IMCB Invited Speaker

Speaker : **Dr. Daniel Messerschmidt**
Senior Research Fellow, Mammalian Development Group,
Institute of Medical Biology (IMB), Singapore

Date : 4 April 2013 (Thursday)

Time : 2:30PM - 3:30PM

Venue : IMCB Seminar Room 3-46, Level 3, Proteos, Biopolis

Host : Prof. Wang Yue

Seminar :

Developmental epigenetics – TRIM28/KAP1 function in the pre-implantation mouse embryo

During oocyte-to-embryo transition nuclear reprogramming resets the epigenome of the zygote and early pre-implantation embryo to a ground state, an essential measure to ensure first toti- and later pluripotency. Radical, global DNA demethylation, occurring actively in the paternal and passively in the maternal genome is a prominent feature of nuclear reprogramming, yet poses a danger to a subset of methylated sequences that must be preserved for their germ-line to soma inheritance. Prominently, imprinted loci, gene clusters with parent-of-origin specific gene expression patterns, must retain their differential methylation status acquired during gametogenesis throughout embryogenesis and in adult tissues. We have identified a complex, formed by maternal TRIM28/KAP1 and its binding partners ZFP57 and SETDB1, playing an essential role preventing detrimental demethylation of imprinted genes during reprogramming. The loss of maternal TRIM28 leads to severe phenotypic and epigenetic variability ultimately resulting in embryonic lethality. Though usually attributed to genetic background variations or environmental influence, we show the phenotypic variability to be derived from early and minute epigenetic variations in single blastomeres. A full rescue of all developmental defects can however be achieved by mere pronuclear transfer of maternal mutant pronuclei into normal enucleated zygotes, thus timing the requirement of maternal TRIM28 protein to the zygote shortly after fertilization, proving it expendable for oocyte growth and maturation. Our results not only shed light on the long elusive players protecting imprinting marks in the shifting epigenetic environment of the early preimplantation embryo, but also reveal the long-ranging effects of a maternal gene deletion on epigenetic memory and illustrate the delicate timing and equilibrium of maternal and zygotic factors during nuclear reprogramming.

About the Speaker :

Dr. D. Messerschmidt completed his master in biochemistry at the Max Planck Institute for Developmental Biology and the University of Tuebingen (Germany) where he studied organ formation and protein interactions in nematodes. He then embarked on his doctoral work at the Max Planck Institute for Immunobiology (Freiburg, Germany) in order to study early differentiation events in mouse embryos. His work on lineage segregation and differentiation in the blastocyst and embryonic stem cells ultimately showed a non-cell autonomous requirement of the pluripotency transcription factor NANOG for primitive endoderm formation in vivo. For his post-doctoral work he joined the laboratory of Barbara Knowles and Davor Solter at the Institute of Medical Biology (Singapore), to follow his interests in epigenetic aspects of differentiation and early embryonic development. His work addresses particularly epigenetic reprogramming during oocyte-to-embryo transition, an essential measure to ensure totipotency in the mammalian zygote and early embryo.

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