A three-dimensional immunocompetent intestine-on-chip model as *in vitro* platform for functional and microbial interaction studies.

Maurer M, Gresnigt MS, Last A, Wollny T, Berlinghof F, Pospich R, Cseresnyes Z, Medyukhina A, Graf K, Gröger M, Raasch M, Siwczak F, Nietzsche S, Jacobsen ID, Figge MT, Hube B, Huber O, Mosig AS (2019) A three-dimensional immunocompetent intestine-on-chip model as *in vitro* platform for functional and microbial interaction studies. *Biomaterials* 220, 119396.

Details

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Abstract

Alterations of the microbial composition in the gut and the concomitant dysregulation of the mucosal immune response are associated with the pathogenesis of opportunistic infections, chronic inflammation, and inflammatory bowel disease. To create a platform for the investigation of the underlying mechanisms, we established a three-dimensional microphysiological model of the human intestine. This model resembles organotypic microanatomical structures and includes tissue resident innate immune cells exhibiting features of mucosal macrophages and dendritic cells. The model displays the physiological immune tolerance of the intestinal lumen to microbial-associated molecular patterns and can, therefore, be colonised with living microorganisms. Functional studies on microbial interaction between probiotic *Lactobacillus rhamnosus* and the opportunistic pathogen *Candida albicans* show that pre-colonization of the intestinal lumen of the model by *L. rhamnosus* reduces *C. albicans*-induced tissue damage, lowers its translocation, and

limits fungal burden. We demonstrate that microbial interactions can be efficiently investigated using the *in vitro* model creating a more physiological and immunocompetent microenvironment. The intestinal model allows a detailed characterisation of the immune response, microbial pathogenicity mechanisms, and quantification of cellular dysfunction attributed to alterations in the microbial composition.

Involved units

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