Baicalein Enhances p27kip Degradation in Oral Cancer Cells

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Backgrounds:
While most studies in cancer cell lines report that baicalein causes cell cycle arrest by increasing the expression of p27kip, we found that in our preliminary data, the p27kip was decreased rather than increased in baicalein treated oral cancer cells, HSC-3. The reduction of p27kip was concomitant to the reduction of cyclinD1 and CDK4 as well as phosphorylated Rb (p-Rb), indicating its association with phosphorylation of Rb and growth inhibition. Thus, the purpose of the study is to elucidate how baicalein regulates p27kip expression in the oral cancer cell model.

Methods and Results:
Using cell cycle analysis, we found that baicalein treated cells was arrested at S phase at 24hr treatment. Data by Western Blot showed that p27kip was decreased at 12 and 24hr whereas phosphorylated p27kip (p-p27) was increased in baicalein treated cells. The reduction of p27kip in baicalein treated cells was time-correlated to the decrease of Akt and increase of p-Akt. This suggests that baicalein induces the phosphorylation of p27kip, which is mediated by activation of Akt. It is known that the increase of p-p27 eventually leads to the degradation of p27kip and thus, decrease the expression of p27kip. Interestingly, phosphorylated GSK-3β (p-GSK-3β) was also increased at the time when p-Akt was increased and p27kip was decreased, suggesting that GSK-3β pathway might be also involved in the modulation of p27kip.

Conclusion:
Our data indicates that baicalein modulates the degradation of p27kip through Akt pathway in HSC-3. GSK-3β, the downstream protein molecule of Akt pathway might be an indirect effect of Akt on regulating the expression of p27kip. Downregulation of p27kip has been reported to correlate to the malignancy and prognosis of oral cancers. The impact of baicalein on the reduction of p27kip in oral cancer cells shall be determined in terms of migration and invasion, in addition to its effect on growth inhibition.