Universidad de Navarra

Máster en Investigación Biomédica
Facultad de Ciencias

Research Project Proposal
Academic year 2015-2016

Project Nº 26

Title: Study of the coordinated regulation of aquaglyceroporins in insulin-sensitive tissues in obesity and type 2 diabetes

Department/ Laboratory Metabolic Research Laboratory, Clínica Universidad de Navarra

Director 1: Amaia Rodríguez
Contact: arodmur@unav.es Phone: 948 42 56 00 (ext. 80 3357)
Codirector: Gema Frühbeck
Contact: gfruhbeck@unav.es Phone: 948 25 54 00 (ext. 4484)

Summary

Aquaporins (AQPs) are integral membrane proteins that allow the movement of water across biological membranes. According to their permeability, AQPs can be classified into 2 groups: aquaporins (pure water channels) and aquaglyceroporins (channels permeated by water and glycerol). The physiological and pathophysiological relevance of aquaglyceroporins (AQP3, AQP7, AQP9 and AQP10) in humans has not been completely disentangled. Glycerol can be obtained by diet intake, adipocyte-derived lipolysis or renal reabsorption and it constitutes one of the substrates for hepatic gluconeogenesis. Several studies performed in mice have shown that the coordinated regulation of aquaglyceroporins in the adipose tissue and the liver is relevant for glycerol efflux from adipocytes and glycerol intake into hepatocytes for de novo synthesis of glucose. The aim of the present study is to analyse the impact of obesity and type 2 diabetes on the expression of aquaglyceroporins in key organs for the absorption and release of glycerol, namely adipose tissue, gut and small intestine. Furthermore, the in vivo regulation of these glycerol channels by the hormone leptin in wild type and leptin-deficient (ob/ob) mice as well as the impact of bariatric surgery (sleeve gastrectomy and Roux-en-Y gastric bypass) and caloric restriction in diet-induced obese rats will be also studied. A deeper understanding of the coordinated regulation of aquaglyceroporins in key metabolic organs for glucose and lipid metabolism might be useful to design drugs specifically targeting these glycerol channels aimed at obesity and/or type 2 diabetes control.

References

1. Frühbeck G. Obesity: aquaporin enters the picture. Nature 2005;438(7067):436-7.

2. Rodríguez A et al. Insulin- and Leptin-Mediated Control of Aquaglyceroporins in Human Adipocytes and Hepatocytes Is Mediated via the PI3K/Akt/mTOR Signaling Cascade. J Clin Endocrinol Metab 2011;96:E586-97.
3. Rodríguez A et al. Reduced hepatic aquaporin-9 and glycerol permeability are related to insulin resistance in non-alcoholic fatty liver disease. Int J Obes 2014: 38(9):1213-20

POSSIBILITY OF PhD

YES*

* (PhD grant required)