Titre du sujet de stage :
Crohn’s Disease-associated polymorphisms affecting the autophagy machinery: consequences on intestinal barrier integrity and immunological surveillance.

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Sujet de stage :
Crohn’s Disease (CD) is a chronic pro-inflammatory disorder that affects the gastrointestinal tract. The etiology of CD is incompletely understood yet it is clear that the disease involves a deregulated relationship between the genetic of patients, the microflora of the intestine and the immune system. CD susceptibility is associated with frequent polymorphism of genes that are involved in autophagy, a cellular function that ensures cell homeostasis and adaptation to changes in the micro-environment through lysosomal degradation/recycling of cytosolic component such as protein aggregates or damaged organelles. Autophagy can also contribute to cell autonomous defense against invading microbes such as intracellular bacteria in both epithelial and immune cells.

The present project aims at examining the possible consequence of CD-associated mutation affecting factors involved in autophagy at large (ATG16L1, LRRK2, NDP52, NOD2) on both the barrier function of intestinal epithelial cells and the capacity to modulate immune cells in the context of infections. The main questions to be addressed are as follows: (I) What is the precise impact of these mutations on the functioning of the autophagy machinery in intestinal epithelial cells? (II) Could these mutations affect the barrier function that characterizes a monolayer of epithelial cells after differentiation? (III) What is the impact of such mutations on the trans-epithelial sensing of pathogenic bacteria by immune cells. These
studies should bring novel insights on the consequences of CD-associated, autophagy-related mutations on the epithelial cell-immune cell interactions that take place at the intestinal mucosa.

Technologies utilisées :
Biologie moléculaire, culture cellulaire, western Blot, microscopie confocale

Mots clés :
Autophagie, maladie de Crohn, Polymorphismes, barrière épithéliale, réponse immunitaire