

Researchers discover surprisingly wide variation across species in genetic systems that influence aging

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Anne Bronikowski

A new Iowa State University study focusing on insulin signaling uncovered surprising genetic diversity across reptiles, birds and mammals.

The research sets the stage for an improved understanding of metabolism, growth and aging and may have implications for medicine

and human health, said Anne Bronikowski, an associate professor of ecology, evolution and organismal biology and a lead author of the study.

Insulin signaling is a critical biological process that governs the rate at which cells grow and divide and ultimately regulates aging. Scientists previously assumed the process remained much the same throughout the animal kingdom. But the new research shows that the genetic pathways in reptiles evolved to include protein forms not observed in mammals, a finding that suggests these proteins carry out new or additional functions in reptiles.

The researchers looked at a molecular network known as the insulin/insulin-like signaling and target of rapamycin network (IIS/TOR). Because the IIS/TOR network regulates critical aspects of animal biology, scientists have long speculated that the network would work more or less the same in most animal species.

Bronikowski and Fred Janzen, a professor of ecology, evolution and organismal biology, completed the study along with former and current members of their labs. The research team compared the genomes of mammals and birds with 17 reptile species. The team found an abundance of variation in the hormones and receptors of the network, which bucks the conventional wisdom and indicates that hormones delivered through insulin likely undertake additional functions in [reptiles](#).

"The study provides a critical step toward understanding how the IIS/TOR network may regulate variation in metabolism, modes of reproduction and rates of aging," Bronikowski said. "It highlights genetic variants that occur in nature that may be useful in a [human health](#) context. It therefore lays the groundwork for future research to identify natural genetic variants that may work together to alter the function of this network, which may lend insight into metabolic and aging diseases

and treatments."

Previous studies of [insulin](#) signaling have focused on species commonly used as laboratory models, such as mice, fruit flies and nematodes. The new study compared 66 species, including 17 [reptile species](#) for which the research group had to generate transcriptome data – or the set of all RNA molecules in a particular genome – because the data didn't exist previously. The team was able to sequence the reptile data with the help of support from the ISU Center for Integrated Animal Genomics.

The wide range of variation discovered by the study may suggest that the [insulin signaling](#) network could be targeted by new medical therapies to treat conditions associated with aging, Bronikowski said.

"The variation indicates that there might be some flexibility in how these genes work," she said. "The next step might be to look at how we can influence the genes to produce better medical outcomes."

The paper was published in the *Proceedings of the National Academy of Science*, a peer-reviewed academic journal. All of the authors either currently work at Iowa State or were one-time graduate students or post-doctoral researchers at Iowa State.

More information: "Rapid molecular evolution across amniotes of the IIS/TOR network." *PNAS* 2015 ; published ahead of print May 19, 2015, [DOI: 10.1073/pnas.1419659112](https://doi.org/10.1073/pnas.1419659112)

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