UNIL | Université de Lausanne

European Research Council
Established by the European Commission

PROF. GRETA GUARDA
(FBM / DB)

PROJECT TYPE ERC Starting Grant (FP7)

TITLE NLRs as Transcriptional Regulators

ACRONYM TranscriptionalNLRs

DURATION 01.03.2013 – 28.02.2018

BUDGET 1 499 154 €

MHC molecules are central to our immune system and are therefore also involved in several pathologies. MHCII transcription is controlled by proximal promoter sequences, which are cooperatively bound by several factors forming the 'MHC enhanceosome'. Upon recruitment to this complex, the NLR family member CIITA promotes MHCII transcription.

We recently found that our mice deficient for the NLR NLRC5 exhibit markedly reduced MHCI expression in lymphocytes. Importantly, endogenous NLRC5 occupies H-2 proximal promoter regions and drives gene transcription.

We now plan to characterize novel NLR-mediated transcriptional regulatory pathways controlling MHC expression. We will investigate the enhanceosome and the transcriptional regulators interacting with NLRC5 as well as the role of NLRC5 in gene expression more broadly. We will also address the function of other NLRs that are potentially controlling gene transcription, paying particular attention at their potential role in the regulation of classical and non-classical MHC genes. Finally, we will try to detail the underlying molecular mechanisms.

Novel aspects of MHC transcriptional regulation are emerging, highlighting a combinatorial system wherein NLRs play a more general role than realized so far. A better understanding of the mechanisms regulating MHC transcription is fundamental to design novel therapeutic approaches relevant to immune disorders, malignancies, and infertility.