MedicalXpress

Ronin an alternate control for embryonic stem cells

June 26 2008

Like the masterless samurai for whom it is named, the protein Ronin chooses an independent path, maintaining embryonic stem cells in their undifferentiated state and playing essential roles in genesis of embryos and their development, said Baylor College of Medicine researchers who reported on this novel cellular regulator in the current issue of the journal *Cell*.

Three proteins – Oct4, Sox2 and Nanog -- had previously been considered the "master" regulators of embryonic stem cells, but "Ronin could be as important as these three," said Dr. Thomas Zwaka, assistant professor in the Stem Cells and Regenerative Medicine (STaR) Center at BCM. In fact, he said, if the action of Oct4, considered the most important, is reduced in embryonic stem cells, Ronin can compensate for the loss.

Embryonic stem cells are pluripotent, meaning they have the potential for becoming all other kinds of cells in the body. They are also capable of self-renewal. Oct4, Sox2 and Nanog were previously thought the major method by which embryonic stem cells remained in their pristine state. Now, Ronin represents a different and parallel pathway to achieve the same result.

Ronin is also expressed in early embryonic development of mice. If it is not present, the embryos die, said Zwaka. It is also found in mature oocytes or egg cells.

"Ronin is a potent transcription repressor," he said. In fact, it prevents the action of genes that promote the differentiation of cells into the various tissues and organs of the body.

"It does it more effectively than the other three factors together," he said. It silences the differentiation genes epigenetically through specific chemical mechanisms that modify histones, the chief packaging proteins for DNA.

He and his colleagues found Ronin as a follow-up to an earlier study that showed a component of the cell death system called caspase-3 actually cleaved and reduced the amount of Nanog protein. This caused the embryonic stem cells to stop self-renewal and begin differentiation into other kinds of cells.

Zwaka and his colleagues searched for other proteins affected by the caspase and found Ronin, which was previously unknown.

The finding prompts other questions. Can Ronin be used to reprogram differentiated cells into those that more closely resemble embryonic stem cells? What is the significance of the portion of Ronin that resembles a "jumping gene" or transponson called P element transposase, usually found in the genomes of fruit flies?

Ronin is also found in areas of the brain such as the hippocampus and the Purkinje cells of the cerebellum.

"What role does it play in the brain?" asked Zwaka.

Source: Baylor College of Medicine