Turning off the "master switch" for cancer

Researchers at the British Columbia Cancer Agency (BCCA) have made a major breakthrough with the discovery of a "master switch" that can turn off tumour growth in several common types of cancer. The findings could result in promising new treatments for cancer (*Proc Natl Acad Sci USA* 2000;97[7]:3207-12).

Dr. Shoukat Dedhar, a senior scientist at the agency, and his colleagues at Vancouver's Kinetek Pharmaceuticals have found a connection between a key tumour suppressor gene called *PTEN* and the integrin-linked kinase (ILK) protein, which plays a major role in the growth of cancer cells.

ILK prevents tumour cell death, allowing tumours to grow (the "on" switch). In normal cells, the *PTEN* gene controls ILK (providing the "off" switch). However, *PTEN* is mutated or absent in 60% of all solid types of cancer. Dedhar's research indicates that ILK is hyperactive in many of these types of cancer, including prostate, breast, brain, lung and colon cancer. Using human lung, prostate and colon cancer cells, Dedhar and Kinetek's Dr. Jasbinder Sanghera have developed promising ILK-inhibiting compounds that block the formation of new blood vessels and prevent the spread of tumour cells. Experimenting with mice in which human tumours had been transplanted, as well as in human prostate cancer cells, the researchers found that ILK inhibitors induced cell death in prostate cancer cells and reduced the spread of the tumours.

"This is both amazing and exhilarating," said Dedhar. "Inhibiting ILK may not only result in inhibiting growth of the primary tumour but may also lead to reducing the subsequent spread of the tumour cells. And unlike standard chemotherapy agents, these inhibitors do not appear to kill or harm healthy cells. We now know that if we inhibit ILK, we might be able to treat tumours in novel ways. We envisage that these anti-ILK compounds may be used with low-dose conventional chemotherapy."

Dr. Victor Ling, vice-president of research at the BCCA, commented: "This is exciting news for cancer patients everywhere. A targeted therapy with fewer side effects will mean better results for those living with cancer."

Phase 1 clinical trials of ILK inhibitors are expected to start within 2 years. — *Heather Kent*, Vancouver

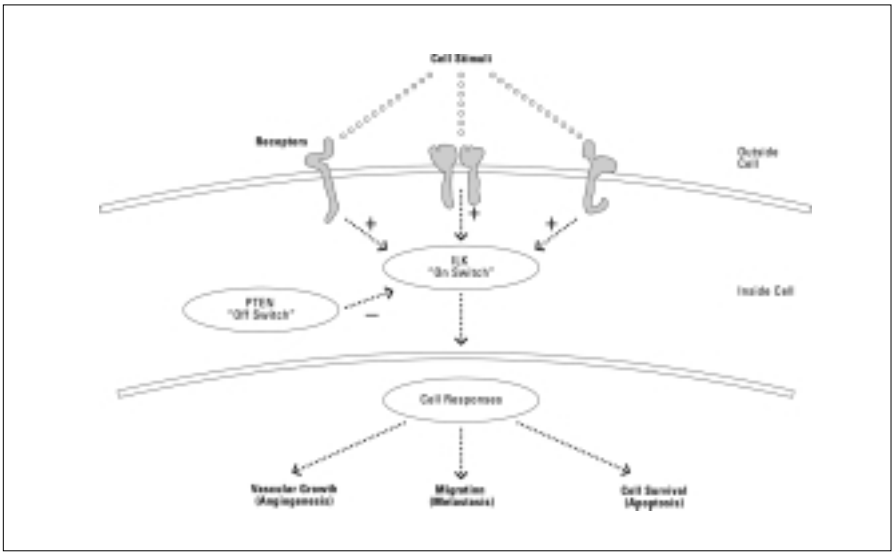

Diagram shows how ILK functions as the "on" switch within cells, inducing cell responses seen in cancer, whereas the *PTEN* gene functions as the "off" switch, preventing this process.

Briefly . . .

Virus found in patients with ALS

For the first time, researchers have found solid evidence of a viral infection in patients with amyotrophic lateral sclerosis (*Neurology* 2000;54 [1]:20-5). The cause remains unknown, but there has been speculation about the role of a persistent enteroviral infection. Now French researchers have found RNA from an enterovirus (probably echovirus 7) in 15 of 17 patients with ALS. The viral RNA was found in only 1 of 29 control subjects tested. The researchers caution that further work is required to confirm the involvement of the virus in ALS, but the finding lends weight to the theory of a viral cause.

Stems cells, high-dose chemotherapy and breast cancer

In an article published in the Apr. 13 *New England Journal of Medicine* and released early on the Internet, a large US trial has shown that stem-cell transplantation plus high-dose chemotherapy provides no more benefits than conventional chemotherapy in treating metastatic breast cancer. Two trials conducted in the late 1980s had shown excellent results in metastatic breast cancer after high-dose chemotherapy and autologous transplantation of hematopoietic stem cells, leading to great demand for the treatment. In this trial, 310 patients with a partial or complete response to induction chemotherapy were randomly assigned to either conventional chemotherapy or stem-cell transplantation plus high-dose chemotherapy. Survival after 3 years and time until disease progression did not differ significantly between the 2 groups.