RESEARCH PROJECT FOR MASTER STUDENTS
Year 2015 – 2016

Field of the Master: Health, infectious diseases; M2
Required skills: microbiology, immunology, molecular biology
Duration: 6 months; Period: from January to June 2016

Title of the research project: Role of the tryptophan-kynurenine pathway in Candida albicans interactions with the host and with Pseudomonas aeruginosa

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Context: In mammalian cells, tryptophan to kynurenine metabolism is controlled by dioxygenases (TDO and IDO). Collectively the activity of the metabolites of tryptophan (Trp) such as kynurenine or quinolinic acid, contribute to immune tolerance to tumors or pathogens by modulating both adaptive and innate immunity. Kynurenine acts as a regulatory molecule through the induction of TReg and Th17 cells and IL-17, IL-22 production (figure).

The ThEx team has characterized the tryptophan-kynurenine pathway in Pseudomonas aeruginosa and demonstrated its role in bacterial virulence and immune tolerance through neutrophil function inhibition (Genestet et al. 2014). In addition, this immuno-modulatory effect was demonstrated in a murine model of invasive candidiasis where IDO inhibition led to exacerbated infection and inflammation and was associated with increased filamentation of the yeasts. By contrast, patients with septicemia due to Candida spp. exhibited higher IL-17 and kynurenine levels than non-infected patients.

We have identified the TDO homolog in C. albicans and the tryptophan-kynurenine-quinolinic acid pathway exists in the model yeast Saccharomyces cerevisiae, suggesting the conservation of the pathway in C. albicans.

Objectives: Firstly, we will characterize the pathway of Trp catabolism in C. albicans by targeted metabolomic assay (HPLC-MS/MS). Then, we will construct the C. albicans tdo mutants and analyze their phenotypes related to virulence (growth, morphogenesis, resistance to stresses) and interaction with cells of the innate immunity (neutrophils and macrophages).

Secondly, we will analyze the effect of the kynurenine produced by Pseudomonas aeruginosa on C. albicans pathogenesis.

Expected results: Candida albicans produces kynurenines, which inhibit its virulence and control innate immune response in vitro. The kynurenines that are produced by P. aeruginosa induces the same effect on C. albicans. These results will probably help to describe a new signalling molecule and will increase knowledge of interkingdom dialog, which is important for microbiota and symbiose.