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3D intestinal co-culture analysis of the interaction of secreted proteins from intestinal nematode parasites with the mucosal habitat

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Intestinal nematodes represent multicellular organisms within the gut microbiota, which colonize their habitat for years and which sustain tolerance mechanisms, thereby containing inflammatory host responses to prevent their expulsion. Of major relevance, concurrently this parasite's influence attenuates adverse inflammatory responses associated with autoimmune diseases like Crohn's disease and ulcerative colitis. The major effect is attributed to excretory/secretory (E/S) products released from the parasite affecting and modulating host local immune system. We are investigating E/S proteins from the intestinal *Strongyloides ratti* and *Trichuris suis* for immunomodulatory effects. We here report our preliminary characterization of the two *S. ratti* proteins, secreted protein acidic and rich-in-cysteine (Sr-SPARC) and thioredoxin-like protein (Sr-Trx-lp) and the *T. suis* E/S protein Ts-Trx-lp. The genes of these proteins were identified, cloned and recombinantly expressed under optimized conditions. The effect of the secreted parasite proteins on host cells were studied applying a novel *in vitro* 3D mucosal model that mimics the *in vivo* natural intestinal microenvironment. In the 3D co-cultures which comprise human intestinal epithelial and dendritic cells growing on a collagen scaffold, an initial pro-inflammatory response (TNF-α) after 24 hours was followed by an increased anti-inflammatory response after 48-72 hours detecting the Th2-type-related cytokines IL-22, IL-10 and TSLP. Thus, Sr-SPARC, Sr-Trx-lp and Ts-Trx-lp can contribute in the reported immunoregulatory potential of intestinal helminth infection. 3D intestinal mucosal co-cultures represent a novel appropriate model to investigate the interaction of intestinal parasites and their released products with the host tissue habitat.

Biography

Emmanuela Maria Anandarajah is currently a PhD student from the Westphalian Wilhelms-University of Munster, Germany and finalizing her thesis at the Bernhard Nocht Institute for Tropical Medicine in Hamburg, Germany. She has completed her BSc in 2011 and MSc in 2013 at the Westphalian Wilhelms-University of Munster.

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