

Scientists get the upperhand in biological pathway that leads to heart formation

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Dr. Eric Olson, Director of the Hamon Center for Regenerative Science and Medicine, and Chairman of Molecular Biology. Credit: UT Southwestern

Researchers at UT Southwestern Medical Center's Hamon Center for Regenerative Science and Medicine have identified a pathway essential to heart formation and, in the process, unveiled a mechanism that may explain how some previously puzzling segments of the genome work.

The DNA sequence they studied - which they named *Upperhand* (*Uph*) - is located just before a gene called *Hand2*, which controls the development of the heart as it grows in the womb.

"These findings uncover a new and unexpected step in the control of [heart formation](#) whereby one gene, *Upperhand*, regulates the expression of the neighboring gene, *Hand2*, by an unusual mechanism," said Dr. Eric Olson, Director of the Hamon Center for Regenerative Science and Medicine, and Chairman of Molecular Biology.

Upperhand works something like a safe, which

holds the controls for *Hand2* locked inside it.

Upperhand has to be opened up first for the *Hand2* controls to be exposed. That ultimately allows *Hand2* to set in motion a whole sequence of events that are crucial to formation of the heart.

Upperhand also may help explain the mystery behind why some DNA sequences don't serve as templates for synthesizing proteins like other DNA sequences. Those that don't are called non-coding DNA and scientists have been pondering what they do and how they work.

"These non-coding sequences are the mysterious "dark matter" of the genome," said Dr. Olson, who holds the Robert A. Welch Distinguished Chair in Science, the Pogue Distinguished Chair in Research on Cardiac Birth Defects, and the Annie and Willie Nelson Professorship in Stem Cell Research.

Upperhand is one such "non-coding" DNA that doesn't serve as the template for a protein.

"Why would it be located before *Hand2*, we wondered? What we learned is that the [controls] for *Hand2* just happen to be trapped inside *Upperhand*," Dr. Olson said. "This is probably a general mechanism for the control of many genes that are important in development, because so many cardiac control genes are adjacent to non-coding RNAs and nobody ever understood why that is."

The research which appears online in *Nature*.

More information: Transcription of the non-coding RNA upperhand controls *Hand2* expression and heart development, *Nature*, nature.com/articles/doi:10.1038/nature20128

Provided by UT Southwestern Medical Center

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