'Innocent bystanders' can be the cause of tumor development

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Tumor growth has commonly been viewed as a result of mutations in a given cell that will therefore proliferate uncontrollably. However, a study conducted at the University of Helsinki, Finland, has demonstrated that in certain type of gastrointestinal polyps, the cause of tumor development are mutations in the smooth muscle cells, previously regarded as “innocent bystanders”. The results emphasize the importance of interactions between tissue types, and open up possibilities to develop new treatment strategies targeting the intercellular signaling.

Gastrointestinal polyps are tumors that can both block the digestion and progress to cancer. The cell-type making up the bulk of the polyps and therefore responsible for the adverse effects are the hyper proliferating epithelial cells, which normally line the inner surface of the gastrointestinal tract.

Therefore studies addressing the possible mechanisms of polyp development have traditionally focused on epithelial cells. However, the results from professor Tomi Mäkelä’s research group demonstrate that origin of at least certain polyps is found elsewhere than in the pathologically growing epithelium. By restricting the mutations in mice to the smooth muscle cells that encircle the epithelium, researcher Pekka Katajisto discovered that deletion of the tumor suppressor gene Lkb1 leads to excessive proliferation of neighboring epithelial cells and tumor development.

The results demonstrate that Lkb1 deletion in smooth muscle cells

disturbes the signaling between cells. Normally the smooth muscle cells appear to hold-back the proliferation of their neighboring epithelial cells by signals mediated by the growth factor TGFß, but this signaling is reduced in the studied tumors. As a consequence, the epithelium undergoes accelerated proliferation. The same intercellular signaling defect was also noted in the Peutz-Jeghers polyposis caused by hereditary LKB1 mutations.

The study results has been published in *Nature Genetics* (online) 2nd March, 2008.

Source: University of Helsinki