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A new role for insulin in cell survival, cell metabolism and stress response

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Researchers at the Buck Institute for Age Research have discovered a novel way in which insulin affects cell metabolism and cell survival. Surprisingly the insulin signaling pathway, which is involved in aging, diabetes and stress response, is active at a deeper level of cell activity than scientists expected. The study appears in the September 8th issue of *Cell Metabolism*.

Insulin is vitally involved in many cell functions. Buck Institute faculty and lead author Gordon Lithgow, PhD, says scientists have known for years that insulin is involved at the level of cell activity called transcription, where DNA produces RNA. Lithgow said the new research, in the nematode worm C. elegans, revealed that insulin is also active at the level known as translation, where RNA specifies protein synthesis.

Lithgow says the discovery of this new level of regulation opens a host of opportunities. "We are desperate to understand why aging is a risk factor for disease, we want to know why diabetes is associated with aging," said Lithgow. "Here we have a insulin signaling pathway involved in aging, diabetes and stress response. This gives us more precise avenues to explore how we might intervene in disease," he said.

Using long-lived mutant worms, researchers demonstrated that increased tolerance to stress, due to lower insulin signaling, is not dependent on stress-induced responses at the level of transcription, but instead requires active protein translation.

Lithgow says the research fits in with work being done in the Buck Institute laboratories of Brian Kennedy and Pankaj Kapahi, all of which point to the importance of translation. Lithgow, who directs the Institute's Geroscience program, says the research will lead to new collaborations. "This work highlights the importance of protein homeostasis - the maintenance of metabolic equilibrium," said Lithgow. "What proteins are made within the cell? When are they made? How and when are they gotten rid of? What happens when they are damaged?" Lithgow thinks control of protein homeostasis is vital for healthy aging and is intrinsically involved in diseases such as Parkinson's and Alzheimer's where protein homeostasis seems to get muddled up. "It's about connections," said Lithgow, "Now we need to connect with what is known about insulin signaling in diabetes with various disease states; we need to know how this small part of cell metabolism fits into the bigger picture of aging and disease."

Provided by Buck Institute for Age Research