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VIRAL GENE DELIVERY TOOLS IN OPTIMIZATION OF HUMAN MESENCHYMAL STEM CELLS' OSTEOBLAST DIFFERENTIATION

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Introduction: Human skeleton is completely remodelled by mesenchymal stem cells (MSC) within roughly four-and-half years. Bone morphogenetic proteins (BMP) are main inducers of bone formation and maintenance apart of their crucial roles in morphogenesis of other tissues and organs. Optimal activity of BMPs in bone usually requires coordinate signals with the Wnt pathway. Consequently, several bone diseases occur when BMP or Wnt pathways are misregulated. Therefore, proper optimization of the osteogenesis requires efficient gene delivery tools on the way of modulation of osteoblast differentiation of MSC. Unfortunately, classical transfection with multiple transfection reagents triggers massive cell death in transduced MSC. On the other hand, viral tools for gene delivery allow to get 100% of efficiently transduced stem cells without any detection of toxicity.

Methodology: Human MSC cell were isolated from bone marrow aspirates obtained under patients' consent from surgical material upon hip joint arthroplasty or from patients' fat using a liposuction. Adv5-based vectors were used for efficient overexpression of recombinant genes into the mesenchymal precursor cells and lentiviral vectors were used for small hairpin RNA (shRNA)-mediated knockdown of gene expression.

Results & Discussions: The set of adenoviral and lentiviral vectors generated at our lab allows to overexpress or correspondingly downregulate expression of different genes important in regulation of osteogenesis. Usage of the gene delivery tools generated at our lab allowed us to describe a molecular mechanism that mediates osteogenesis regulation by secreted phosphoprotein 2.

Conclusions: Modern viral gene delivery tools open a wide window for biomedical studies aiming to investigate the molecular mechanisms of human MSC differentiation and to optimize the efficacy of regenerative skeletal tissues engineering based on MSC incorporation into the grafts.

Biography

O Korchynskyi has completed his PhD from Institute of Animal Biology, Lviv, Ukraine and Postdoctoral studies at the Netherlands Cancer Institute, Amsterdam, Netherlands and University of North Carolina, Chapel Hill, NC, USA. Currently he is the Associate Professor at the Rzeszow University, Poland and the Senior Scientist at the Institute of Cell Biology, Lviv, Ukraine. He has published more than 30 papers in reputed journals including Nature and Science.

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