Baicalein Activates Aryl Hydrocarbon Receptor and Decreases the Expression of CDK4 and Cyclin D1 to Induce G1 Phase Arrest in Oral Cancer Cells

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Baicalein is a flavonoid known to have anti-inflammatory and anti-cancer effects. Its function as an aryl hydrocarbon receptor (AhR) ligand that modulates AhR-mediated dioxin toxicity was recently proposed. This study investigated if the antiproliferative effect by baicalein was mediated by AhR. The results from MTT assay showed baicalein at concentrations of 7 to 56 μg/ml inhibited cell proliferation in a dose-dependent way in oral cancer cells, HSC-3. Cell cycle analysis showed that baicalein (28μg/ml) arrested cells at G1 phase. The G1 phase arrest in baicalein-treated cells, through the detection of Western blot method, was associated with decreased CDK4, cyclin D1 and retinoblastoma (Rb) phosphorylation. Results from luciferase assay revealed that baicalein activated AhR activity in HSC-3. Furthermore, the hypophosphorylation of Rb was partially reversed when using siRNA to suppress the expression of AhR in baicalein-treated cells. However, the reduction of CDK4 and cyclin D1 by baicalein was not different between cells with or without AhR knockdown. These data indicate that baicalein inhibits cell proliferation by causing cell cycle arrests at G1 phase. The molecular mechanism of baicalein on G1 phase arrest is mediated by the hypophosphorylation of Rb. The activation of AhR, and the reduction of CDK4 and cyclin D1 contributes to the de-phosphorylation of Rb in baicalein-treated cells. The data of the study suggest that baicalein can be a chemopreventive agent to inhibit AhR- and cyclin D1-associated cancer cell proliferation.