Suppressing cancer with a master control gene

February 23 2009

Starting with the tiny fruit fly and then moving into mice and humans, researchers at VIB and K. U. Leuven show that expression of the same gene suppresses cancer in all three organisms. Reciprocally, switching off the gene - called Ato in flies and ATOH1 in mammals - leads to cancer. The authors show there is a good chance that the gene can be switched on again with a drug. They report their findings in two papers in the leading online open access journal *PLoS Biology*.

All of us begin our lives as a single cell (made when an egg and sperm fuse) which repeatedly divides into the few billion cells that constitute an adult human. During these divisions cells become increasingly differentiated from each other, until in an adult almost all cells are highly specialized to perform a specific function - skin cells, liver cells, eye lens cells, nerve cells, etc. Cancer is a collection of cells without a function, which grow when normal genetic controls of cell division are interrupted. Cancer cells are less differentiated than normal cells - leading to the hypothesis that the final steps of differentiation prevent cells from becoming cancerous.

New work conducted by Wouter Bossuyt, Bassem Hassan, and colleagues at VIB and K. U. Leuven has tested this theory. They demonstrate that in the fruit fly, master control genes steering the specialization step inhibit tumor formation.

In collaboration with colleagues from the United States, they show that loss of one of those genes, Atonal homolog 1 (ATOH1), causes colon

cancer in mice. The gene regulates the last step in the specialization to epithelial cells of the colon. Humans with colon cancer frequently have an inactivated ATOH1 gene, the researchers show.

The researchers could reactivate the gene in human colon cancer cells grown in culture. This caused the tumor cells to stop growing and commit suicide. This exciting, but preliminary, result suggests that it may be possible to switch the gene back on in living patients to target their cancers. Taking this work in the test tube and using it to develop a therapy is an exciting but complicated challenge. Therefore, more work will be required to further understand the role of ATOH1 in suppressing cancer formation.

More information:

1st paper:
Bossuyt W, De Geest N, Aerts S, Leenaerts I, Marynen P, et al. (2009) The Atonal proneural transcription factor links differentiation and tumor formation in Drosophila. PLoS Biol 7(2): e1000040. doi:10.1371/journal.pbio.1000040
biology.plosjournals.org/perls … journal.pbio.1000040

2nd paper:
Bossuyt W, Kazanjian A, De Geest N, Van Kelst S, De Hertogh G, et al. (2009) Atonal homolog 1 is a tumor suppressor gene. PLoS Biol 7(2): e1000039. doi:10.1371/journal.pbio.1000039
biology.plosjournals.org/perls … journal.pbio.1000039

Source: Public Library of Science