Bioprocessing Technology Institute
A*STAR

SEMINAR ANNOUNCEMENT

SPEAKER : **ASSOC PROF PETER W. ZANDSTRA**
Institute of Biomaterials and Biomedical Engineering
University of Toronto
Ontario, Canada

(1) TEMPORAL AND SPATIAL CONTROL OF EMBRYONIC STEM CELL SELF-RENEWAL

DATE : **Monday, 4 December 2006**
TIME : **11 am**
VENUE : **Aspiration, Level 2M, Matrix**

(2) STEM CELL BIOPROCESS ENGINEERING

DATE : **Tuesday, 5 December 2006**
TIME : **2 pm**
VENUE : **BTI Board Room, Level 6, Centros**

..Plse see next page for abstracts & a short biography

(1) Temporal and spatial control of embryonic stem cell self-renewal
(Monday, 4 December 2006)

Seminar Abstract

In vivo, stem cells reside in temporally dynamic and adaptive 3-D microenvironments comprised of multiple cell types, signaling factors and adhesion molecules. Together, these exogenously regulated signals interact to form a stem cell niche. Our long term goal is to engineer an artificial stem cell niche capable of guiding stem cell fate. We are approaching this problem by designing novel technologies to recapitulate critical niche components *in vitro,* and by quantitatively measuring and understanding the contribution of isolated niche-components to cell fate decisions. This presentation will review our developing understanding of intra- and intercellular communication networks and the role of cell composition and growth factor presentation on directing mouse and human embryonic stem cell fate.

(2) Stem cell bioprocess engineering
(Tuesday, 5 December 2006)

Seminar Abstract

Stem cell based technologies promise a renewable source of cells and tissue for research, pharmaceutical testing, and cell-based therapies. Despite this enormous potential, significant challenges remain in order to translate the demonstrated biological properties of stem cells into robust and efficacious therapies. Fundamentally, a strategy to control and predict stem cell responses to changes in molecular, cellular and microenvironmental conditions is required. At the molecular and cellular levels, an understanding of the parameters that govern the decision of an individual stem cell to undergo self-renewal vs. differentiation divisions, as well as how interactions between stem cells and their progeny impact culture output, is required. From a microenvironmental perspective, cost effective approaches to implement molecular and cellular requirements for cell growth must be incorporated into stem cell culture technologies. This presentation will review recent progress in our use of engineering – based approaches such modeling and bioreactor design, to enable stem cell based therapies and technologies. Examples from embryonic stem cell – based differentiation into cardiac and blood cells will be presented.

BIOGRAPHICAL SKETCH

Peter W. Zandstra, Associate Professor

EDUCATION/TRAINING

McGill University, B. Eng.	Chemical Engineering and Biotechnology
University of British Columbia, Ph.D.	Chemical Engineering and Biotechnology
Massachusetts Institute of Technology, PDF	Center for Biomedical Engineering

POSITIONS AND HONORS

University of Toronto (Toronto, ON, Canada)		***Jan 1999-present***
Associate Professor	Institute of Biomaterials & Biomedical Engineering	*July 2003-present*
Assistant Professor	Institute of Biomaterials & Biomedical Engineering	*Jan 1999-2003*
Massachusetts Institute of Technology (Cambridge, MA)		***1998-present***
Adjunct Faculty –	Biotechnology Process Engineering Center,	
York University (Toronto, ON)		***2005-present***
Term Appointment -	Mathematics & Statistics Department	*July 2005–2008*

AWARDS AND HONORS (Selected)

- E.W.R. Steacie Memorial Fellowship (July. 2005 – 2011)
- Canada Research Chair in Stem Cell Bioengineering (Jan. 2006 – 2011)
- Canada Research Chair in Stem Cell Bioengineering (Jan. 2001 – 2006)
- Premiers Research Excellence Award (Feb. 2000 - 2004)
- NSERC Postdoctoral Fellowship (Sept. 1998 – 1999)

EDITORIAL BOARD (Selected)

- Associate Editor, Stem Cells (Oct. 2005 – Present)
- Associate Editor, Biotechnology and Bioengineering (Jan. 2004 - Present)
- Associate Editor, Journal of Biotechnology and Applied Biochemistry (July 2002 – May 2006)
- Associate Editor, Experimental Hematology (Aug. 2001 – 2005)

PEER-REVIEWED PUBLICATIONS (Selected)

Manuscripts Submitted For Review

Varelas, X., Rao, R., Dembowy, J., Yaffe, M.B., Zandstra, P.W., and Wrana, J.L. (Submitted Sept. 2006). Hierarchical control of SMAD shuttling regulates human embryonic stem cell pluripotency.

Davey, R., Onishi, K., Mahdavi, A., and Zandstra, P.W. (Submitted Sept. 2006). LIF-mediated control of ESC self-renewal emerges due to an autoregulatory loop.

Purpura, K., Dang, S.M., George, S., Nagy, A., and Zandstra, P.W. (Submitted Sept. 2006). Soluble VEGFR-1 regulates VEGFR-2 activation to control hematopoietic and endothelial development in an oxygen responsive manner.

Mahdavi, A., Davey, R.E., Onishi, K., and Zandstra, P.W. (Submitted Oct. 2006). Sensitivity analysis of transient signaling kinetics finds control modules of stem cell fate control.

Baksh, D., Zandstra, P.W., Davies, J.E., (Submitted Aug. 2006). Osteogenic cells derived from a CD49 below subpopulation of bone marrow-derived cells can undergo long-term expansion in non-contact suspension culture.

Published Manuscripts

Madlambayan, G., Rogers, I., Purpura, K., Ito, C., Yu, M., Kirouac, D., Casper, R.F. and Zandstra, P.W. (2006). Clinically relevant expansion of HSCs with conserved hematopoietic potential in a single-use, closed-system bioprocess. *Biology of Blood and Marrow Transplantation. 12(10): 1020-1030.*

Davey, R.E. and Zandstra P.W. (2006). Spatial organization of embryonic stem cell responsiveness to autocrine GP130 ligands reveals an autoregulatory stem cell niche. *Stem Cells Express.* (doi:10.1634/stemcells.2006-0216).

Kirouac, D. and Zandstra, P.W. (2006). Understanding cellular networks to improve hematopoietic stem cell expansion cultures. *Current Opinion in Biotechnology,* 17 (5): 538-547.

Rosu-Myles M, Stewart E, Trowbridge J, Ito CY, Zandstra P. and Bhatia M. (2005). A unique population of bone marrow cells migrates to skeletal muscle via hepatocyte growth factor/c-met axis. *Journal of Cell Science* 118(Pt 19):4343-52.

Baksh, D., Zandstra P.W. and Davies J.E. (2005). Soluble factor crosstalk between human bone marrow-derived hematopoietic and mesenchymal cells enhances in vitro CFU-F and CFU-O growth and reveals heterogeneity in the mesenchymal stem cell compartment. *Blood* 106(9):3012-9.

Madlambayan, G.J., Rogers I., Kirouac D.C., Yamanaka N., Mazurier F., Doedens M., Casper R.F., Dick J.E. and Zandstra P.W. (2005). Dynamic changes in cellular and microenvironmental composition can be controlled to elicit in vitro human hematopoietic stem cell expansion. *Experimental Hematology* 33(10):1229-1239.

Fok, E. and Zandstra P.W. (2005). Shear-controlled single-step mouse embryonic stem cell expansion and embryoid body-based differentiation. *Stem Cells* 23(9):1333-42.

Viswanathan, S., Davey R.E., Cheng D., Raghu R.C., Lauffenburger D.A. and Zandstra P.W. (2005). Clonal evolution of stem and differentiated cells can be predicted by integrating cell-intrinsic and extrinsic parameters. *Biotechnology and Applied Biochemistry* 42(2):119-131.

Alperin, C., Zandstra P.W. and Woodhouse K.A. (2005). Polyurethane films seeded with embryonic stem cell-derived cardiomyocytes for use in cardiac tissue engineering applications. *Biomaterials* 26(35):7377-86.

Bauwens, C., Yin T., Dang S., Peerani R. and Zandstra P.W. (2005). Development of a perfusion fed bioreactor for embryonic stem cell-derived cardiomyocyte generation: oxygen-mediated enhancement of cardiomyocyte output. *Biotechnology and Bioengineering* 90(4):452-61. Dang, S.M. and Zandstra P.W. (2005). Scalable production of embryonic stem cell-derived cells. *Methods in Molecular Biology* 290:353-64.

Chang, K.H. and Zandstra P.W. (2004). Quantitative screening of embryonic stem cell differentiation: endoderm formation as a model. *Biotechnology and Bioengineering* 88(3):287-298.

Prud'homme, W., Daley G.Q., Zandstra P. and Lauffenburger D.A. (2004). Multivariate proteomic analysis of murine embryonic stem cell self-renewal versus differentiation signaling. *Proceedings of the National Academy of Sciences USA* 2;101(9):2900-5.

Dang, S.M., Gerecht-Nir S., Chen J., Itskovitz-Eldor J. and Zandstra P.W. (2004). Controlled, scalable embryonic stem cell differentiation culture. *Stem Cells* 22(3):275-282.

Purpura, K.A., Aubin J.E. and Zandstra P.W. (2004). Sustained in vitro expansion of bone progenitors is cell density dependent. *Stem Cells* 22(1):39-50.

Purpura, K.A., Zandstra P.W. and Aubin J.E. (2003a). Fluorescence activated cell sorting reveals heterogeneous and cell non-autonomous osteoprogenitor differentiation in fetal rat calvaria cell populations", *Journal of Cellular Biochemistry*. 1:90(1):109-120.

Purpura, K.A., Aubin J.E. and Zandstra P.W. (2003b). Two-colour image analysis discriminates between mineralized and unmineralized bone nodules in vitro. *Biotechniques* 34(6):1188-1192

Viswanathan, S., Benatar T., Mileikovsky M., Lauffenburger D.A., Nagy A. and Zandstra P.W. (2003). Supplementation-dependent differences in the rates of embryonic stem cell self-renewal, differentiation and apoptosis. *Biotechnology and Bioengineering* 84(5):505-517.

Baksh, D., Davies J.E. and Zandstra P.W. (2003). Adult human bone marrow derived mesenchymal progenitor cells are capable of adhesion independent survival and expansion. *Experimental Hematology* 31(8):723-732.

Zandstra, P.W., Bauwens C., Yin T., Liu Q., Schiller H., Zweigerdt R., Pasumarthi K.B.S. and Field L.J. (2003). Scalable production of embryonic stem cell-derived cardiomyocytes. *Tissue Engineering* 9(4):767-778.