2 signals -- from within and out of cell -- specify motor neuron differentiation

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Two signals - an external one from retinoic acid and an internal one from the transcription factor Neurogenin2 - cooperate to activate chromatin (the basic material of chromosomes) and help determine that certain nerve progenitor cells become motor neurons, said researchers from Baylor College of Medicine in a report in the current issue of the journal *Neuron*.

"This finding is important for many reasons. For example, as we understand more about what happens, the more likely we will be able to generate motor neurons from different types of stem cells," said Dr. Soo-Kyung Lee (http://www.bcm.edu/db/db_fac-lees.html), assistant professor of molecular and human genetics and molecular and cellular biology at BCM. (A motor neuron conducts impulses from the spinal cord to a muscle fiber, controlling movement and other activities.) "It will also be useful as a tool for drug screening, allowing us to determine whether a drug is killing or enhancing the activity of motor neurons."

In a delicate series of experiments, she and her colleagues showed that a complex consisting of Neurogenin2 and the retinoic acid receptor, when bound to retinoic acid, recruit a particular enzyme (histone acetyltransferase CBP) to their complex. This causes a chemical reaction called acetylation of the histones (the spools around which DNA winds in the chromatin), stimulating the transcription of the gene into the protein for which it holds the genetic code.

"These changes lead to strong expression of the motor neuron genes in

nerve progenitor cells, converting them to motor neurons," said Lee. "What is striking is that the retinoic acid receptor uses the Neurogenin2 site to bind to the DNA."

In mice that lack CBP, she said, there is marked reduction in motor neurons. The finding could play a role in unraveling the secrets of diseases such as the muscular dystrophies.

Source: Baylor College of Medicine (news : web)