Medical Xpress

Nuclear hormone receptors, microRNAs form developmental switch

April 2 2009

A particular nuclear hormone receptor called DAF-12 and molecules called microRNAs in the let-7 family form a molecular switch that encourages cells in the larvae of a model worm to shift to a more developed state, said a consortium led by researchers from Baylor College of Medicine in a report that appears online today in the journal *Science*.

As organisms go through the stages of life, hormones coordinate the changes. Nuclear receptors respond to hormones to coordinate stage transitions, but how they do so is not well understood.

"We knew that nuclear hormone receptors were involved in stage 2 to stage 3 transitions in Caenorhabditis elegans," said Dr. Adam Antebi, associate professor in the Huffington Center on Aging at BCM and the report's senior author. "Another class of molecules called microRNAs is also involved in that transition. We hypothesized that maybe if they are involved in the same process, one turns on the other."

That turns out to be the case in C. elegans and may be true in more advanced organisms as well, he said.

Scientists use the tiny worm called Caenorhabditis elegans to study such processes because it has a simple anatomy and life cycle. *C. elegans* develops from embryo through four larval stages into adulthood.

Each "stage" has specific programs of cell division, migration,

differentiation and death that are crucial to the organism's final development. Particular master regulators in the worm determine each stage transition and are responsible for organizing developmental time.

"Expression of the let-7 family of microRNAs is dependent on the nuclear receptor and its hormone," Antebi said. "We can show in the worm and in cell culture that DAF-12 and its steroid hormone are directly activating these microRNAs."

But how does this cause stage transitions? The tiny molecules called microRNAs work as switches to turn off other genes. In this case, the nuclear hormone receptor DAF-12 and its ligand turn on the microRNAs, which then turn off the earlier developmental "programming" of the cell (stage 2), allowing the later programming (stage 3) to take over.

Specifically, the microRNAs dial-back the activity of a protein called "hunchback," which specifies that the cells are in stage 2. That enables stage 3 to start and development to continue.

"We think this could also give insight into cancers," Antebi said, "particularly those that are hormone-dependent, such as breast or prostate cancer. When worm skin cells go from stage 2 to stage 3 they reduce their cell proliferation. When they fail this transition, skin cells overproliferate (grow uncontrollably)."

It is known that both nuclear receptors and microRNAs play a role in human cancers. These studies could help bridge understanding of the effects of the two.

Antebi also thinks that this system links development to the environment. DAF-12 plays a role in a long-lived quiescent stage called the dauer diapause, which the worms enter in times of starvation and

overcrowding.

"In good times, the DAF-12 steroid ligand is made, the microRNAs are turned on, and the worm goes through all stages of development to adult," said Antebi. (A ligand is a molecule that binds to the receptor to form a biologically active complex.)

"In bad times, the ligand is not made and the nuclear receptor (DAF-12) causes the animals to go into the long lived dauer stage, shutting down the microRNAs and the developmental clock," he said.

In this way, environmental signals actually affect the worm's rate of development, and perhaps even its aging, said Antebi.

Source: Baylor College of Medicine (news : web)

Citation: Nuclear hormone receptors, microRNAs form developmental switch (2009, April 2) retrieved 4 May 2024 from https://medicalxpress.com/news/2009-04-nuclear-hormone-receptors-micrornas-developmental.html

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.