Gastro-enterology

Jan Niess
Department of Biomedicine
Division of Gastroenterology and Hepatology
University Hospital Basel

Group Members

Berna Kaya
(PhD Student)
Dr. Katarina Radulovic
(Postdoc)
Anna Steinert
(PhD Student)
Philipp Wuggenig
(PhD Student)
*left during report period

Mononuclear phagocytes in mucosal immune responses

Inflammatory bowel diseases (IBD), such as Crohn`s disease and ulcerative colitis, are chronic relapsing diseases with increasing incidence and prevalence in the developed world. Innate and adaptive immune responses to constituents of the intestinal microbiota are essential for the development of IBD. Intestinal mononuclear phagocytes are in direct contact with the intestinal microbiota, initiate innate immune responses and shape adaptive immune responses. Phagocytes are located in the lamina propria of the gastrointestinal tract, in cryptopatches and isolated lymph follicles in close proximity to innate lymphoid cells (ILCs). Infection of animals with the mouse pathogen C. rodentium leads to IL-22 production by ILCs, which regulates the expression of REG family proteins required for the defense to infections with enteric pathogens. The depletion of phagocytes decreased IL-22 production by ILCs. This means that phagocytes support IL-22 production by ILCs required for host defense in the gut (Manta et al, Mucosal Immunol, 2013).
Mononuclear phagocytes may also initiate adaptive immune responses in the gut as indicated by the close proximity of phagocytes to T cells in the lamina propria of the gastrointestinal tract. Colonic phagocytes sample continuously fluorescent labelled E. coli. To reduce the complex interactions between phagocytes and T cells in presence of the intestinal microflora with vast array pf potential antigens, an antigen-specific colitis model was developed. In this model the challenge of E. coli expressing the antigen ovalbumin induces colitis in immunodeficient animals (RAG animals) reconstituted with antigen-specific T cells. *Ex vivo* confocal imaging allows the visualization of phagocytes that have sampled E.coli in proximity to T cells. *In vitro* studies indicated that the phagocytes deliver the antigen to dendritic cells, which migrate to mesenteric lymph nodes. In mesenteric lymph nodes the dendritic cells prime T cells, which home back to the lamina propria. In the lamina propria phagocytes are able to activate the effector T cells (Rossini et al, Mucosal Immunol, 2014).
These findings support the hypothesis that mononuclear phagocytes in the gastro-intestinal tract are of importance for the sampling of constituents of the microbiota, the initiation of innate and adaptive immune responses. Likely, mononuclear phagocytes play a key role in the pathogenesis of IBD.

Selected Publications

Manta C, Heupel E, Radulovic K, Rossini V, Garbi N, Riedel CU, Niess JH. (2013) CX(3)CR1(+) macrophages support IL-22 production by innate lymphoid cells during infection with Citrobacter rodentium. Mucosal Immunol. 6, 177–88

Radulovic K, Rossini V, Manta C, Holzmann K, Kestler HA, Niess JH. (2013) The early activation marker CD69 regulates the expression of chemokines and CD4 T cell accumulation in intestine. PLoS One 8(6):e65413

Rossini V, Zhurina D, Radulovic K, Manta C, Walther P, Riedel CU, Niess JH. (2014) CX3CR1+ cells facilitate the activation of CD4 T cells in the colonic lamina propria during antigen-driven colitis. Mucosal Immunol. 7, 533–48

Schulz O, Ugur M, Friedrichsen M, Radulovic K, Niess JH, Jalkanen S, Krueger A, Pabst O. (2014) Hypertrophy of infected Peyer's patches arises from global, interferon-receptor, and CD69-independent shutdown of lymphocyte egress. Mucosal Immunol. 7, 892–904

Steinert A, Radulovic K, Niess J. (2016). Gastro-intestinal tract: The leading role of mucosal immunity. Swiss Med Wkly. 5, 146:w14293

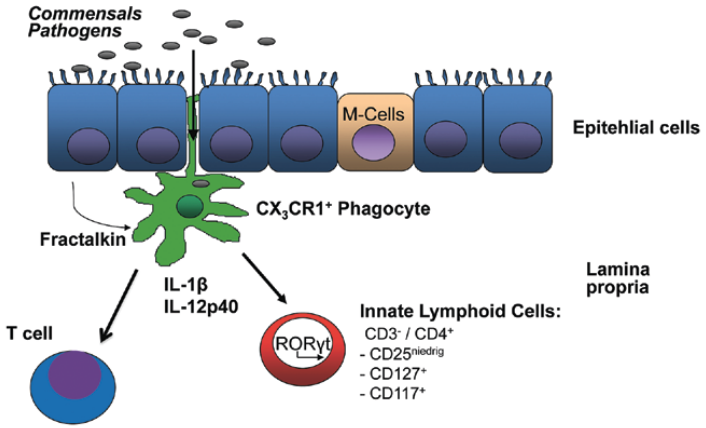

Fig. 1: Mononuclear phagocytes sample constituents of the intestinal microflora, initiate effector T cell responses (adaptive immunity) and facilitate IL-22 production by innate lymphoid cells (innate immunity).