2006 IOF+ANZBMS Combined Meeting

Combined Meeting of the
3rd IOF Asia-Pacific Regional Conference on Osteoporosis *and the*
16th Annual Meeting of the ANZ Bone & Mineral Society
~ 22-26 October 2006, Port Douglas, Australia ~
www.anzbms.org.au/asm/asm2006

Invited Plenary Abstract
P7

Signalling for cartilage differentiation

Toshihisa Komori
Department of Cell Biology, Unit of Basic Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences, 1-7-1 Sakamoto, Nagasaki 852-8588, Japan

Sox9 is an essential transcription factor for mesenchymal condensation in the formation of cartilage anlagen, and Sox9, 5, and 6 are required for acquiring chondrocyte phenotype. After acquiring the phenotype of chondrocytes, the immature chondrocytes further differentiate to hypertrophic chondrocytes in the process of endochondral ossification. Many factors, including PTHrP, FGFs, and BMPs, regulate chondrocyte differentiation at the late stage. Runx2 and Runx3 are essential transcription factors in the late stage of chondrocyte differentiation.

Runx2 and Runx3 are transcription factors that belong to Runx family (Runx1, Runx2, and Runx3). Each of the Runx family genes encodes a DNA-binding domain, runt that is homologous with the Drosophila pair-rule gene runt. Runx2 is induced by BMPs, FGFs, retinoic acid, and TGFβ, and Runx2 interacts with many other transcription factors and co-regulators in the transcriptional regulation of its target genes. Cbfb forms heterodimers with Runx2 and is required for Runx2-dependent transcriptional regulation.

Runx2 regulates bone formation by regulating osteoblast differentiation as well as chondrocyte maturation. Runx2 is essential for the commitment of multipotent mesenchymal cells into the osteoblastic lineage. Runx2 triggers the gene expression of bone matrix proteins, while keeping the osteoblastic cells in an immature stage. Runx2 and Runx3 have redundant functions in chondrocytes, and they are essential for chondrocyte maturation. They prevent chondrocytes from acquiring the phenotype of permanent cartilage. Runx2 directly induces Ihh, which plays an important role in chondrocyte proliferation. Further, PTHrP, which is induced by Ihh, inhibits Runx2 expression. Therefore, the Runx2-Ihh-PTHrP cascade coordinates the proliferation and differentiation of chondrocytes. The regulation of chondrocyte differentiation by Runx family transcription factors will be discussed in detail.