Universidad de Navarra

Máster en Investigación Biomédica
Facultad de Ciencias

Research Project Proposal
Academic year 2015-2016

Project Nº 42

Title: UNDERSTANDING HOW HOMEOBOX PROTEIN NKX2-3 TRIGGERS B-CELL RECEPTOR SIGNALING AND PROMOTES MARGINAL-ZONE LYMPHOMAGENESIS

Department/ Laboratory
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Summary

Constitutive B-cell receptor (BCR) signaling plays a critical role in the development o virtually all marginal-zone B-cell lymphomas. In many cases, however, the cause of BCR activation remains unknown. Whereas the homeobox NKX2-3 transcription factor is no expressed in normal B lymphocytes, we observed ectopic expression of NKX2-3 in 30% o marginal-zone lymphomas. B cells from Eμ-NKX2-3 transgenic mice driving expression o NKX2-3 in B lymphocytes showed increased expression of multiple surface molecules tha boosted B-cell migration and homing to secondary lymphoid tissues, leading t progressive B-cell accumulation. Molecularly, NKX2-3 induced constitutive BCR signalin and downstream cascades to promote cell proliferation and survival. Eventually, Eμ-NKX2 3 mice developed marginal-zone B-cell lymphomas with clinic-biological features mirrorin human disease. In this project we will use NKX2-3 transgenic mice and additiona experimental models of human lymphoma as tools to elucidate how NKX2-3 activates BCR signaling and modulates lymphocyte dynamics to eventually drive marginal-zone lymphomagenesis. We will also determine the implication of NKX2-3 in human marginal zone lymphoma samples, aiming to translate basic knowledge to the clinical setting Therefore, the Specific Aims of this project are:

1. Define the mechanistic basis by which NKX2-3 activates BCR signaling and promotes marginal-zone lymphoma development in mice
2. Determine the functional role of NKX2-3 in favouring migration, homing and adhesion of mouse B cells in extranodal tissues to drive lymphomagenesis
3. Characterize the functional role of NKX2-3 in human marginal-zone lymphoma samples
4. Define the biological and clinical features of patients with NKX2-3-expressing marginal-zone lymphomas

POSSIBILITY OF PhD

YES*

* (PhD grant required)