A bottom-up approach to study the interplay between signaling and mechanics in early mammalian embryogenesis

Chii Jou Chan[1], Prachiti Moghe[1], Atef Asnacios[2], François Graner[2], Takashi Hiiragi[1]

[1] EMBL Heidelberg, Heidelberg, Germany

[2] Laboratoire Matière et Systèmes Complexes, Université Paris Diderot, France

During early mouse embryonic development, as the blastocyst cavity begins to form and expand, the inner cell mass (ICM) undergoes lineage and spatial segregation to form the primitive endoderm (PrE) facing the blastocyst cavity, and the epiblast (EPI) enclosed between the PrE and the outer trophectoderm. However, the mechanisms driving such cell sorting behavior remain unknown. Furthermore, it remains unclear whether cell position determines their fate, or that the cells are pre-specified in a random manner before sorting out their positions. Here, using a combination of embryological and biophysical approach, we revealed a fluid-to-solid transition that underlies the ICM morphogenesis, which is characterized by a pronounced increase in tissue stiffness and viscosity during ICM maturation. We further showed that increased tissue fluidity correlates with dynamic cellular rearrangements and extensive nuclear shape fluctuations during the sorting phase, while the solid-like phase at the mature stage is accompanied by PrE epithelialization. Notably, cell sorting behavior correlates with changes in nuclear deformability and FGF-mediated actomyosin contractility in the two cell types. Overall, this bottom-up approach allows us to dissect the interplay between cell sorting and fate specification and to establish the mechanochemical feedback loops regulating ICM morphogenesis.