

## **Dental Pulp Stem Cells (DPSCs), differentiating into osteoblasts, become a source of the pro-apoptotic factor TRAIL: evaluation of an experimental model for cancer therapy**

Giorgio Mori<sup>1</sup>, Giacomina Brunetti<sup>2</sup>, Angela Oranger<sup>2</sup>, Francesca Sardone<sup>2</sup>, Claudia Carbone<sup>2</sup>, Andrea Ballini<sup>3</sup>, Roberto Grassi<sup>3</sup>, Silvia Colucci<sup>2</sup>, Maria Grano<sup>2</sup>

<sup>1</sup> Dipartimento di Scienze Biomediche, Università di Foggia, Italy

<sup>2</sup> Dipartimento di Anatomia Umana e Istologia "Rodolfo Amprino", Università di Bari Italy

<sup>3</sup> Dipartimento di Odontostomatologia e Chirurgia, Università di Bari Italy

The DPSCs belong to the family of mesenchymal stem cells (MSCs) and are capable, if properly stimulated to differentiate into different cell types including osteoblasts. It has been shown, in animal models, that MSCs derived from bone marrow, producing TNF-related apoptosis-inducing ligand (TRAIL), inhibit the growth of tumors that metastasize to the bone tissue, including lung cancer; however, the expression of TRAIL by the MSCs to be effective, must be stimulated with genetic engineering techniques with the involvement of bacterial vectors. TRAIL is a pro-apoptotic factor, member of the super-family of tumor necrosis factors, known for its peculiarity to selectively induce apoptosis in cancer cells. TRAIL can activate apoptotic signals by binding two different death receptors, DR4 and DR5. In our work we evaluated the production of TRAIL by DPSCs differentiated toward the osteoblastic phenotype. Microarray experiments, also supported by real-time PCR, showed that in DPSCs after differentiation, the expression of TRAIL increased fifteen times. Moreover, cell viability tests have shown that DPSCs differentiating into osteoblasts become resistant to the pro-apoptotic effect of the molecule. This strong resistance derives from a significant decrease in the expression of TRAIL receptors DR4 and DR5, and is confirmed by the weak activation of intracellular apoptotic signal (caspase 3) following the exposure to the molecule. Conversely, the tumor cell lines expressed high levels of DR4 and DR5, and in the presence of TRAIL, activate the intracellular apoptotic signals (caspase 3-8). Thus, the DPSCs, differentiated into osteoblasts, expressing high levels of TRAIL and developing a resistance to the apoptotic effect of the molecule, could represent a valuable therapeutic approach to cancer therapy.

### Keywords

DPSCs, stem cells, TRAIL, osteoblast differentiation, cancer cells apoptosis