

Full Paper

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PPAR γ agonists inhibit growth and expansion of CD133+ brain tumour stem cells

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Abstract

Brain tumour stem cells (BTSCs) are a small population of cells that has self-renewal, transplantation, multidrug resistance and recurrence properties, thus remain novel therapeutic target for brain tumour. Recent studies have shown that peroxisome proliferator-activated receptor gamma (PPAR γ) agonists induce growth arrest and apoptosis in glioblastoma cells, but their effects on BTSCs are largely unknown. In this study, we generated gliospheres with more than 50% CD133+ BTSC by culturing U87MG and T98G human glioblastoma cells with epidermal growth factor (EGF) and basic fibroblast growth factor (bFGF). *In vitro* treatment with PPAR γ agonist, 15-Deoxy- $\Delta^{12,14}$ -Prostaglandin J₂ (15d-PGJ₂) or all-*trans* retinoic acid resulted in a reversible inhibition of gliosphere formation in culture. Peroxisome proliferator-activated receptor gamma agonists inhibited the proliferation and expansion of glioma and gliosphere cells in a dose-dependent manner. Peroxisome proliferator-activated receptor gamma agonists also induced cell cycle arrest and apoptosis in association with the inhibition of EGF/bFGF signalling through Tyk2-Stat3 pathway and expression of PPAR γ in gliosphere cells. These findings demonstrate that PPAR γ agonists regulate growth and expansion of BTSCs and extend their use to target BTSCs in the treatment of brain tumour.

Keywords: brain tumour stem cells, glioblastoma, PPAR γ , anti-cancer drug, Jak-Stat pathway