Research Project Proposal  
Academic year 2016-2017

**Project Nº 3 (ASIGNADO)**  
**Title:** Emerging therapies for acute intermittent porphyria.  
**Department/ Laboratory** Hepatology Program, Laboratory 402, Center for Applied Medical Research (CIMA)  
**Director:** Antonio Fontanellas Romá  
**Contact:** afontanellas@unav.es

**Summary**

Acute intermittent porphyria (AIP) is an autosomal dominant metabolic disease caused by hepatic deficiency of porphobilinogen deaminase (PBGD), the third enzyme of the heme synthesis pathway. The dominant clinical feature is acute neurovisceral attack associated with high production of potentially neurotoxic porphyrin precursors due to increased hepatic heme consumption. Current Standard of Care is based on a down-regulation of hepatic heme synthesis using heme replacement therapy. Recurrent hyper-activation of the hepatic heme synthesis pathway affects about 5% of patients and can be associated with neurological and metabolic manifestations and long-term complications including chronic kidney disease or increased risk of hepatocellular carcinoma. Prophylactic heme infusion is an effective strategy in some of these patients, but it induces tolerance and its frequent application may be associated with thromboembolic disease and hepatic siderosis. Liver transplantation is the only curative treatment. Emerging therapies including replacement enzyme therapy or gene therapies (PBGD-gene transfer and ALAS1-gene expression inhibition) are being developed to improve quality of life, reduce the significant morbidity associated with current therapies and prevent late complications such as kidney disease and malignancy.

**References:**

3. Collantes M, Serrano-Mendioroz I, Benito M, Molinet-Dronda F, Delgado M, Vinaixa

POSSIBILITY OF PhD

YES*

* (PhD grant required) Candidates will apply for scholarships/fellowships to support their research.