Jan O Gordeladze, J Stem Cell Res Ther 2014, 4:9
http://dx.doi.org/10.4172/2157-7633.S1.007

OMICS Group Conferences
Accelerating Scientific Discovery

3rd International Conference and Exhibition on
Cell & Gene Therapy
October 27-29, 2014 Embassy Suites Las Vegas, USA

# Key regulatory junctions stabilizing the osteoblast phenotype: Implications for cell and tissue engineering

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MicroRNAs are short, non-coding RNAs, which bind to the 3'UTR of messenger RNAs, thus suppressing the translation process. MicroRNAs may be intragenic and positioned more or less adjacent to their targets. However, it has been asserted that transcription factors (TFs) and microRNAs engaged in feed-forward/feed-back loops are stabilizing cell phenotypes. Many researchers, engaged in osteoblast and bone engineering, have focused on Runx2 and Osterix (SP7), being two TFs instrumental in osteoblastogenesis, as well as various microRNA species targeting them. However, when using bioinformatics (the Mir@nt@n algorithm), it appears that other osteoblast-"specific" TFs, like SP1, are involved in regulatory loops. The work presented here indicates that stabilizing the interactions of SP1 with microRNA species targeting it (e.g. mir-204, mir-211, mir-24, -mir-149, and mir-328) may lead to a better differentiation of stem cells to osteoblasts, thus producing a better bone tissue more able to withstand an inflammatory environment compared to over-expressing the TFs Runx2 and Osterix (SP7). The experiments conducted are based on manipulations of TF or microRNA levels using polycistronic constructs of pre-mirs and antago-mirs, up- or down-regulation of TFs using gene-expressing vectors and sh-RNA expressing lentiviral constructs, adipose stem cells grown in an osteoblast-differentiating medium ± cytokines from Th-17 cells, co-cultures with osteoclasts differentiating from PBMCs, as well as manipulated osteoblasts injected into the tibial muscle of SCID mice. Other important transcription factors involved in regulatory loops are SP3, Ets-1, as well as SPI1, JUN, and FOS. Finally, we make an attempt to rank SP1 compared to SP3 and Ets-1 featuring their "stabilizing potency".

## Biography

Jan O Gordeladze, PhD, holds a triple Professor competence (medical biochemistry, physiology, and pharmacology), and is presently working as a Professor at the Department of Biochemistry, Institute of Basic Medical Science, University of Oslo, Norway. He has previously been employed as the Medical Director of MSD, Norway, serving two years as a Fulbright Scholar at the NIH, Bethesda, Maryland, USA, and from 2006-2009 also being employed as Associate Professor at the University of Montpellier, France. He is a member of the Norwegian Stem Cell Center, and his research has over the past 5-6 years been devoted to differentiation of osteochondral cells from stem cells focusing on the impact of transcription factors and microRNA species constituting regulatory loop interactions with functional target genes. He has published more than 120 scientific articles, reviews/book chapters and presented more than 250 abstracts/posters/talks at conferences world-wide.

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