research.

**Dr. Ney**, Professor in the Department of Nutritional Sciences at the University of Wisconsin-Madison, will continue to evaluate GMP, synthetic amino acids, and casein control diets on osteopenia in the PKU mouse model and wild type litter mates. Dr. Ney has already demonstrated that GMP diets lower the Phe in both blood and brain in the PKU mouse model. There have been observations documented that osteopenia does occur in PKU patients. Dr. Ney's hypothesis is that the GMP diet provides a source for more substantial systemic protein synthesis, a reduction in acid levels that would favor bone formation and more proline to support cartilage and scaffolding to enhance bone formation.

**Dr. Harding**, Associate Professor of Molecular and Medical Genetics at Oregon Health & Science University in Portland, Oregon, has been working on gene therapy to cure PKU in the PAH mouse models for more than 10 years with support from NIH. In order to translate this research into the clinic, vectors carrying the human PAH cDNA must be designed and carefully evaluated in a preclinical study. Specific gene therapy methods will be incorporated to improve the liver PAH expression from the human PAH cDNA and will be compared head-to-head in a short 8-week trial in PAH mice following portal vein injections and measuring the blood Phe levels. A second specific aim is to use sequences from the human 285 ribosomal RNA gene (rDNA) in an effort to get permanent integration with the recipient genome so PAH expression will not diminish over time and thus could lead to a cure for PKU in humans.
Postdoctoral Fellowships

Dr. Gramignoli is a Visiting Scholar in the Department of Pathology at the University of Pittsburgh School of Medicine, which is internationally renowned in the field of liver and hepatocyte transplantation. Hepatocyte transplantation has been successfully used to treat other metabolic disorders, but its efficacy in treating PKU had not yet been studied. During the last year, he has made significant progress in developing the mouse PKU model to test hepatocyte transplantation as a cure for PKU. Dr. Gramignoli and his team possess a level of commitment, excitement, and expertise that was evident in a successful site visit to the University of Pittsburgh lab last fall. Based on this visit, the NPKUA is pleased to support this post-doctoral fellowship award for a second year.

Dr. Kristen Skvorak-Vallieu has been working at the University of Pittsburgh with Dr. Gramignoli and has entitled her project, “Hepatocyte and Induced Pluripotent Stem (IPS) Cell Transplants to Correct Phenylketonuria”. Her work will focus on two hypotheses. The first hypothesis is that repopulation of the liver of PAH-deficient recipient mice with PAH proficient IPS-derived hepatocytes will result in long-term correction of hyperphenylalaninemia. The second hypothesis is to test that PAH deficiency leads to alterations in brain catecholamine and monoamine levels which result in the chronic CNS damage of the disease. The NPKUA Scientific Advisory Board observed that the lab has a very well-trained, experienced team working in this arena that could in fact result in a cure.

NPKUA Research Selection Process

The overall funding strategy of the NPKUA is to support projects that will promote advances in the treatment and management of PKU, with a long-term goal of facilitating the development of a cure and to facilitate the growth and expansion of young, innovative researchers working in the inherited metabolic disease field. The NPKUA’s Scientific Advisory Board is made up of eminently qualified physicians, researchers, and clinicians who are leaders in their fields to evaluate proposals, including Thomas Franklin, PhD; Emil Kakkis, MD, PhD; Harvey Levy, MD; Kathryn Mosely, MS, RD; Ray Stevens, PhD; and Bryan Hainline, MD. Each year this board goes through a rigorous evaluation process to select those proposals that will meet the above funding strategy.