Universidad de Navarra

Máster en Investigación Biomédica
Facultad de Ciencias

Research Project Proposal
Academic year 2015-2016

Project Nº 9
Title: Does MMP-10 play a role in cardiac repair after ischemia?
Department/ Laboratory Laboratory of Atherothrombosis. Program of Cardiovascular Diseases. CIMA
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Summary Cardiovascular diseases of ischemic nature, such as myocardial infarction (MI) or stroke, are the leading cause of morbi-mortality in western societies. After an ischemic episode the heart undergoes extensive remodelling. Metalloproteinases (MMPs) play a role in atherosclerotic plaque progression, thrombosis, fibrinolysis, ischemic damage and tissue repair. MMP-10 is required for proper skeletal muscle regeneration after hindlimb ischemia or toxin induced damage, and has also been involved in liver repair after injury (1-3). However, no information is available on the expression of MMP-10 in cardiac tissue or its implication in remodelling after myocardial ischemia. We will study the relevance of MMP-10 in heart repair and remodelling after MI, using an experimental model of permanent ligation of the left descending coronary artery in wild type (WT) and MMP-10 deficient (Mmp10-/-) mice. Cardiac tissues will be harvested at different time points after occlusion (day 3/early wound healing, and days 15 and 30/late remodelling) to do an extensive morphological analysis. In addition, we will identify new pathways and MMP-10 substrates involved in tissue repair after myocardial ischemia by using genomics and proteomics. That will be the base to investigate in vitro novel molecular pathways and mechanism regulated by MMP-10. The knowledge of MMP-10 functions in repair and remodelling, together with the mechanisms involved, will provide new therapeutic targets in tissue regeneration after myocardial ischemia.

References

1. Gomez-Rodriguez V, Orbe J, Martinez-Aguilar E, Rodriguez JA, Fernandez-Alonso L, Serneels J, Bobadilla M, Perez-Ruiz A, Collantes M, Mazzone M, Paramo JA, Roncal C. Functional MMP-10 is required for efficient tissue repair after experimental hind limb ischemia. FASEB J. 2015 Mar;29(3):960-72.

2. Bobadilla M, Sáinz N, Rodriguez JA, Abizanda G, Orbe J, de Martino A, García Verdugo JM, Páramo JA, Prósper F, Pérez-Ruiz A. MMP-10 is required for efficient muscle regeneration in mouse models of injury and muscular dystrophy. Stem Cells. 2014 Feb;32(2):447-61

3. Garcia-Irigoyen O, Carotti S, Latasa MU, Uriarte I, Fernández-Barrena MG, Elizalde M, Urtasun R, Vespasiani-Gentilucci U, Morini S, Banales JM, Parks WC, Rodriguez JA, Orbe J, Prieto J, Páramo JA, Berasain C, Ávila MA. Matrix metalloproteinase-10 expression is induced during hepatic injury and plays a fundamental role in liver tissue repair. Liver Int. 2014 Aug;34(7):e257-70.

POSSIBILITY OF PhD

YES*

* (PhD grant required)