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**Impact of bacterial mucin proteases on intestinal microbial communities.**

Crohn's disease is a debilitating and incurable chronic inflammatory bowel disease affecting more than 2.5 million individuals in the Western world. A general dysbiosis of gut microbiota has been well established in CD patients with a high prevalence of the invasive E coli strains, designated adherent-invasive E coli (AIEC). AIECs product proteases that degrade mucins promoting bacteria penetration of the mucus and intestinal colonization. The aims of this project are (i) to decipher the role of the secreted mucin-proteases, as newly identified components of AIEC virulence, in alteration of intestinal mucosa-associated microbiota and mucus barrier associated to CD and (ii) to develop selective inhibitors of these proteases. In mice mimicking CD susceptibility and gnotobiotic mice, we will determine whether mucin-protease-producing AIEC are able to disrupt mucosal barrier and the spatial organization of intestinal mucosa-associated microbiota. Impact of mucinases on commensal bacterial biofilm will be assessed in vitro. Mucinase inhibitors will be identified by molecular docking. We will give insights into how mucin-proteases degrading mucins contribute to gut bacterial encroachment that can eventually cause inflammation and infection.

Gibold L, Garenaux E, Dalmasso G, Gallucci C, Cia D, Mottet-Auselo B, Faïs T, Darfeuille-Michaud A, Nguyen HT, Barnich N, Bonnet R, **Delmas J**. The Vat-AIEC protease promotes crossing of the intestinal mucus layer by Crohn's disease-associated Escherichia coli. Cellular Microbiology. 2015