Mechanisms of pluripotency and epigenesis in human embryonic stem cells.

Roger A. Pedersen

Recent developments in the stem cell field have highlighted the potential for medical applications arising from studies of human embryonic stem cells. Our group has chosen to focus on understanding fundamental mechanisms that underlie the biology of these pluripotent cells as the foundation for future progression to their possible therapeutic use. Our principal objective is to define the molecular and genetic basis for the maintenance of the pluripotent status of human embryonic stem cells, and similarly, the basis for their differentiation into the primary body lineages: mesoderm, endoderm and ectoderm. Previous studies had revealed that pluripotency of human embryonic stem cells was not maintained by similar mechanisms as for mouse embryonic stem cells, whose self-renewal depends on Leukemia Inhibitor Factor and Bone Morphogenetic Protein. Accordingly, we have examined the effects of other growth factors known to be important in cell fate decisions of mammalian and other vertebrate embryos. Surprisingly, we found that signaling through the Activin/Nodal pathway is critical for maintenance of pluripotency and that basic Fibroblast Growth Factor augments this pathway. Because Activin and Nodal are considered responsible for directing differentiation along the mesoderm and endoderm lineages during embryonic development, we hypothesise that their effects in human embryonic stem cells involve alternative intermediate transcription factor(s) and target genes. Of particular interest are Smad binding partners capable of altering the epigenetic status of the cells. As background for understanding such epigenetic mechanisms, we have analysed the expression of imprinted genes and their regulation by DNA methylation in human embryonic stem cells. We find that the overall epigenetic status of human embryonic stem cells is relatively stable during their derivation and extended culture, in marked contrast to that of mouse embryonic stem cells. Taken together, these findings illustrate the distinct biological nature of human embryonic stem cells in comparison to their mouse counterparts and underscore the need for further studies of the mechanisms underlying their differentiation into clinically useful lineages.

Initial results from the Singapore Stem Cell Laboratory

Mahendra S. Rao

The Singapore Stem Cell Consortium under the leadership of the executive committee chaired by Dr. Eng-Hin Lee and Dr. Pedersen proposed the establishment of a stem cell laboratory, a stem cell bank and a GMP facility with an initial focus on the laboratory. Work was initiated in January and a staffed laboratory was inaugurated in April. Stem cell scientists at the LSCB have initiated research programs in cell culture, differentiation and characterization of cells and established local and international collaborations. I will present a brief outline of where we are and where we expect to be by the end of the year.