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Attenuation of chronic Morphine-mediated cAMP upregulation in SH-SY5Y cells by mesenchymal stem cells

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The cAMP upregulation induced by chronic morphine is regarded as one of the molecular mechanisms leading to its tolerance and dependence. In the present work, we differentiated SH-SY5Y cells into neuron-like cells by retinoic acid (RA), pretreated these cells by morphine, the highly addictive drug, and tested their cAMP levels under different conditions, including co-culture with bone marrow-derived human mesenchymal stem cells (hMSCs) and human dermal fibroblast cells (hDFCs). We found that chronic treatment with 10μM morphine led to cAMP upregulation in these differentiated SH-SY5Y cells and the morphine mediated-cAMP upregulation was significantly attenuated by co-culturing with the hMSCs at early passages ($P \leq 5$), though this attenuation did not occur in co-cultures with the hMSCs at late passages ($P > 5$) or hDFCs. In addition, hMSCs improved the mu-opioid receptor-mediated endocytosis in SH-SY5Y cells in preventing the development of morphine tolerance. In summary, early passaged hMSCs can successfully inhibit morphine induced cAMP upregulation in RA-differentiated SH-SY5Y cells by cell-cell contact and/or their released molecules, suggesting that hMSCs may serve as valuable therapeutics for treating morphine tolerance and dependence to minimize the risk of drug abuse and addiction. This research is supported by grants of DoD (PR100499P1) & the Boothroyd Foundation to T. QU.

Biography

Hongna Yang is a visiting student of Psychiatry of UIC, from Shandong University in China. Her focus is on the stem cell therapy (NSCs, MSCs) of neurodegenerative diseases and morphine tolerance.

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