Centre de Recherche en Biologie Cellulaire de Montpellier

CRBM external seminar
Thursday Oct 27th 11:00 am Salle Marcel Dorée

Modeling microvillus atrophy and regeneration: from *C. elegans* and mouse intestinal organoids to patients

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Grégoire is a cell biologist, group leader at the IGDR, Rennes. He is interested in the dynamics of epithelial polarity using a multiscale approach, from molecules to whole organism, using C. elegans as a model organism and intestinal organoids a mammalian non-animal model. He is collaborating with physicians to address the clinical relevance of his discoveries. After a PhD with Michel LABOUESSE at Strasbourg, and a post-doc with Dan CUTLER in London, he got an ATIP/AVENIR grant to set up his team in Rennes. He is an expert in C. elegans, membrane trafficking, and intestine.

Abstract

Intestinal microvillus atrophy is a major cause of enteropathies such as idiopathic or congenital diarrhea, that are often associated with severe morbidity. It can be caused by genetic disorders, inflammatory diseases such as Crohn's and celiac diseases, or pathogens. In particular genetic microvillus atrophy can be triggered by mutations in MYO5B, STX3 or MUNC18.2 which alter epithelial polarity by affecting apical trafficking in intestinal epithelial cells. Using live super-resolution microscopy and endogenously expressed probes we first described microvillus growth and dynamics throughout embryonic and larval development in C. elegans. We next established a genetic worm model of an inherited disorder leading to microvillus atrophy by depleting the V0 domain of the V-ATPase. We then transposed this model to mouse intestinal organoids where it also triggers a very severe microvillus atrophy. We are now integrating the function of this new factor in the broader framework of apical trafficking and inherited microvillus atrophy. By combining a genetically tractable model, intestinal organoids and observations in patients, we aim to propose new therapeutic options to treat microvillus atrophy and trigger their regeneration. Indeed, while regeneration is essential for life, it is mostly investigated at the tissue or organ level; microvilli regrowth provides a unique model for subcellular regeneration which could be useful to treat not only genetic disorders but also all the other causes of microvillus atrophy.

Selected publications

Bidaud-Meynard A, Demouchy F, Nicolle O, Pacquelet A, Suman SK, Plancke C, Robin F, Michaux G. High resolution dynamic mapping of the C. elegans intestinal brush border. 2021, Development, 148, dev200029.

Bidaud-Meynard A, Nicolle O, Heck M, Michaux G. V0-ATPase-dependent apical trafficking maintains the polarity of the intestinal absorptive membrane. 2019, Development, 146, dev174508.

Mosa MH, Nicolle O, Maschalidi S, Sepulveda FE, Bidaud-Meynard A, Menche C, Michels BE, Michaux G, de Saint Basile G and Farin HF. Dynamic formation of microvillus inclusions during enterocyte differentiation in Munc18-2 deficient intestinal organoids. 2018, Cell Mol Gastroenterol Hepatol, 6, 477-493.

Michaux G, Massey-Harroche D, Nicolle O, Rabant M, Brousse N, Goulet O, Le Bivic A, Ruemmele FM. The localisation of the apical Par/Cdc42 polarity module is specifically affected in microvillus inclusion disease. 2016, Biology of the Cell, 108, 19-28.

Shafaq-Zadah M, Brocard L, Solari F, Michaux G. AP-1 is required for the maintenance of apico-basal polarity in the C. elegans intestine. 2012, Development, 139, 2061-2070.