CMB PhD School Seminars 2022-2023

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Instructions for infection: a study of the competitive scenario between intestinal bacteria using organoids

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The human gastrointestinal tract is colonized by a complex ecological community of microorganisms, known as microbiota, responsible for vital functions, including the induction of immune system development, regulation of intestinal barrier integrity and synthesis of crucial molecules for human health. Bacterial pathogens, opportunistic pathogens and pathobionts are able to colonize the intestinal tract by outcompeting the resident flora through the expression of specific virulence factors. On the other hand, the role of beneficial strains, such as probiotics, is to restrain invading pathogens from conquering a specific niche by the colonization resistance phenomenon, thereby improving human health. Intestinal organoids represent an "in vivo-like" model of the intestinal epithelial surface to study where this competition battle is played. Hence, we compared the efficacy of the probiotic Escherichia coli strain Nissle 1917 to prevent enteropathogenic E. coli (EPEC, strain E2348/69) infection in intestinal organoids. Time course co-infection experiments were performed on 2D and 3D cultured mouse intestinal organoids mimicking the apical and the basolateral contact, respectively. At the selected time points organoids were either lyzed for bacterial counting or stained for fluorescence experiments. Results showed an enhanced capability of Nissle strain to adhere to the apical side of intestinal cells, thereby reducing EPEC attachment. Furthermore, we observed for the first time the ability of EPEC to contact intestinal tissues from the basal side and this interaction was not affected by the presence of the Nissle strain. In conclusion, results demonstrated that intestinal organoids are the most suitable in vitro model to test the efficiency of specific probiotic strains in protecting intestinal tissues from pathogens. Moreover, they offer the possibility to unveil new virulence traits enabling intestinal pathogen to interact with the basal side of the epithelium.