

BDR SEMINAR in Kobe

"CDB SEMINAR" and "QBiC SEMINAR" have been renamed "BDR SEMINAR".

Nicolas Rivron

Hubrecht Institute and MERLN Institute, The Netherlands

Thursday, September 6, 2018

17:30-18:30, Seminar Room, Building A 7F

Synthetic entities: blastocyst-like structures generated solely from stem cells

Summary

The blastocyst, the early mammalian embryo, forms all embryonic and extra-embryonic tissues, including the placenta. It consists of a spherical thin-walled layer, the trophoblast, that surrounds a fluid-filled cavity sheltering the embryonic cells.

From mouse blastocysts, both trophoblast and embryonic stem cell lines can be derived, which are *in vitro* analogues of the trophoblast and embryonic compartments, respectively. Our lab showed that trophoblast and embryonic stem cells cooperate *in vitro* to form structures that morphologically and transcriptionally resemble E3.5 blastocysts (*blastoids*). *Blastoids* are permissive to the formation of primitive endoderm-like cells, the second extra-embryonic lineage, and implant upon *in utero* transfer.

Like blastocysts, *blastoids* form *via* inductive signals originating from the inner embryonic cells and driving outer trophoblast development. The nature and function of these signals are largely unexplored. Genetically and physically uncoupling the embryonic and trophoblast compartments, along with single cell transcriptomics, revealed an extensive list of inductive signals. We specifically show that the embryonic cells maintain trophoblast proliferation and self-renewal, while fine-tuning trophoblast epithelial morphogenesis. Altogether, these embryonic inductions are paramount to form a trophoblast state that robustly implants and triggers a genuine decidualization *in utero*. Thus, at this stage, the nascent embryo fuels the development and implantation of the future placenta.

Our lab now investigates how synergies between the different compartmented cell types (epiblast, primitive endoderm, and trophoblast) regulate implantation and post-implantation development. The *blastoid* is a unique and powerful tool that can be reproducibly generated in large numbers, finely tuned, contains all the cell types to form the *conceptus*, and implants *in utero*.

References:

Rivron NC [corresponding author] et al. Blastocyst-like structures generated solely from stem cells. *Nature* (2018). doi:10.1038/s41586-018-0051-0.

Rivron NC. Formation of blastoids from mouse embryonic and trophoblast stem cells. *Protocol Exchange* (2018) doi:10.1038/protex.2018.051



RIKEN Center for Biosystems Dynamics Research (BDR)

Host: **Kyogo Kawaguchi**
Nonequilibrium physics of living matter RIKEN Hakubi Research Team
(Scheduled to start September 1, 2018)
Contact: bdr-mtg@ml.riken.jp

