Universidad de Navarra

Máster en Investigación Biomédica
Facultad de Ciencias

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)
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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 us kidney disease and malignancy.

R**eferences:**

1. Puy, H., Gouya, L. and Deybach, J.C. (2010) Porphyrias. Lancet 375(9718), 924-37

2. Harper, P. and Sardh, E. (2014) Management of acute intermittent porphyria. Expert Opinion on Orphan Drugs 2, 349-68. Available from: http://dx.doi.org/10.1517/21678707.2014.891456.

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

M, Sampedro A, Enríquez de Salamanca R, Prieto E, Pozo MA, Peñuelas I, Corrales FJ, Barajas M, Fontanellas A. Glucose metabolism during fasting is altered in experimental porphobilinogen deaminase deficiency. Hum Mol Genet. 2016 Apr 1;25(7):1318-27.

POSSIBILITY OF PhD

YES*

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