Roscovitine

Purine analogue roscovitine, a cyclin-dependent kinase (CDK) inhibitor, has shown strong anti-proliferative and pro-apoptotic effects in solid and hematologic cancers such as non small-cell lung cancer and lymphomas. It targets CDK2, 7 and 9 preferentially, which are also overexpressed in glioblastoma. Therefore, the biological effects of roscovitine in glioblastoma cell lines were investigated. Glioblastoma A172 and G28 cell lines were incubated with serial concentrations of roscovitine for 24-120 h. Proliferation was measured using the xCELLigence Real-Time Cell Analyzer, an impedance-based cell viability system. Cell cycle distribution was assessed by flow cytometry and gene expression was quantified by quantitative RT-PCR and western blot analysis. Roscovitine exhibited a clear dose-dependent anti-proliferative and pro-apoptotic effect in the A172 cell line, while G28 cells showed a anti-proliferative effect only at 100 µM. The results of the flow cytometric (FACS) analysis revealed a dose-dependent increase of the G2/M and sub-G1 fractions in A172 cells, while G28 cells responded with an elevated sub-G1 fraction only at the highest concentration. Roscovitine led to a dose-dependent decrease of transcripts of p53, CDK 7 and cyclins A and E and an increase of >4-fold of p21 in A172 cells. In G28 cells, a dose-dependent induction of CDK2, p21 and cyclin D was observed between 10 and 50 µM roscovitine after 72 h, however, at the highest concentration of 100 µM, all investigated genes were downregulated. Roscovitine exerted clear dose-dependent anti-proliferative and pro-apoptotic effects in A172 cells and less distinct effects on G28 cells. In A172 cells, roscovitine led to G2/M arrest and induced apoptosis, an effect accompanied by induced p21 and a reduced expression of CDK2, 7 and 9 and cyclins A and E. These effects requre further studies on a larger scale to confirm whether roscovitine can be used as a therapeutic agent against glioblastoma [1)].

1)
Kolodziej M, Goetz C, Di Fazio P, Montalbano R, Ocker M, Strik H, Quint K. Roscovitine has anti-proliferative and pro-apoptotic effects on glioblastoma cell lines: A pilot study. Oncol Rep. 2015 Jul 3. doi: 10.3892/or.2015.4105. [Epub ahead of print] PubMed PMID: 26151768.