MECHANISMS AND MOLECULAR ACTORS OF THE INTESTINAL RESPONSE TO INFECTION IN THE CONTEXT OF HLA-B27

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We have acquired expertise in using *Drosophila* to explore the molecular and cellular mechanisms underlying human pathologies. Part of our work, therefore, focuses on studying a major genetic factor predisposing individuals to ankylosing spondylitis. Spondyloarthritis (SpA) is a group of chronic inflammatory joint disorders. They have a significant hereditary component, the HLA-B27 allele of the major histocompatibility complex (MHC). However, the mechanisms by which HLA-B27 contributes to SpA remain poorly understood, despite 50 years of research. This research has highlighted the non-canonical effects of the HLA-B27 antigen, independent of its role in adaptive immunity. In

collaboration with Prof. Breban's team (U1173, INSERM-UVSQ), we have developed a Drosophila model that allows us to study, in vivo, the effects of HLA-B27 at the cellular level and on innate immunity. A genetic approach has enabled us to show that HLA-B27 interacts with TGF signaling pathway receptors, which could disrupt the differentiation and regulation of CD4+ T cells (Grandon et al. 2019, Lauraine et al. 2024). This interaction has been found in patient cells. The continuation of this ANR-funded work has enabled us to develop the genetic tools needed to study the effect of HLA-B27 in the intestine. Our ongoing work aims to understand why this rheumatic disease is strongly associated with inflammatory bowel disease (IBD).

Grandon *et al*. (2019) Annals of the Rheumatic Diseases, doi: 10.1136/annrheumdis-2019-215832 (hal-02975533)

Lauraine *et al*. (2024) Arthritis Research and Therapy, doi: 10.1186/s13075-024-03370-1. hal-04362225