Insulin-like signaling in aging and dietary restriction

Insulin and Insulin-like Signaling in Aging and Disease

Bethany Barrow
Xin Li
Sharon Paige
3 ligands

5 receptors

Insulin Pathway
Tissue-Specific Effects Are Mediated by Different IRS Proteins

Endocrine Regulation of IGF

Hypothalamus → GRF/SS → Pituitary → GH → Liver → IGF-1

Genetic Homology Across Species

C. elegans Insulin-like Signaling Pathway

Pha-4 Response to Dietary Restriction

Pha-4 expression directly correlates with lifespan in C. elegans

Superoxide Dismutase Regulation
Effect of Mutant DAF-16 on Lifespan in *C. elegans*

Pathways Controlling Longevity in Collaboration with DAF-16/FOXO

• Systemic Inactivation of insulin or IGF1 receptors in Mice
  IGF1 receptor-/-: die owing to development defects
  Insulin receptor-/-: die owing to severe hyperglycemia
  Insulin receptor+/-: life span has not been reported
  IGF1 receptor+/-: live on average 26% longer than wild

• Tissue-specific insulin receptor knockouts
  fat specific insulin receptor knockout mice have a 20% longer median and maximal life span than controls

• IRS protein signaling
Figure 3: Pathophysiology of hyperglycaemia and increased circulating fatty acids in type 2 diabetes.
Thank You

• Sharon Paige
• Bethany Barrow
• Xin Li