

34th Stem Cell Club Meeting

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

Date: April, 7th, 2008 (**Monday**)

Time: 6:00 pm

Venue: Breakthrough, Level 4, Matrix

Host: Simon Cool, IMCB

Time Title

6:00-7:00 Human mesenchymal (skeletal) stem cells: basic biology and clinical application for bone tissue regeneration

**7:00 - Wine and Cheese
(at Invitrogen facilities, 4th floor Chromos)**

Speaker

Moustapha Kassem
*University of
Southern Denmark,
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This event is sponsored by



Human Mesenchymal (Skeletal) Stem cells: Basic biology and clinical applications for bone tissue regeneration

Moustapha Kassem

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Human bone marrow stromal cells (hMSC) contain a population of stem cells called skeletal (mesenchymal) stem cells that are capable for differentiation into several mesodermal-type lineages including osteoblasts, adipocytes and chondrocytes. The aim of our research program is to understand the biological characteristics of hMSCs so that it will be possible to make full use of them in the context of clinical applications. The following topics will be discussed: a) approaches to isolate an homogenous population of hMSCs with stem cell characteristics from the bone marrow using specific criteria, b) one major challenge for the use of hMSCs in clinical applications is their limited in vitro proliferative potential and the senescence-associated growth arrest phenotype exhibited by the cells during long-term culture. I will present results from studies in our lab showing that transducing hMSCs with human telomerase reverse transcriptase (hTERT) extended the life span of the cells and maintained their “stemness” characteristics, c) I will present recent data regarding the molecular control of hMSC differentiation and some new factors that maintain hMSCs in an undifferentiated state and others that promote their differentiation into the osteoblastic phenotype. I will also present our experience with applying state-of-the-art proteomic approaches to studying the biology of hMSCs.

References from our group that will be discussed:

1. J. Simonsen, C.Rosada, N.Sernici, J. Justesen, K.Stenderup, S.Rattan, T.Jensen, M.Kassem (2002). Telomerase expression extends lifespan and prevents senescence-associated impairment of osteoblast functions. *Nature Biotechnology* 20:592
2. K.Stenderup, J.Justesen, C.Clausen, M.Kassem (2003). Aging is associated with decreased maximal life span and accelerated senescence of bone marrow stromal cells *Bone* 33:919
3. Abdallah BM, Jensen CH, Gutierrez G, Leslie RG, Jensen TG, Kassem M (2004) Regulation of human skeletal stem cells differentiation by Dlk1/Pref-1. *J Bone Miner Res.* 19:841
4. Abdallah BM, Haack-Sorensen M, Burns JS, Elsnab B, Jakob F, Hokland P, Kassem M (2005) Maintenance of differentiation potential of human bone marrow mesenchymal stem cells immortalized by human telomerase reverse transcriptase gene despite of extensive proliferation. *Biochem Biophys Res Commun.* 326:527
5. Kratchmarova I, Blagoev B, Haack-Sorensen M, Kassem M, Mann M (2005) Mechanisms of divergent growth factor effects in mesenchymal stem cell differentiation. *Science* 308:1472
6. Foster LJ, Zeemann PA, Li C, Mann M, Jensen ON, Kassem M (2005) Differential expression profiling of membrane proteins by quantitative proteomics in a human mesenchymal stem cell line undergoing osteoblast differentiation. *Stem Cells* 23:1367
7. Abdallah BM, Haack-Sorensen M, Fink T, Kassem M (2006) Inhibition of osteoblast differentiation but not adipocyte differentiation of mesenchymal stem cells by sera obtained from aged females. *Bone.* 39:181

8. Serakinci N, Hoare SF, Kassem M, Atkinson SP, Keith N (2006) Telomerase promoter reprogramming and interaction with general transcription factors in human mesenchymal stem cells. *Regenerative Medicine* 1:125
9. Abdallah BM, Boissy P, Tan Q, Dahlgaard J, Traustadottir GA, Kupisiewicz K, Laborda J, Delaisse JM, Kassem M (2007) DLK1/FA1 regulates the function of human bone marrow mesenchymal stem cells (hMSC) by modulating gene expression of pro-inflammatory cytokines and immune-response-related factors. *J Biol Chem.* 282:7339
10. Abdallah BM, Ding M, Jensen CH, Ditzel N, Flyvbjerg A, Jensen TG, Dagnaes-Hansen F, Gasser JA, Kassem M (2007). Dlk1/FA1 is a novel endocrine regulator of bone and fat mass and its serum level is modulated by growth hormone. *Endocrinology.* 148:3111

Reviews:

1. Abdallah BM, Kassem M (2007) Human mesenchymal stem cells: from basic biology to clinical applications. *Gene Ther.* [Epub ahead of print]
2. Gimble JM, Zvonic S, Floyd ZE, Kassem M, Nuttall ME (2006) Playing with bone and fat. *J Cell Biochem.* 98:251

Biography

Professor Moustapha Kassem received his medical degree from Cairo University, Egypt (1985) and did his post-graduate training in Internal Medicine and Endocrinology in Denmark and USA. After obtaining his PhD and DSc degrees from the University of Aarhus, Denmark, he did a post-doctoral fellowship at the Mayo Clinic, Rochester, Minnesota, USA. Prof Kassem heads the Molecular Endocrinology Unit at the Faculty of Health Sciences, University of Southern Denmark, Odense, Denmark and the Molecular Endocrinology Laboratory at the Medical Biotechnology Center. He also is consultant endocrinologist at the University Hospital of Odense (OUH), Denmark.

Prof Kassem has extensive research experience with human mesenchymal stem cells (MSC) and their osteoblastic differentiation potential. He has studied the biological aging of hMSC and human bone cells and the effects of donor age on the biological functions of the cells. He has also investigated the interaction between donor age and hormone levels, particularly sex steroids and growth hormone, on the biological characteristics of bone cells. His lab was the first in Denmark to obtain approval to develop human embryonic stem cells (hESC), and has generated 6 hESC lines that are being used for cell differentiation studies. Prof Kassem has received numerous awards in recognition of his research. These include the 1995 Young Investigator award from the American Society for Bone and Mineral Research and the 2004 research prize from Dansk Frimurer. He has published more than 70 original papers in journals including *Nature* and *Science*, and more than 30 reviews and book chapters.