

## Proceedings of German Society for Stem Cell Research (PGSSCR)

### MicroRNA regulation of osteogenic differentiation

Genever P

Biomedical Tissue Research Group, Department of Biology, University of York, York, YO10 5YW, Great Britain

Published on 16 May 2007

Understanding molecular mechanisms that control differentiation of multipotent mesenchymal stromal cells or mesenchymal stem cells (MSCs) is central to the development of novel therapies. Many studies have successfully identified critical factors involved in initiating and maintaining lineage-specific transcriptional changes although the role of post-transcriptional gene silencing during differentiation remains unclear.

In the last decade, it has emerged that RNA may play a major role in the regulation of gene and protein expression in all eukaryotic cells. The transcriptome describes the repertoire of RNAs transcribed from the genome of a particular organism. Gene expression profiling, using defined cell populations, can determine which mRNA species are transcribed, the proteins they encode (though not necessarily translated) and the potential functional consequences. However mature mRNAs represent only about 2% of the total transcriptional output of complex genomes and there is growing evidence that non-coding RNAs profoundly influence gene expression profiles and therefore cellular function.

MicroRNAs (miRNAs) are a superfamily of evolutionary conserved, small non-coding RNAs that bind to the 3' UTR of mRNAs to inhibit protein translation. Consequently, miRNAs can influence a broad range of biological activities, which are instrumental in conferring tissue identity and function. We have determined the expression function of miRNAs during osteogenic differentiation of MSCs and osteoprogenitors *in vitro*. Expression was determined by microarray analysis of 984 known and predicted miRNAs using RNA isolated from undifferentiated cells or following differentiation in the presence of osteogenic supplements (dexamethasone, ascorbic acid and beta-glycerolphosphate) over 21 days. Differentiation was confirmed by induction of alkaline phosphatase, von-Kossa positive mineralisation and qRT-PCR, revealing temporally relevant changes in expression of osteogenic markers (cbfa-1, alkaline phosphatase, type-I collagen, osteopontin and osteocalcin). The analyses revealed constitutive and differentiation-dependent expression of different miRNAs. The functional role of miRNAs was determined using anti-mir microRNA inhibitors transfected into progenitors before osteogenic stimulation and bioinformatic

analyses using predictive algorithms were used to identify potential miRNA targets. Our evidence suggests an important functional role of miRNAs during osteogenesis which may have pervasive implications for our understanding of MSC biology.

JSRM  
www.pubstemcell.com