NEURON-LIKE CELLS DERIVED FROM BONE MARROW STROMAL CELLS: EXPRESSION AND FUNCTIONING OF $GABA_B$ RECEPTORS

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Bone Marrow Stromal Cells (BMSCs) are reported to differentiate in neuronal-like cells, based on expression of neuron markers and morphologic features; nevertheless, doubts are raised on the true neuronal differentiation potential of mesenchymal stem cells and on their ability to attain functional neuron features. To investigate on functional relevance of BMSC differentiation, we focus on receptors for the neurotransmitter GABA, acting as a trophic factor during neurogenesis. Briefly, rat BMSCs and fibroblasts were exposed to neuron differentiating procedure according to Woodbury; semi-quantitative RT-PCR and Real-Time PCR was performed and relative gene expression calculated; intracellular cyclic AMP accumulation was measured by radioimmunoassay. After 24-hour induction BMSCs displayed neuronal-like morphological phenotype and increased gene expression for Nestin, Neurofilament–M and Tau: we refer to these cells as to BMSC Derived Neuron Like cells (BDNL cells). GABA-Aβ3 mRNA was detected in BDNL cells; GABA-Aβ2, GABA-Aβ3, GABA-Aα1, GABA-Aε subunits were expressed at higher level in BDNL cells, suggesting possible assembly of heterotrimeric $GABA_A$ receptors. GABA-B1 mRNA was present in BMSCs and BDNL cells, BDNL cells also expressing GABA-B2 subunit. Inhibition of forskolin-evoked cAMP accumulation by the $GABA_B$ receptor agonist baclofen, ineffective in BMSC (and baclofen antagonism by phaclofen, CGP 35348, or CGP 52432), confirmed the presence of functional $GABA_B$ receptors negatively coupled to cAMP production in BDNL cells. Fibroblasts undergoing induction protocol expressed GABA-Aβ2, GABA-Aβ3 GABA-Aα1, and GABA-Aε; GABA-B1, but not GABA-B2, transcript was induced; forskolin-stimulated cAMP accumulation was unaffected by baclofen. To conclude, GABA-B1 and GABA-B2 subunit mRNAs were detected in BDNL cells, meeting requirements for functional $GABA_B$ receptor expression; functional analysis confirmed that expression and assembly of $GABA_B$ receptors (exhibiting the profile of classical phaclofen- CGP 35348-, CGP 52432-sensitive $GABA_B$ receptors) coupled to transduction mechanism was selectively induced in BMSCs, an not in other cells tested. $GABA_B$ receptors seem to play roles in neuron migration and in modulation of neuron activity during development; presence of functional $GABA_B$ receptor in BDNL cells would suggest that BMSCs can be converted in cells equipped with appropriate receptors, potentially responding to the neurotransmitter GABA. **Supported by PRIN 2004057732**