## **Research Fellow**

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## Description

This position is at the interface between cell biology and biophysics. It will include collaboration with theoretical physicists. The aim of the project is to understand interplay between mechanical forces, during the self-organization of intestinal organoids. Intestinal organoids have been proven to capture essential features of the intestinal epithelium such as crypt folding, cellular compartmentalization, collective dynamics and cell extrusion, although the latter is less studied. These behaviours are likely coordinated by mechanosensitive processes, although the impact of mechanics remains to be elucidated.

We will investigate specific mechano-transduction processes that link mechanical stresses, intestinal differentiation and fate of extruding cells in the regulation of the homeostatic behaviour of the intestinal organoids. Integrating mechanics, engineering and cell signalling approaches across scales from sub-cellular, cellular and multicellular levels, we aim at understanding the physical principles and molecular mechanisms that control cell extrusion processes.

We will combine cell imaging, micromechanics and microfabrication to investigate the role of mechanics in controlling the self-organization of intestinal organoids. We will particularly focus on the role of the actomyosin cytoskeleton in cell extrusion focusing on the extruded cell and its immediate neighbours in correlation with caspase activity. We will analyse cells under tensile or compressive stresses together with shape descriptors and stress measurements.

The candidate will be responsible for carrying out experimental research on the project using techniques including organoid culture, live cell microscopy, micropatterning, mechanical measurements (already implemented in the lab), image and data analysis.

This position is funded through an ERC advanced grant for 2 years in the first instance and preferred start date is June first 2022.

## **Key Requirements**

The successful candidate will have a PhD in a relevant area of cell biology (or at least have submitted the thesis) with outstanding track record of research and publications. Extensive experience in cell biology and optical microscopy is essential with a particular interest in interdisciplinary science, quantitative biology and biophysics.

Additional experience with organoids or stem cells is desirable. You must have demonstrated ability for creative, original independent research. You must be adept at multi-tasking and organising your work to meet deadlines. You must have a proven track record of working in multi-disciplinary teams.

## **References:**

L. Balasubramaniam, A. Doostmohammadi, T. B. Saw, G.H.N Sankara Narayana, R. Mueller, T. Dang, S. Gupta, S. Sonam, A. S. Yap, R-M. Mège, J. Yeomans & B. Ladoux, Investigating the nature of active forces in tissues reveals how contractile cells can form extensile monolayers, Nature Materials, 20, 1156-1166 (2021).

A. P. Le, J-F. Rupprecht, T. B. Saw, R-M. Mège, Y. Toyama, C. T. Lim & B. Ladoux, Adhesion-mediated heterogeneous actin organization governs apoptotic cell extrusion, Nature Communications, 12(1), 397 (2021). T. B. Saw, A. Doostmohammadi, V. Nier, L. Kocgozlu, S. Thampi, Y. Toyama, P. Marcq, C. T. Lim, J. M. Yeomans & B. Ladoux, Topological defects in epithelia govern cell death and extrusion, Nature, 544, 212-216 (2017).