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Development of bioactive small molecules for controlling mesenchymal stem cells fate

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Histones acetylation, along with methylation, ubiquinitation, sumoylation and phosphorylation, regulates access to DNA through chromatin reorganization. These epigenetic events appear to affect a wide range of physiological processes within cell differentiation, including those implicated in differentiation of mesenchymal stem cells (MSCs) towards mesodermal lineage. During in vitro differentiation from osteoprogenitor to mature osteoblast, three distinct phases can be distinguished that reflect the maturation stages of osteoblasts in vivo. A proliferation phase is followed by a matrix maturation phase, after which the extracellular matrix becomes mineralized. Different markers have been associated with each of these events such as alkaline phosphatase (ALP) for the matrix maturation phase and osteocalcin (OCN) for the matrix mineralization phase. Exploiting access to DNA through chromatin reorganization by histone acetylation and ALP activity, we have developed a novel and efficient cell-based screening assay using MSCs and identified bioactive small molecules after isolation from natural product medicines and high-throughput screening on a library of signal transduction inhibitors. Exploiting ALP activity helped to identify a set of small molecules potential candidates for controlling MSCs differentiation towards mesodermal lineage since ALP is not restricted to osteoblasts. Among selected ALP activators, three isolated small molecules and one synthetic small molecule have been successful on controlling mesenchymal stem cells towards osteogenic, adipogenic and myogenic differentiations using our in-house cell therapy. This research's inventions find their applications both in cancer therapy and in the tissue engineering, specially in the treatment of orthopedic disorders where growth factors such as BMPs are pending to afford satisfactory results.

Biography

Michel N. Mifundu has completed his Ph.D in March 2012 from Kyoto University at Graduate school of Pharmaceutical Sciences (Kyoto, Japan). He also obtained a Master degree in Pharmaceutical Sciences from Osaka University (Osaka, Japan) in March 2009. Prior coming to Japan, he was a Junior Lecture at University of Kinshasa, Faculty of Sciences where he completed his Licence (M.Sc.) degree in Chemical Sciences. Michel's current research interests are: Stem cell in Drug Discovery and Development, Chemical Genomics and Bioinformatics.

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