



Abstracts

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POSTER SESSION B

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Topic 2

Stem Cells, Development and
Regenerative Medicine

Topic 4

Cell Stress: Survival and Apoptosis

P2.21

Differentiation of ES cells and deficiency of Suv39h histone methyltransferases is accompanied by distinct levels of A- and B-type lamins

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Nuclear lamins are major architectural elements of the mammalian cell nucleus, and they have been implicated in the functional organization of the nuclear interior, possibly by providing structural scaffold for nuclear compartments. Mutations in LMNA gene have been shown to cause a whole range of human disorders, called laminopathies. Here, we have studied, by the use of western blots, changes in the levels of A- and B-type lamins in human embryonic stem cells (hESCs) undergoing differentiation and after siRNA to LMNA mRNA. In addition, we have analyzed in which extent the levels of lamins can be influenced by deficiency of histone methyltransferases (HMTs) Suv39h1 and Suv39h2. Our preliminary experiments confirmed that interaction between lamins and histone modifiers could be important for higher-order chromatin arrangement. Moreover, differentiation of hESCs, characterized by distinct epigenetic profiles, was also accompanied by changes in the levels of A- and B-type lamins. Especially an absence of A-type lamins is of functional significance in hESCs.

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P2.22

PTHrP isoform expression in adipo- and osteo-differentiating human mesenchymal stem cellsA. Longo¹, I. Catanzaro¹, F. Caradonna¹, E. Tobiasch², C. Luparello¹¹Dept STEMBIO (Sez. Cellular Biology), Univ. of Palermo, Palermo, Italy²Dept of Natural Sciences, Bonn-Rhine-Sieg Univ. of Applied Sciences, Rheinbach, Germany

Multipotent mesenchymal stem cells (MSC) can differentiate *in vitro* towards osteoblasts and adipocytes, and although the early steps of the differentiation process have been examined thoroughly, still specific markers for the characterization of defined differentiation steps are lacking. To search for stemness/differentiation markers, we examined the expression of the splicing isoforms of parathyroid hormone-related peptide (PTHrP), a regulator of proliferation, differentiation and apoptosis. The PTHrP gene, coding for three protein variants of 139, 141 and 173 aa, has a complex organization with three transcriptional start sites, i.e. two TATA promoters, P1 and P3, and a GC-rich promoter, P2, and nine exons undergoing to alternative splicing. In the undifferentiated MSC we have found four transcripts encoding for the 139 and 173 aa isoforms, whereas osteo-differentiating cells produced only two transcripts encoding for the same protein isoforms, and adipo-differentiating cells only one transcript encoding for the 173 aa isoform. Therefore, our results strongly suggest that during osteo- and adipo-differentiation, the expression of PTHrP isoforms by MSC becomes increasingly selective and P2 is always silenced. Consequently, PTHrP isoform expression could be considered a putative marker of MSC differentiation. We examined the methylation state of PTHrP P2 promoter in undifferentiated and osteo-differentiating MSC, to investigate the possible correlation between methylation and silencing of this promoter in some cell preparations. In agreement with the gene expression data, three CpG island internal sites of this promoter were found to be hypermethylated in DNA preparations from undifferentiated and differentiated cells. Further studies will be performed to underline these findings also for P3 promoter. We conclude that PTHrP plays a role in the differentiation of MSC through both the selective regulation of these isoforms and the mechanism of promoter methylation.