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**Titre du sujet : Signatures microARNs de la réponse lymphocytaire T CD4+ modulée par l’interféron de type I**

We study the immunomodulatory activity of type I interferon family (IFNα/β) on the human CD4+ T cell response in healthy donors and in a pathologic context with multiple sclerosis (MS) patients. This chronic autoimmune and inflammatory disease targets the central nervous system and leads to axonal demyelination and neurodegeneration, with gradual physical and cognitive disabilities. The relapsing-remitting disease (RRMS) is the most common form that can be treated by IFNβ as a first-line therapy. However, the disease mainly evolves in time towards a secondary progressive form. In this context, there is a need for prognostic biomarkers of disease severity and progression.

Based on RNA-seq data and other data obtained with the Nanostring methodology, we have identified microRNAs (miRNAs) whose the level of expression is modulated by IFNβ in activated CD4+ T cells of healthy donors. MiRNAs are small non-coding RNAs that bind to the 3’ untranslated region of messenger RNAs, causing their degradation and/or reduced translation. They play a critical role in the post-transcriptional regulation of genes that are involved in T cell differentiation. Moreover, their expression and activity differ according to the immune cell type and activation context.

The objectives of the project are: 1- to select IFN-modulated miRNAs of interest based on our previous data, bibliography and computational prediction. 2- to confirm the IFN-dependent modulation of the miRNAs by RT-qPCR with miRNA-specific primers in CD4+ T cells of additional healthy donors. 2- to study the functional impact of some miRNAs in the modulation of the CD4+ T cell response using a T cell line model and primary CD4+ T cells. 3- to investigate if some miRNAs may help to determine a molecular signature of immune cell subsets that play a pathogenic role in the MS disease. For that, distinct CD4+ T cells subsets will be sorted by flow cytometry from PBMCs of healthy donors and RRMS patients.

**Références**

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