Proliferative Effect of Hypericine on Human Skin Fibroblast Cells in vitro

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Hypericine is used traditionally as a wound healing agent; therefore it’s a potential promoter for reprogramming induced pluripotent stem cells (IPSCs) which possesses several problems due to drawbacks associated with efficiency and viral genome integration. In order to improve reprogramming efficiency and compensate for viral transduction new chemicals have been searching in IPSCs researches. The aim of this project is to investigate the proliferative effect of Hypericine on human skin fibroblast cells (SF) in-vitro and to identify the mechanism of action in molecular level. The proliferation was measured using the Clonogenic and MTT assays. Real time quantitative polymerase chain reaction (Q-PCR) was performed to detect the mRNA levels of cyclins (D1 and B1) and cell cycle controller genes (p53 and p21). SF cells were treated with different doses (1nM-100µM) of Hypericine for 24 and 48 h. A significant cell proliferation was observed in moderate concentrations (0, 1 - 15 µM; %110-134), but in high concentrations (25-50µM) cytotoxic effects emerged in SF cells (IC50 = 23, 62 µM, R^2 = 0,915). Q-PCR results showed that the most proliferative dose of Hypericine (15µM) stimulates cyclin D1. The anti-proliferative activity of Hypericine was accompanied by inhibition of cyclin B1 mRNA, whereas it induced expression of the p53 and p21 genes, and thus apoptosis was observed by DNA laddering at the same dose (50µM). This study demonstrates that Hypericine can compensate for viral transduction and improve reprogramming efficiency by enforcing G1 phase of SF cells.