

Biologists describe key mechanism in early embryo development

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New York University and University of Iowa biologists have identified a key mechanism controlling early embryonic development that is critical in determining how structures such as appendages -- arms and legs in humans -- grow in the right place and at the right time.

In a paper published in the journal <u>PLoS Genetics</u>, John Manak, an assistant professor of biology in the UI College of Liberal Arts and Sciences, and Chris Rushlow, a professor in NYU's Department of Biology, write that much research has focused on the spatial <u>regulatory networks</u> that control early <u>developmental processes</u>. However, they note, less attention has been paid to how such networks can be precisely coordinated over time.

Rushlow and Manak find that a <u>protein</u> called Zelda is responsible for turning on groups of genes essential to development in an exquisitely coordinated fashion.

"Zelda does more than initiate <u>gene networks</u>—it orchestrates their activities so that the embryo undergoes developmental processes in a robust manner at the proper time and in the correct order," says Rushlow, part of NYU's Center for Developmental Genetics.

"Our results demonstrate the significance of a timing mechanism in coordinating regulatory gene networks during early development, and bring a new perspective to classical concepts of how spatial regulation can be achieved," says Manak, who is also assistant professor of



pediatrics in the Roy J. and Lucille A. Carver College of Medicine and researcher in the UI Roy J. Carver Center for Genomics.

The researchers note that their findings break new ground.

"We discovered a key transcriptional regulator, Zelda, which is the long-sought-after factor that activates the early zygotic genome," says Rushlow.

"Initially, the embryo relies on maternally deposited gene products to begin developing, and the transition to dependence on its own zygotic genome is called the maternal-to-zygotic transition," she adds. "Two hallmark events that occur during this transition are zygotic gene transcription and maternal RNA degradation, and interestingly, Zelda appears to be involved in both processes."

The research showed that when Zelda was absent, activation of genes was delayed, thus interfering with the proper order of gene interactions and ultimately disrupting gene expression patterns, the researchers noted, adding that the consequence to the embryo of altered expression patterns is a drastic change in the body plan such that many tissues and organs are not formed properly, if at all.

The researchers used Drosophila, or fruit flies, to investigate these regulatory networks. The fruit fly has the advantage of being a tractable genetic model system with a rapid developmental time, and many of the genetic processes identified in flies are conserved in humans. Additionally, pioneering fly research has led to many of the key discoveries of the molecular mechanisms underlying developmental processes in complex animals.

The study brought together Rushlow, who discovered Zelda and is an expert in genetic regulatory networks in development, and Manak, a



genomics expert whose laboratory focuses on how a genome is constructed and coordinately functions.

"I had always wanted to work with Chris, and this was a wonderful opportunity for us to combine our complementary areas of expertise in a truly synergistic fashion," says Manak.

"Our collaboration is a marvelous example of how a problem can be viewed from two different perspectives, a systems view of early gene networks and an individualistic view of single genes and single embryos, and result in novel and significant discoveries," says Rushlow.

Provided by New York University

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