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Cell Fate Clusters in ICM Organoids Arise from Cell Fate Heredity & Division –a Modelling Approach

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During the mammalian preimplantation phase, cells undergo two subsequent cell fate decisions. Within the second decision, the inner cell mass (ICM) segregates into the epiblast and the primitive endoderm. Recently, ICM organoids have been published as an in vitro model system towards preimplantational development. ICM organoids mimic the cell fate decision taking place in the in vivo mouse embryos. In a previous study, the spatial pattern of the different cell types was investigated. The study revealed that cells of the same fate tend to cluster stronger than expected for the currently hypothesised purely random cell fate distribution. Three major processes contribute to the final cell fate arrangements at the mid and late blastocysts or 24 h old and 48 h old ICM organoids, respectively: 1) intra- and intercellular chemical signalling; 2) a cell sorting process; 3) cell proliferation.

To quantify the influence of cell proliferation on the emergence of the cell type clustering behaviour, a computational model was developed. The model accounts for mechanical cell-cell interactions, cell growth and cell division and was applied to compare several assumptions of how ICM neighbourhood structures are generated. The model supports the hypothesis that initial cell fate acquisition is a stochastically driven process. The model further shows that the observed neighbourhood structures can emerge due to cell fate heredity during cell division and allows the inference of a time point for the cell fate decision.

Simulations show that cell divisions involving cell fate heredity seem sufficient to lead to the local clustering observed in 24 h old ICM organoids, and that the initial cell differentiation process takes place only during a small time window. Our results leave little room for extracellular signalling believed to be important in cell fate decision, therefore we are discussing an alternative role of chemical signalling in this process.

Primary authors: LIEBISCH, Tim (Goethe University Frankfurt am Main); Mr DRUSKO, Armin (Goehte University); Dr MATHEW, Biena (Goethe University); Prof. STELZER, Ernst (Goethe University); Prof. FISCHER, Sabine (Julius Maximilian University of Würzburg); Prof. MATTHÄUS, Franziska (Frankfurt Institute for Advanced Studies)

Presenter: LIEBISCH, Tim (Goethe University Frankfurt am Main)

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