

## **Soy Isoflavones to be Studied for Their Anti-Diabetic Effects**

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**Final report** (covers period of 7/1/2003-6/30/2006)

### **Executive Summary**

Type 2 diabetes mellitus (DM), obesity, nonalcoholic steatohepatitis (NASH), the metabolic syndrome, and cardiovascular disease (CVD) are all interrelated and major public health concerns. Our research team has demonstrated novel insulin-sensitizing effects of bioactive factors in soybeans, eliciting not only an improvement in glucose tolerance, but also an attenuation of fatty liver and dyslipidemia, similar to the effects of the new generation antidiabetic drugs (e.g., peroxisome proliferator-activated receptor - PPAR agonists/thiazolidinediones - TZD). In the male Zucker Diabetic Fatty (ZDF) rat model, these soy components are even more effective than the TZD, rosiglitazone, in controlling specific diabetic complications. Understanding these soy-induced effects will provide critical knowledge pertinent to the prevention and treatment of insulin-resistance. Further validation of these results through the proposed mechanistic studies may indicate that soyfoods or soy-based components could reduce or prevent the need for costly prescription drugs and offer therapies that avoid drug-associated side effects. Soy chemicals could also elicit the desired metabolic effects on specific genes and target tissues without undesirable effects on other tissues. These experiments combined receptor binding studies, cell culture assays of receptor-mediated gene regulation, and evaluation of gene arrays for recognition of potential selective or tissue-specific activity. We have performed and published testing of the soy compounds in the preclinical models. Additionally, we have published and evaluated gene arrays in rat tissue to assist with the recognition of potential selective or tissue-specific activity (AIM II). We have tested and published receptor binding studies (AIM I). We believe we have made significant progress on this project. We have answered many basic mechanistic questions regarding the anti-diabetic effects of soy. This project has provided us with a strong foundation for future preclinical and clinical studies regarding the anti-diabetic effects of soy.

(see list of publications).

### **SPECIFIC AIMS**

**AIM I: Investigate key molecular mechanisms that may be responsible for the antidiabetic effects of soybean components, especially on PPAR- $\gamma$ , PPAR- $\alpha$ , and ER nuclear receptor pathways.**

**AIM II: Determine whether the effects of soy components result in similar or different effects on gene expression.**

**This project directly contributes to the mission of IMBA:** Socioeconomically, increased soy in the diet will improve health and general quality of life by fighting the disease conditions associated with insulin resistance; this in turn, will enhance profitability, increasing the demand and utilization of soybeans and potentially increasing the value of crops as raw material for producing bio-based products. In addition, content of bioactive components (e.g. isoflavones) in soy could potential be enhanced by marker-assisted breeding or transgenic technologies (ongoing research at

SIU). Healthful bioactive varieties of soybeans would expand markets both domestically and internationally, especially in the functional food/ nutraceutical industry. Strengthened marketability of soybeans would directly benefit the MO and IL agricultural industry.

## PUBLICATIONS

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## RESEARCH AGREEMENTS, PATENTS & MATERIAL TRANSFER AGREEMENTS

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Banz, W.J., M. Peluso, M. Shanahan, and T.A. Winters. Methods of Treating Clinical Diseases (Hepatic Steatosis, Steatohepatitis) with Isoflavones. Issued on July 15, 2003. U.S. Patent No. 6,592,910.

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