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## Hesperitin, a Potential Therapy for Carcinoid Cancer

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**Background:** Many studies have been conducted to elucidate the role of naturally occurring compounds in the treatment of various forms of cancer. One of these compounds, Hesperitin, has been shown to inhibit proliferation of human pancreatic cancer cells and murine melanoma cells. Although these compounds show promise, few studies have been performed to evaluate their effects in carcinoid tumors. Our lab has previously shown that carcinoid cancer cell growth can be suppressed via activation of the Notch signaling pathway. In this study, we sought to examine Hesperitin as a potential Notch activating drug and carcinoid tumor suppressor.

**Methods:** A high throughput drug screen utilizing a Notch 1 activating assay revealed that Hesperitin induced the Notch signaling pathway. We treated human BON GI carcinoid cells with Hesperitin (up to 125 $\mu$ M) and assessed growth with MTT assays. Western blots for human achaete-scute complex-like 1 (ASCL-1) and Chromogranin A (CgA) were used to measure production of neuroendocrine tumor markers. We then examined the expression of Notch 1 using real-time PCR.

**Results:** The MTT assay demonstrated Hesperitin induced cell death in BON cells in a dose dependent manner. Western blot analysis confirmed that Hesperitin suppressed expression of both ASCL-1 and CgA with a 2 day treatment. Real-time PCR confirmed that Hesperitin increased the levels of Notch 1 over controls.

**Conclusion:** This study demonstrates that Hesperitin can induce Notch 1 in carcinoid cells, leading to suppression of tumor cell proliferation and bioactive hormone production. Based on these findings, further research into the role of Hesperitin as a treatment for patients with carcinoid cancer is warranted.

