

**Research Project Proposal**  
Academic year 2015-2016

<b>Project Nº</b> 54
<b>Title:</b> Role of the NADPH oxidase 5 in vascular and metabolic complications in experimental obesity
<b>Department/ Laboratory:</b> Biochemistry and Genetics, School of Sciences
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<p><b>Summary</b></p> <p>Diabetes is reaching epidemic proportions in industrialized countries, and has been associated with an increased risk of cardiovascular disease. There has been proposed a key implication of oxidative stress in these processes.</p> <p>NADPH oxidases are key reactive oxygen species (ROS)-generating enzymes implicated in the pathophysiology of vascular and metabolic disorders. An excessive production of ROS dependent on the activity of different NOX isoforms has been reported in adipocytes, vascular and phagocytic cells, and may promote endothelial dysfunction, inflammation, and apoptosis. NADPH oxidase 5 (NOX5) is a novel isoform that is present in endothelial cells. High glucose increases NOX5-mediated ROS production in these cells thus suggesting this pathway may have important implications in the development of vascular complications in metabolic diseases. In fact, NOX5 expression is enhanced in human diabetic nephropathy.</p> <p>The main objective of this project is to analyze the role of NOX5 in the overall development of vascular damage in experimental obesity. In detail, the main objective is to perform an experimental study in the transgenic mouse overexpressing human NOX5 cDNA gene specifically in endothelium (End-Nox5Tg, generated by the Dr. Guillermo Zalba from the department of Biochemistry and Genetics), that had been fed with control or high-fat diet (diet of obesity). In this project the candidate will develop skills with a mouse model and will perform molecular biology techniques, such as western blot and quantitative PCR.</p> <p>The results of this study will provide new insights into the molecular mechanisms involved in the regulation of NOX5, and the effect of the activation of this oxidase in metabolic disorders and its impact on the development of vascular complications.</p> <p><u>References</u></p> <p>Palacios-Ortega S, Varela-Guruceaga M, Milagro FI, Martínez JA, de Miguel C. Expression of Caveolin 1 is enhanced by DNA demethylation during adipocyte differentiation. status of insulin signaling. <b>PLoS One</b> 2014;9:e95100</p> <p>Moreno MU, San José G, Pejenaute Á, Landecho MF, Díez J, Beloqui Ó, Fortuño A, Zalba G. Association of phagocytic NADPH oxidase activity with hypertensive heart disease: a role for cardiotrophin-1? <b>Hypertension</b> 2014;63:468-474</p>



Gómez-Ruiz A, Milagro FI, Campión J, Martínez JA, de Miguel C. High-fat diet feeding alters metabolic response to fasting/non fasting conditions. Effect on caveolin expression and insulin signalling. **Lipids Health Dis** 2011;10:55

**POSSIBILITY OF PhD**

YES\*

\* (PhD grant required)