Researchers discover key to cell specialization

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Researchers at then Albert Einstein College of Medicine of Yeshiva University have uncovered a mechanism that governs how cells become specialized during development. Their findings could have implications for human health and disease and appear in the November 10 online edition of the journal *Cell*.

A fundamental question in biology is how a fertilized egg gives rise to many different cells in the body, such as nerve, blood and liver. By providing insight into that process, known as differentiation, the findings by the Einstein researchers are relevant to cancer, stem cell research and regenerative medicine.

The scientists studied cell differentiation in the fruit fly, Drosophila melanogaster. They found that cell specialization depends on a pair of proteins that act as super regulators of proteins that were already known—one super-regulating protein encouraging a cell to differentiate and the other trying to hold back the process.

The research was conducted by senior author Nicholas Baker, Ph.D., professor of genetics, of developmental and molecular biology, and of ophthalmology and visual sciences at Einstein, and graduate student Abhishek Bhattacharya, the paper's lead author. They studied Helix-Loop-Helix proteins, "master-regulating" proteins that were known to play a role in the differentiation of fruit fly cells such as muscle, fat and nervous-system cells. By examining eye development in the fruit fly, they found that these master-regulating Helix-Loop-Helix proteins are in turn controlled by "super-regulating" proteins that bind with them.

Successful cell differentiation requires the presence of both master-regulating and super-regulating proteins. "If you don't turn both of those keys, cell differentiation doesn't work properly," said Dr. Baker.

One of these super-regulating proteins, called E-protein Daughterless (Da), binds with Helix-Loop-Helix proteins to activate them. Da also triggers expression of a protein called Extramacrochaetae (Emc), which turns the Helix-Loop-Helix proteins off. Through this feedback-loop mechanism, Da and Emc allow Helix-Loop-Helix proteins to function during specific times during fruit-fly development to create the fly's specialized cells.

Similar findings seem to apply to the Helix-Loop-Helix proteins that are present in human cells, where they are involved in cancer as well as in the differentiation of stem cells into specialized tissues. "We would expect that there will be people in the stem cell field that would be quite interested in what we have found," Dr. Baker said.

More information: The paper is titled "A network of broadly-expressed HLH genes regulates tissue-specific cell fates."

Provided by Albert Einstein College of Medicine