

Working in harmony: New insights into how packages of DNA orchestrate development

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New research from Huntsman Cancer Institute (HCI) at the University of Utah (U of U) illuminates aspects of how an early embryo, the product of fertilization of a female egg cell by a male sperm cell, can give rise to all the many cell types of the adult animal. Researchers demonstrated that the hundreds of genes important for controlling embryonic development are all packaged in a unique manner in the early

embryo - and even as far back as the paternal sperm - and that this packaging helps control how, when, and where different genes are expressed in the embryo. The findings, published today in the journal *Cell*, have significant implications for understanding how early development is orchestrated, and provides a mechanism for how parental environment might impact the expression of these genes in the offspring.

Brad Cairns, PhD, HCI senior director of basic science and professor and chair of Oncological Sciences at the U of U, and his colleagues, including postdoctoral fellow Patrick Murphy PhD, used zebrafish in this work, a model system that maintains significant similarities to human [development](#). They demonstrated that DNA segments (genes) important for controlling development are packaged in physical structures that help turn 'on' and 'off' genes at different stages of development. These physical structures serve as platforms that help activate or poise these genes, as needed, for normal development. The researchers also identified the protein machines that place these physical structures into the genome, and the proteins that remove them, to ensure their proper placement and function. This work builds upon several prior studies from the Cairns lab that show that show how genes prepare themselves for different aspects of [embryonic development](#).

"A key question in embryonic development is how the early embryo achieves the state of totipotency that it displays - that is ability to become any type of cell in the body. We reasoned that the central answer might be to package all the decision-making genes in a special physical state that helps identify and regulate them," explains Cairns.

Researchers have long sought to better understand whether and how genes from mom and dad might be packaged in a manner that influences expression and development in the embryo, and how those packaging states are maintained or reprogrammed during the development process. This study identifies that packaging - termed histone variant H2AFV -

and provides a mechanism for inheriting gene packaging, and therefore has important implications for developmental potential and inheritance. Remarkably, although the initial packaging of genes in the paternal sperm differs somewhat from packaging in the maternal egg, the maternal packaging was shown to reprogram to the same packaging state of the paternal genome, thus harmonizing the packaging states from the parents in the early embryo to arrive at the same cellular development state.

The implications of this work include a possible mechanism for how environmental factors - for example, smoking - might influence inheritance of traits, by affecting how [developmental genes](#) are packaged. "These [packaging](#) states help to define whether and how genes are expressed in normal development. Such [genes](#), if misregulated can lead to developmental disorders, and perhaps to predisposition for cancer," says Cairns. "By better understanding what happens in normal development, it opens up new possibilities for being able to identify the precursors to diseases like cancer, when cell development goes haywire."

Provided by University of Utah

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