

## **Gut Immunomodulating Properties of Phenolic Compounds in Oklahoma Grown Pecans: Potential Health and Long-term Economic Impacts**

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Over the past decade, significant advances have been made in our understanding of the role of inflammatory processes in a broad spectrum of chronic diseases. For example, it is now appreciated that the hypertrophy of adipocytes occurring in obesity stimulates the secretion of pro-inflammatory molecules that can promote the development of atherosclerosis and impair insulin sensitivity, leading to diabetes. Likewise, inflammation plays a central role in the initiation and promotion of many cancers, including colorectal, cervical, pancreatic and prostate cancer. Chronic activation and alterations in immune cell populations, especially T cell subsets (e.g., T helper 17 [TH17] and T regulatory [TREG] cells) have been identified as the major culprits in the pathophysiology of these diseases.

Gut mucosal immunity comprises more than 70% of the body's total immune system. The gut mucosal immune system requires complex interactions between epithelial cells that line the mucosa of the ileum and colon with underlying immune cells (e.g., dendritic cells and T cells) within the lymphoid tissues of the Peyer's patches and lamina propria. Preliminary data from our recent animal studies suggest that fruits rich in phenolic compounds (e.g., plums and cherry) mediate their effects in the gut in part by regulating T-cell differentiation.

One of the most concentrated sources of phenolics in the diet is the tree nut. In this project the effects of pecan phenolics on the interactions between intestinal epithelial cells and T cells will be investigated using an *in vitro* model of gut mucosal immunity. The **hypothesis** to be tested is that phenolic compounds from pecans will down-regulate the differentiation and activation of T<sub>H</sub>17 cells under normal and inflammatory conditions, while simultaneously promoting the differentiation toward a TREG phenotype. Moreover, this response will be mediated via transforming growth factor (TGF) $\beta$  signaling. The following objectives have been developed to test these hypotheses.

**Objective 1:** *To investigate how phenolic compounds from pecans alter CD4+T-cell differentiation and activation under normal and inflammatory conditions using an in vitro co-culture model of gut mucosal immunity.*

**Objective 2:** *To determine the extent to which the phenolic compounds isolated from pecans result from TGF- $\beta$  signaling.*

If the phenolic compounds in pecans prove to have favorable effects on the immune system of the gut, this new information could enhance the marketing potential of pecan growers for their crops. Pecans have the potential to be a very profitable crop for Oklahoma growers, offering more profit potential per acre than most row crops or cow/calf farms, according to researchers at The Samuel Robert Noble Foundation in Ardmore, Oklahoma. As such, a greater understanding of the health benefits associated with their bioactive components could also have positive economic implications for the state.