FOXO Transcription Factor: A Novel Therapeutic for Cardiometabolic Disease

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The risk of cardiovascular disease, the world's leading cause of death, is greatly increased by metabolic syndrome, a combination of hyperlipidemia, hypertension, and type-2-diabetes. A rapidly growing global health challenge across all age groups, cardiometabolic disease affects 25% of adults globally and 10% of children and 50% of adults over 60 in the US. Typically, components of cardiometabolic disease are treated individually. To address underlying molecular pathways of cardiometabolic disease components, FOXO proteins were investigated as a novel drug target. FOXO proteins target key metabolic pathways in adipose tissue; lipid metabolism, insulin signaling, adipocyte function and differentiation, oxidative stress resistance, lipogenesis, autophagy, and cholesterol biosynthesis inhibition. FOXO transcription factor was expressed in adipose tissue by crossing two Drosophila transgenic lines, GAL4-driver line and dFOXO line, and raised on lipogenic diets to induce cardiac and metabolic decline. Abdomens were surgically dissected without damaging beating hearts, and videos were analyzed. Cardiac tissue was fixed, fluorescence-stained, and actin-myofibrils imaged. FOXO-expressing flies on lipogenic diet exhibited therapeutic benefits of reduced cardiac dysfunction: heart rate improved 27%, arrhythmicity 76%, contractility 120% ($p<0.05$). When expressed prior to lipogenic diet placement, FOXO exhibited protective roles: heart rate improved 43%, arrhythmicity 76%, contractility 155% ($p<0.05$). Structurally, FOXO prevented cardiac hypertrophy and myofibrillar disarray. Successfully reducing mortalities and treating diet-induced arrhythmias, tachycardia, and hypertrophy, FOXO presents a novel drug target with both therapeutic and protective roles.

Awards Won:

Intel ISEF Best of Category Award of $5,000

First Award of $5,000

Intel Foundation Cultural and Scientific Visit to China Award