Univerza v Ljubljani

CELSA
Central Europe Leuven Strategic Alliance

Project: The role of snoRNAs in the etiology of inflammatory bowel disease

Duration: 1 Oct 2022 – 30 Sept 2024

Coordinator: University: KU Leuven (KUL), Department of Human Genetics (izr. prof. dr. Isabelle Cleynen)
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Project summary:

Inflamatory bowel disease (IBD) constitutes a group of progressive and debilitating disorders characterized by chronic inflammation of the intestine, with poorly understood etiology. Our recent data indicate that expression of small nucleolar RNAs (snoRNAs), a family of short non-coding RNAs traditionally implicated in guiding ribosomal RNA modification, marks recurrent Crohn's disease (a form of IBD). We have also shown that lack of dyskerin, a well-known protein partner of snoRNAs, leads to IBD-like symptoms in a zebrafish model, further supporting a potential link between snoRNAs and IBD. To examine the role of snoRNAs in IBD we will apply an interdisciplinary approach, combining complementary expertise from three research groups. Specifically, at KUL we will analyse differential expression of snoRNAs in intestinal biopsies and peripheral blood immune cells of IBD patients vs healthy controls using short RNA sequencing. Using a similar approach, we will identify perturbed snoRNAs in chemically inducible zebrafish and intestinal cell models of IBD at ELTE and UL, respectively. These data will set ground for mechanistic studies, where individual dysregulated snoRNAs will be knocked-out or overexpressed in both disease models using advanced molecular biology methods. Their role in IBD will be verified by monitoring morphological, histochemical and gene expression changes. Furthermore, we will use our state-of-the-art methods of RNA interactome interrogation to identify molecular targets of dysregulated snoRNAs in live cells, assisting in revealing their link to IBD symptoms. The overarching goal of the proposed project is to find reliable snoRNA diagnostic biomarkers with functional relevance to IBD, which in future should aid in accurate disease diagnosis, thereby allowing early and effective treatment. Last but not least, the animal and cell models generated in this project might find use for preclinical screens to identify new or repurposed therapeutics for IBD.

Web page: Selected projects (celsalliance.eu)