24th Stem Cell Club Meeting

Embryonic and Hematopoietic Stem Cells

(Organised by the Stem Cells Research Singapore Website Committee http://www.stemcell.edu.sg)

Date: June, 14th, 2007 (**Thursday!**)
Time: 5:30 pm
Venue: Matrix, Creation, Level 4

Host: Justine Burley

Time	Title	Speakers
5:30-6:10	***Embryonic identity of hESC***	**Ludovic Vallier** *MRC, Cambridge*
6:10-6:50	***MicroRNAs regulating human hematopoietic development***	**Curt Civin** *Samuelson Professor of Cancer Research* *Kimmel Cancer Center* *Johns Hopkins University*
7:00-	**Wine and Cheese (at Invitrogen facilities, 4th floor, Chromos)**	

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Embryonic identity of hESC

Ludovic Vallier, MRC Cambridge

Embryonic stem cells are pluripotent cells derived by culturing embryos at the blastocyst stage. Despite the common origin and the similar properties of differentiation of mouse and human embryonic stem cells, recent studies have revealed that they rely on different signalling pathways to maintain their pluripotent status. Mouse embryonic stem cells are dependent on LIF whereas their human counterparts rely on Activin/Nodal and FGF. Recent results obtained in our laboratory demonstrate that Activin/Nodal signalling has an evolutionarily conserved role in the maintenance of pluripotency in mammals providing for the first time a developmental explanation for the differences between mouse and human embryonic stem cells.

MicroRNAs regulating human hematopoietic development

Curt Civin, Samuelson Professor of Cancer Research, Kimmel Cancer Center, Johns Hopkins University

MicroRNAs bind to partially complementary target sites in the 3* untranslated regions (3*UTRs) of mRNAs and inhibit their translation to protein. Because a microRNA binds with imperfect complementarity to its target sequences in mRNAs, one microRNA can recognize different target sequences in the 3*UTRs of many different mRNAs. By inhibiting expression of multiple proteins in one or more pathways, microRNAs can serve as *multi/master switches* to potently regulate cellular functions, particularly cellular development. Pursuant to our long-term studies on regulation of hematopoiesis, we recently profiled microRNA expression in hematopoietic stem-progenitor cells (HSPCs) and identified 31 mature and 2 precursor microRNAs expressed by human CD34+ cells from both mobilized peripheral blood stem-progenitor cells (PBSCs) and bone marrow (BM). We combined these microRNA expression data with our prior human HSPC mRNA expression results{Georgantas et al, Cancer Research 2004}, and with our microRNA-mRNA target predictions, into a novel *Transcriptome Interaction Database* (TID){Georgantas et al, PNAS 2007}, which predicted that certain of these HSPC-expressed microRNAs (*HE-microRNAs*) targeted several mRNAs critical to human hematopoietic differentiation. Thus, we formulated a model for microRNA control of hematopoiesis in which many genes specifying hematopoietic differentiation are expressed in HSCs and early HPC subsets, but are held in check by HE-microRNA-mediated selective translational inhibition of expressed mRNAs until further differentiation occurs. This model also fits with our unpublished data that several HSC-expressed mRNAs were not expressed in HSCs at the protein level. We recently published the first study to systematically examine the expression and actions of microRNAs in HSPCs. We defined the microRNAs expressed by primary human CD34+ cells and predicted that a subset of these HE-microRNAs can act to down-regulate translation of a relatively large set of key hematopoiesis-associated mRNAs. For several target mRNAs, we then demonstrated, using luciferase assays, that translation is actually decreased by microRNAs. As proof of principle, we showed in the initial publication{Georgantas et al, PNAS 2007} that mir-155 (aka BIC, the primary microRNA precursor of mir-155) potently inhibits both human
myelo- and erythropoiesis, and we have since found that mir-16 selectively inhibits human erythropoiesis. Thus, certain HE-microRNAs appear to function as powerful master regulators of human hematopoietic differentiation.