38th Stem Cell Club Meeting

Forces and Places in Stem Cell Research

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

Date: August, 20th, 2008 (**Wednesday**)
Time: 5:30 pm
Venue: Aspiration, Level 2M, Matrix

Host: Michael Raghunath

Time	Title	Speaker
5:30-6:00	**How do cells sense mechanical forces? Implications of mechanotransduction in stem cell research**	***Yasuhiro Sawada*** *Department of Biological Sciences, NUS*
6:00-6:30	**Influence of nano-topography on differentiation of human MSCs**	***Evelyn Lim*** *Division of Bioengineering, NUS*
6:30 -	**Wine and Cheese (at Invitrogen facilities, 4th floor Chromos)**	

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How Do Cells Sense Mechanical Forces? – Implications of Mechanotransduction in Stem Cell Research

Yashuhiro Sawada, NUS

Abstract

Cellular responses to mechanical forces underlie numerous biological events including development (morphogenesis), carcinogenesis, cardiovascular disorder, neurogenesis, wound healing, bone homeostasis, and stem cell differentiation (1). Recent studies indicate that various signaling systems and pathways are involved in mechanotransduction. However, specific force receptors, *i.e.* direct mechano-sensors that are directly modulated by mechanical stimuli and initiate intracellular signaling cascades, were not identified at a molecular level, with the exception of mechano-sensitive ion channels.

After over ten years of intensive work on mechanotransduction, we recently demonstrated that the Src family kinase substrate p130Cas (Crk-associated substrate) acts as an ion channel-independent cytoskeletal mechano-sensor through mechanical extension-induced enhancement of substrate susceptibility to phosphorylation (2). Since such "substrate priming" appeared not to be specific for p130Cas but generally involved in the regulation of signaling pathways involving tyrosine phosphorylation (3), we speculated that proteins tyrosine-phosphorylated upon cell stretching would act as mechano-sensors and sought their identities. While we found stretch-dependent tyrosine phosphorylation of several proteins, sequence analysis suggested that the stretch-responsive domains form non-globular structures, consistently with the low mechanical stability observed in p130Cas.

We expect that the exploration of mechanotransduction will provide a novel insight into the mechanisms of how stem cell differentiation is regulated and contribute extensively to the advancement of stem cell research.

References:

1. Engler, A. J., Sen, S., Sweeney, H. L., and Discher, D. E. (2006) *Cell* **126**, 677-689
2. Sawada, Y., Tamada, M., Dubin-Thaler, B. J., Cherniavskaya, O., Sakai, R., Tanaka, S., and Sheetz, M. P. (2006) *Cell* **127**, 1015-1026
3. Tamada, M., Sheetz, M. P., and Sawada, Y. (2004) *Dev Cell* **7**, 709-718

Influence of nano-topography on differentiation of human mesenchymal stem cells

Evelyn K.F. Yim; Division of Bioengineering and Department of Surgery, National University of Singapore

Abstract

Cells are surrounded by various nano-scaled topographical, biochemical and biomechanical cues in their microenvironment during the natural tissue development. An ideal scaffold for tissue engineering application should mimic the natural microenvironment for natural tissue and present the appropriate biochemical and topographical cues in a spatially controlled manner. Recent findings underscore the phenomenon that mammalian cells do respond to nanoscale features on a synthetic surface. Our lab is interested in studying the interaction of adult and embryonic stem cells with nanotopography and how to apply this knowledge to direct stem cell differentiation for tissue engineering applications. We have showed that nanotopography can significantly influence cellular behaviours ranging from attachment to proliferation and differentiation. This presentation will focus on the discussion of the influence of topographical cues on differentiation of human mesenchymal stem cells.