Scientists reveal mechanism that triggers differentiation of embryo cells

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The mechanism whereby embryonic cells stop being flexible and turn into more mature cells that can develop into specific tissues has been discovered by scientists at the Hebrew University of Jerusalem. The discovery has significant consequences towards furthering research that will eventually make possible medical cell replacement therapy based on the use of embryonic cells.

At a very early stage of human development, all cells of the embryo are identical, but unlike adult cells are very flexible and carry within them the potential to become any tissue type, whether it be muscle, skin, liver or brain.

This cell differentiation process begins at about the time that the embryo settles into the uterus. In terms of the inner workings of the cell, this involves two main control mechanisms. On the one hand, the genes that keep the embryo in their fully potent state are turned off, and at the same time, tissue-specific genes are turned on. By activating a certain set of genes, the embryo can make muscle cells. By turning on a different set, these same immature cells can become liver. Other gene sets are responsible for additional tissues.

In a recent paper, published in the journal, *Nature Structural and Molecular Biology*, Professors Yehudit Bergman and Howard Cedar of the Hebrew University-Hadassah Medical School have deciphered the mechanism whereby embryonic cells stop being flexible and turn into more mature cells that can differentiate into specific tissues. Bergman is

the Morley Goldblatt Professor of Cancer Research and Experimental Medicine and Cedar is the Harry and Helen L. Brenner Professor of Molecular Biology at the Medical School.

They found in their experiments, using embryos from laboratory mice and cells that grow in culture, that this entire process is actually controlled by a single gene, called G9a, which itself is capable of directing a whole program of changes that involves turning off a large set of genes so that they remain locked for the entire lifetime of the organism, thereby unable to activate any further cell flexibility.

Their studies shed light not only on this central process, but also can have consequences for medical treatment. One of the biggest challenges today is to generate new tissues for replacing damaged cells in a variety of different diseases, such as Parkinson's disease or diabetes. Many efforts have been aimed at "reprogramming" readily-available adult cells, but scientists have discovered that it is almost impossible to do this, mainly because normal tissues are locked in their fixed program and have lost their ability to convert back to fully potent, flexible, embryonic cells.

Now, with the new information discovered by Bergman and Cedar, the molecular program that is responsible for turning off cell flexibility has been identified, and this may clear the way towards developing new approaches to program cells in a controlled and specific manner.

Source: The Hebrew University of Jerusalem