Institute of Medical Biology
A*STAR

Seminar Announcement

- All Are Welcome -

Speaker: **Dr Drew Titmarsh**
Australian Institute for Bioengineering and Nanotechnology
The University of Queensland
St. Lucia, Queensland, Australia

Title: **"Diagnostic Microbioreactor Arrays for Screening Pluripotent Stem Cell Expansion, Maintenance And Differentiation"**

Date : **20 May 2013 (Monday)**

Time : **11.00am – 12.00pm**

Venue: **Breakthrough Theatrette, Matrix Level 4, Biopolis**

Host : **Dr Simon Cool**
(Tel: 64070176, email: simon.cool@imb.a-star.edu.sg)

Abstract of the Seminar:

Exquisite control over stem cell fate through expansion and differentiation is needed to efficiently produce sufficient, defined cell populations for intended applications in regenerative medicine and drug screening. Yet, this is hindered by poorly defined microenvironmental compositions inherent in conventional static culture formats. We have developed scalable, valveless, continuous-flow microbioreactor arrays that provide a full-factorial set of 27 exogenous factor compositions, and also allow controlled accumulation of paracrine factors.

HES-3 hESCs were screened for maintenance of pluripotency markers against b-FGF and TGF-β1 in a chemically-defined medium background, with retinoic acid included as an internal pro-differentiation control. Factorial analysis revealed the main and interaction effects of the supplied factors on pluripotency marker expression, which was also strongly dependent on sequential position within a column of serial culture chambers, best explained by accumulation of paracrine factors that negatively modulate pluripotency.

The microbioreactor array was then utilised to investigate mesendodermal differentiation of hESCs to a MIXL1+, primitive streak-like population. A MIXL1 gene reporter was activated in specific combinations of BMP-4, Activin A, and BIO (a canonical Wnt activator) treatment, and was dependent on the position within a column of serial culture chambers. Regardless of the factors supplied to cells, significant MIXL1 expression was only activated in downstream chambers, suggesting accumulation of paracrine factors was required and direct action by BMP, Activin and/or canonical Wnt signals was not sufficient to activate robust expression. Modulation and identification of paracrine factors was then possible by directly screening putative paracrine factors or inhibitors of their signaling pathways. Importantly, optimization of these culture conditions with the arrays was readily translatable to improving mesendodermal differentiation in conventional static culture protocols, exemplifying the immediate practicality of the microbioreactor array platform. This platform thus deciphers factor interplay and signalling hierarchies that control of stem cell fate, and is applicable as a universal microenvironmental screening platform for bioprocess optimisation, media formulation design, quality control for cellular therapeutics and cell-based drug toxicity and discovery.

About the Speaker:

Drew Titmarsh received his B.E. (Chem) (Hons) from The University of Queensland in 2006 with a Minor in Biotechnology. He has since focused on multi-disciplinary work throughout his Ph.D. in Bioengineering (The University of Queensland, 2011), during which he developed microbioreactor arrays for human embryonic stem cell expansion and differentiation. Since graduating he has continued the theme of microbioreactors and stem cells as a Postdoctoral Research Fellow, having research interests in microscale cell culture, stem cell differentiation, large-scale screening platforms, and image-based analysis of single cells. In 2012 he began working to commercialise the microbioreactor array technology developed in his thesis, by collaborating with key industrial partners and leading stem cell laboratories.