Drug Screening Methods and Therapeutics for Diabetes, Obesity, and Coronary Heart Diseases

Background: Calcium-independent phospholipases (iPLs) are associated with an array of cellular processes and play a pivotal role in diabetes, obesity, and cardiovascular disease. Combined these major contributors to premature death significantly affect the Western world as well as developing countries. Researchers from Washington University have identified new targets, developed effective inhibitor screening methods and treatments for type 2 diabetes, coronary heart diseases, and obesity.

Technology Description: The team led by Dr. Richard Gross has elucidated the cellular role of a family of human iPLs including iPLA₂β, iPLA₂γ, iPLA₂ε, and iPLA₂η. In brief, the patent portfolio comprises:

1) Methods for expression (nucleic acid sequence), isolation, and purification of iPLs (case 004045).
2) iPLA₂β, iPLA₂γ Inhibitors: therapeutics for hypertension, heart attacks, and obesity (case 003376).
3) Reversibility of ischemic ventricular tachyarrhythmias by inhibition of activated iPLA₂β: exploitable for in vivo mice screening of inhibitors that prevent ischemia-induced phospholipase activation (case 003725).
4) iPLA₂ε catalyzes the anabolic synthesis of triglycerides and plays a pivotal role in the abnormal increase of adipose tissue: exploitable to determine its activity in biological samples and for screening of new therapeutics for the treatment of obesity (case 004045).
5) iPLA₂η, a triglyceride lipase regulating both triglyceride breakdown and synthesis thereby contributing to hypertrophy and hyperplasia: exploitable target in (a) the treatment of obesity, by reduction of triglyceride stores in adipose tissue, and (b) type 2 diabetes, by enhancement of insulin signaling through decreasing elevated serum non-esterified fatty acid levels (case 004483).
6) Cardiolipin as a potential early biomarker for diabetes and as a substrate for both iPLA₂β and iPLA₂γ. Fatty acyl-CoA and congeners disrupt/reverses inhibition of iPLA₂β resulting in its activation: exploitable for drug development targeting iPLA₂β and iPLA₂γ activation during ischemia, diabetes, and heart disease, atherosclerosis, and obesity (case 005831).

Key Advantages:
- New therapeutics for coronary heart disease, and obesity
- New inhibitor screening methods for coronary heart disease, obesity, and type 2 diabetes
- Detection of specific lipase activity


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Application Space
Therapeutics, Diabetes, Obesity, Phospholipases, Enzyme Inhibitors, Screening Assay

WUSTL Case#
003376, 003725, 004045, 004483, 005831