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Cornus Officinalis Significantly Improves Oxidative Capacity and Promotes the Calcium-Dependent Transcription Factor, NFATC2, in Human 1.1B4 Pancreatic Cell Line

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JOURNAL ARTICLE

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Abstract

Type 1 diabetes (T1D) is an autoimmune disease resulting in the destruction of pancreatic β cells (β-cells) and subsequent loss of insulin production. The only treatment for T1D is using exogenous insulin coupled with continual glucose monitoring following significant autoimmune destruction of β-cells. Novel interventional therapies are needed that can preserve and protect existing pancreatic β cells in individuals with early identified T1D autoimmunity. Our initial in-vitro evidence indicates *Cornus officinalis* (CO) may be able to serve in this function. What sets ethnopharmacology apart from conventional medicine is the simultaneous targeting of multiple mechanisms using a single herb due to the composition of numerous bioactive ingredients. CO has been used in TCM (traditional Chinese medicine) for over 2 millennia for the therapeutic effect of improved glucose tolerance and has also demonstrated efficacy in animal models but rarely examined in the context of T1D. We hypothesize that CO treatment may provide a β cell restorative and protective therapy for T1D and inhibit progressive cytokine-mediated β cell loss while enhancing existing β cells. Our preliminary evidence demonstrated a dose-dependent exposure of 1.1B4 cells to CO increased proliferation and protected against cytokine-induced cell death. We examined the metabolic effect of CO using the

Agilent Seahorse XF Analyzer and at a two-hour time point there was a remarkable increase in maximal respiratory and glycolytic capacity following CO treatment. However, the molecular mechanism in which CO is inducing a proliferative and metabolic effect in 1.1B4 cells has not been elucidated. Therefore, we employed transcriptomics by RNA-Seq to analyze the early initiators of this increased metabolic effect. Our strongest and most significantly differentially expressed transcript was calcium-dependent transcription factor, NFATc. Expression of NFATc was validated by qPCR, which displayed a 2-fold increase in gene expression. NFATc is an essential transcription factor for β cell proliferation, endocrine function, and insulin secretion and may be a mediator of CO induced biological effects. Lastly, to date, 300 compounds have been elucidated from CO; therefore we wanted to analyze the components within our CO extracts via HPLC/MS in order to elucidate the bioactive ingredients. We found over 300 compounds, and of those, we found known bioactive ingredients such as, loganin and morroniside, while also finding novel extracts with potential bioactive properties. Altogether, CO increased β cell metabolism while inducing the NFAT pathway to signal for increased proliferation and endocrine function. Further experiments will examine the anti-diabetic effects of individual CO constituents that were identified via HPLC/MS, and the full molecular mechanism related to the NFAT signaling pathway.

Issue Section: Novel Aspects of Diabetes and Metabolic Disease Across Tissues and Developmental Stages