Modulation of THP-1 Macrophage Cytokine Expression by Kava Metabolites

Pinner, Keanu

Kava has been used by Pacific Islanders for years. The purpose of this project was to determine which of the Kava metabolites activate THP-1 macrophages to produce pro/anti-inflammatory cytokines. Specifically, do any of the major secondary metabolites in kava alter the expression of pro- or anti-inflammatory mediators in THP-1 macrophages? The hypothesis was when macrophages are treated with kava metabolites, the macrophages will activate to produce both pro-inflammatory and anti-inflammatory cytokines. THP-1 monocytes were treated with PMA to initiate differentiation to macrophages. Calcein-AM toxicity curves were run on the macrophages treated with the six kava metabolites. THP-1 macrophages were treated with the kava metabolites and LPS to stimulate cytokine mRNA expression and Real-Time PCR was used to evaluate whether the pro-inflammatory molecules were suppressed or expressed. ELISA assays were conducted to record the cytokine protein expression of TNF-a, GM-CSF, and IL-1B. A phagocytosis assay was conducted to see the effect of kava metabolites on phagocytosis with Zymosan Particles. Dyhydrokawain expressed several of the pro-inflammatory cytokine mRNA , but the other kava metabolites showed less response. Flavokawain A inhibited the expression of several cytokines. The ELISA assays confirmed the protein expression, where notably FKA inhibited GM-CSF and strongly inhibited IL-1beta protein levels. Only FKA appears to suppress phagocytosis. Since phagocytosis is associated with bacterial presence, and is how macrophages help to remove infections, FKA may have an immunosuppressive effect. Future research will focus on understanding the effects of kava on the body to either suppress or increase the immunoresponse for specific inflammatory diseases.

Awards Won: