First functional insulin-binding protein in invertebrates

April 15 2008

Insulin-like growth factor (IGF) signaling that helps to regulate mammals' growth, metabolism, reproduction and longevity is well documented. Now research published in the open access journal *Journal of Biology* describes the genetic identification of the first functional insulin-like growth factor binding protein (IGFBP) ortholog in invertebrates.

Insulin and insulin-like growth factors (IGFs) signal through a highly conserved pathway and control growth and metabolism in both vertebrates and invertebrates. The well-studied mammalian IGF binding proteins (IGFBPs) do not, however, have obvious sequence homologs in the fruit fly Drosophila.

The discovery of a functional ortholog transforms Drosophila into a powerful model system in which to explore metabolic regulation and presents a significant advance in our understanding of the mechanisms by which the actions of insulin-like peptides are regulated.

A research team led by Ernst Hafen from the Institute of Molecular Systems Biology at the ETH in Zürich, Switzerland, employed a genetic strategy to search for negative insulin/insulin-like growth factor signaling (IIS) regulators in Drosophila. The team identified a new functional insulin-binding protein that acts as an IIS antagonist. Dubbed imaginal morphogenesis protein-late 2 (Imp-L2), the new antagonist binds the Drosophila insulin-like peptide 2 (Dilp2), inhibiting its growth-promoting function. Imp-L2 not only has a role in growth regulation - it

is also essential for the dampening of insulin signaling under adverse conditions.

The authors hope that better understanding of Imp-L2's role in growth control and insulin signaling in Drosophila will ultimately impact on our understanding of the human ortholog IGFBP-7. This has a regulatory role in pathways that impact upon diabetes and cancer. IGFBP-7 acts as a tumor suppressor in a variety of human organs and differs in the C-terminus from the other IGFBPs.

"Since Imp-L2 and the human tumor suppressor IGFBP-7 display sequence homology in their C-terminal immunoglobulin-like domains, we suggest that their common precursor represents an ancestral insulin-binding protein," says Hafen

Source: BioMed Central