Health Science Center News

University of Florida

Tiny cellular structure plays big role in mammalian gene regulation

Lindy McCollum-Brounley
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University of Florida researchers have discovered a new ingredient in our cellular soup, tiny structures that may lay the groundwork for how new cells form and then function.

The structures, dubbed GW bodies by the UF researchers who identified them in mammalian cells, are described this month in the online edition of Nature Cell Biology. The cellular structures play a crucial role in gene regulation, known as RNA interference, and their discovery heralds a fundamental shift in scientists' understanding of cell biology that could open up new treatments for cancer and autoimmune diseases and lead to better ways of manipulating genes for therapeutic purposes. Similar structures have previously been found in other organisms, such as yeast, where they are known as P bodies.

GW bodies, which are found outside the cell nucleus in the jelly-like material known as the cytoplasm, appear to be part of the body's recipe for regulating how snippets of genetic material called microRNA switch genes off to control cell reproduction and development. UF scientists found this process functioned poorly in the absence of GW bodies. Dysfunction of microRNA in turning off genes could theoretically allow for the uncontrolled cell growth that characterizes cancer.

"The significance of our study is that it is one of the first to stress the importance of this pathway with respect to cell biology by demonstrating that the specific micro-environments of the GW bodies within the cell appear to be crucial for the proper functioning of the RNA interference process," said Andrew Jakymiw, Ph.D., a postdoctoral associate in the UF College of Dentistry's department of oral biology. "This RNA interference pathway is revolutionizing the way people do research and potentially the way people may apply therapies."

The study of RNA interference is a relatively new field in the science of cellular biology. Discovered in 1993, it is nonetheless an ancient cellular mechanism

that predates the divergence of plants and animals to shape life as we know it.

Imagine the cell as a factory making proteins essential to cellular function and health. Strands of messenger RNA, acting as subcellular photocopy machines, use the genetic information within the cell's DNA as a template to produce new protein copies.

But RNA interference acts like a paper jam, blocking RNA's ability to communicate the complete genetic code for the assembly of the protein.

In their study, UF researchers constructed small RNA molecules to induce RNA interference in cell cultures in the laboratory — entirely silencing the targeted messenger RNA and shutting it down for eventual decay. But they were unable to do so without the presence of the GW bodies.

"Our data show that if GW bodies are not present in the cells, then RNA interference is dramatically inhibited," said study co-investigator Edward Chan, Ph.D., a UF professor of oral biology. "So GW bodies are a gateway to successful RNA interference."

Chan and Jakymiw believe their team's discovery of GW bodies as the cellular focal point of RNA interference may one day enable doctors to exploit the process to silence genes that cause cancer cells to madly multiply or to restore health by returning malfunctioning cells to a normal state.

"Abnormal mutation or expression of microRNA, and dysfunction in regulation in the microRNA, can lead to cancer and could play a potential role in autoimmune diseases," Chan said. "RNA interference is an interesting concept for potential clinical therapy; you could target small interfering RNA at any gene you suspect may play a role in helping cure disease."

The UF study of GW body function in mammalian cells is similar to research performed on P body function conducted by scientists at University of Arizona and Cold Spring Harbor Laboratory in New York. Their study is published in Nature Cell Biology as a companion to the UF report.

"The GW bodies are relatively new, so we don't really understand their broader function in the cell," said Roy R. Parker, Ph.D., Regents professor of molecular and cellular biology at the University of Arizona and Howard Hughes Medical Institute investigator. "But it appears that sequestration of the molecules away from the rest of the cytoplasm is important to the silencing, preventing the messenger RNAs from functioning."

Parker said the idea behind using gene therapy to turn genes off or on to treat diseases has been around for a long time, but successfully delivering gene therapy to cells in living organisms is still a work in progress.

“I think it will have to be a combination of everybody doing their share of research to bring the puzzle together,” Jakymiw said. “Hopefully, understanding how the GW bodies work in regard to RNA interference will combine with other studies to one day result in improved therapies.”

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