



# CDB SEMINAR

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Monday, November 19, 2012

16:00~17:00 A7F Seminar Room

### Making fate decisions at the exit of pluripotency: what ES cells tell us about the embryo

#### Summary

Mouse Embryonic Stem (ES) cells are a defined and controllable system to study the process of cell fate decisions in development. Current thinking suggests that ES cells in culture self renew a pluripotent naïve state which reflects the situation in the mammalian blastocyst, Upon experimental manipulation (withdrawal of self renewal inducing factors) cells can be coaxed to differentiate into particular lineages through the application of particular cocktails of signalling molecules. There are questions as to whether -or to what extent- this process reflects the emergence of cell types in the embryo. This will be the topic of under discussion.

Fate choices are always binary, are taken by individual cells and involve intrinsic programmes of gene expression that, when launched, push cells into 'transitions states' which act as substrates for selection. Signals act as the selective agents, with Wnt signalling playing a central role in the selection process and thereby in the establishment of specific fates. Evidence will be presented that there might not be a pluripotent naïve state, but rather that in self renewing conditions cells are already primed for a specific fate and that therefore they are in a 'ground state of differentiation". Developmental, experimental and evolutionary considerations suggest that this state might be a 'transition state" related to particular precursors of the nervous system. This state is used as a basis to generate more cell types through binary decision of the type IF NOT, THEN.

These notions will be illustrated with the early choices that ES cells make in neutral differentiation conditions in culture and how these relate to those that take place in embryos.

#### References

Muñoz Descalzo, S., de Navascues, J and Martinez Arias, A. (2012) Wnt/Noch signaling: an integrated mechanism regulating transitions between cell states. *Bioessays* 34, 110-118.

Trott, J., Hayashi, K., Surani, A., Babu, M. and Martinez Arias, A. (2012) Dissecting ensemble networks in ES cell populations reveals micro-heterogeneity underlying pluripotency. *Molecular Biosystems* 8, 744-752.

Kalmar, T., Lim, C., Hayward, P., Muñoz Descalzo, S., Garcia Ojalvo, J. and Martinez Arias, A. (2009) Regulated fluctuations in Nanog expression mediate cell fate decisions in embryonic stem cells. *PLoS Biol* 7(7): e1000149. doi:10.1371/journal.pbio.1000149

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