

Clocking in and out of gene expression

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A chemical signal acts as time clock in the expression of genes controlled by a master gene called a coactivator, said Baylor College of Medicine researchers in a report that appears in the journal *Cell* today.

“We have long known that our bodies live by a daily and monthly and even yearly clock and that cells have clocks as well,” said Dr. Bert O’Malley, chair of molecular and cellular biology at BCM and senior author of this report. “We have actually taken this concept to the gene now and said that we are made up of 25,000 genes that have clocks too.” Genes get expressed and carry out their functions through proteins, he said. Gene expression involves the machinery of the cell translating the gene’s code into a protein that carries out function. This process has to have a beginning and an end.

“That sets the time clock,” said O’Malley. “The question is, ‘How is this done?’” The answer lies in coactivators – master genes that turn other genes on and off.

“Inherent to the structure of these coactivators is a clock,” he said. “But the clock needs to be set off.” In studies of breast cancer cells, O’Malley and his colleagues showed how the clock works. Using steroid receptor coactivator-3 (SRC-3), they demonstrated that activation requires addition of a phosphate molecule to the protein at one spot and addition of an ubiquitin molecule at another point. Each time the message of the gene is transcribed into a protein, another ubiquitin molecule is chained on. Five ubiquitins in the chain and the protein is automatically destroyed.

“It’s built-in self destruction,” said O’Malley. “It prevents you from activating a potent factor in the cells that just keeps the clock running and the gene continuing to be expressed.” In that scenario, the result could be cancer, too much growth or an abnormal function.

“It means there’s a fixed length of time that the molecule can work. When it’s activated, it’s already preprogrammed to be destroyed. The clock’s running and each time an ubiquitin is added, it is another tick of the clock.” When the clock system fails, problems result.

“If you can’t start the clock, you can’t stop the clock. If you stop the clock before you should or if it is running too slow or too fast, it causes problems in the cells,” he said.

Source: Baylor College of Medicine

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