Peter Buske
Interdisciplinary Center for Bioinformatics, Leipzig University
e-mail: buske@izbi.uni-leipzig.de
Markus Loeffler
Interdisciplinary Center for Bioinformatics, Leipzig University
e-mail: markus.loeffler@imise..uni-leipzig.de
Joerg Galle
Interdisciplinary Center for Bioinformatics, Leipzig University
e-mail: galle@izbi.uni-leipzig.de

Modelling in vitro crypt formation

In vitro cultures of intestinal tissue have been tried for decades. Only recently Sato and co-workers succeeded in establishing organoid cultures from single cells [1]. In these cultures intestinal cells expressing the stem cell marker Lgr5 form crypt-like structures similar to those found *in vivo*. The mechanisms that underlie the formation of these spatially-organised structures are currently a matter of debate.

We here present a 3D biophysical model of de novo crypt formation *in vitro*. The model builds on an individual cell-based model of crypt dynamics recently published by us [2]. We extended this model by introducing a flexible basal membrane. This membrane can be reorganised by cells showing active matrix metabolism.

In this model, shape changes of the basal membrane result from a feedback loop between its curvature and the Wnt-activity of adherent cells. Thereby, increased Wnt-activity increases the adhesion strength of the cells and thus, forces local shape changes of the basal membrane. We demonstrate the formation of crypt-like structures within this model depending on the elasticity and stiffness of the basal membrane and on the adhesion properties and matrix metabolisms of the different cell types.

We suggest the proposed mechanism to be a principal one in epithelial gland formation.

References

[1] T. Sato, *Single Lgr5 stem cells build crypt-villus structures in vitro without a mesenchymal niche.* Nature **459(7244)**:262-51–2.

[2] P. Buske, *A comprehensive model of the spatio-temporal stem cell and tissue organisation in the intestinal crypt.* PLoS Comput Biol. **7(1)**: e1001045.