Micro-RNAs Are Life's Genetic Sculptors

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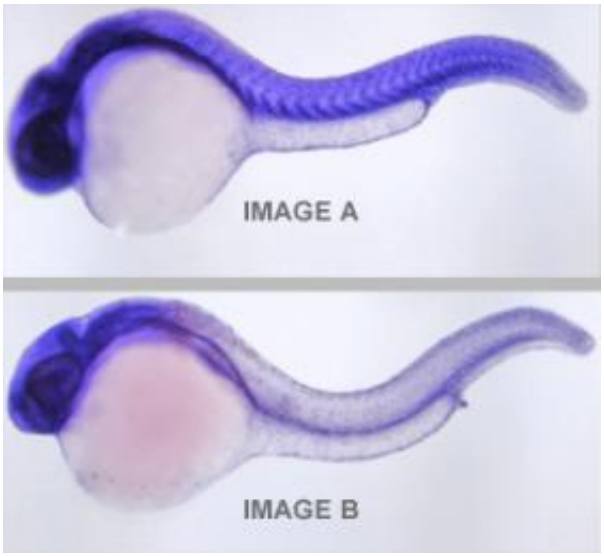

When a micro-RNA is removed, genes governing muscle development shown in blue are activated within the embryo (IMAGE A). In the presence of micro-RNA, the genes are inactive (IMAGE B).

(PhysOrg.com) -- Yale scientists have found a way to study within a living organism the wonders of micro-RNAs - tiny bits of RNA that act like a sculptor and shape the activity of hundreds of genes. The work is reported in the March 1 edition of the journal *Genes & Development.*

The analysis of micro-RNA in the developing muscle tissue of a zebra fish embryo sheds new light on research and therapeutic potential of these tiniest of all genes, the authors say.

Micro-RNAs (miRNAs), snippets of genetic material usually associated with the production of proteins from DNA, are one of the hottest targets of scientific research because they can precisely regulate the activity of many important genes. So far, most researchers have studied their effects only in cell cultures and have found it difficult to map the extent of their influence throughout a living organism.

The Yale study, however, illustrates that two miRNAs influence the gene activity of hundreds of muscle genes to regulate the muscle contraction apparatus in the developing zebra fish embryo. They act like ubiquitous chisels, carving away material suppressing the expression of genes in precise parts of an organism, said Antonio J. Giraldez, the Lois and Franklin H. Top, Jr. Yale Scholar in the genetics department of the Yale School of Medicine and senior author of the study. But some genes are turned on in their absence, allowing for the precise development of muscle tissue.

“It is as if these micro-RNAs are putting the final touch on evolution’s artwork,” Giraldez said.

Micro-RNAs are the smallest genes known, with only 22 building blocks or nucleotides, while most genes average more than 1000 nucleotides. Unlike most genes that are encoded as DNA and produce proteins, these tiny genes act by controlling much larger messenger RNAs, which carry the protein-making instructions of the DNA. Although micro-RNAs account for only about four percent of genes, each one can regulate hundreds of genes.

“It is likely that microRNAs have deep implications not only in how humans and animals are made, but in the development of human diseases,” said Giraldez.

For instance, the same miRNAs that in this study regulate muscle

function during development can also modify the metastatic potential of tumor cells in mice.

Other Yale researchers on the paper were lead author Yuichiro Mishima, Alison A. Staton, Carlos Stahlhut, Chong Shou, Chao Cheng, and Mark Gerstein.

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