How the hostage-taking of Twist hit the mass media

Ioanna Soufleri writes for the Greek daily newspaper *To Vima*. In a series of articles that jointly won her the 2005 ACE (Awarding Excellence in Cancer) Reporter's Award, she has shown that progress in cancer can make fascinating reading without resorting to misleading talk of 'wonder drugs' and 'breakthroughs'. Below we reprint a sample of her work.

An unexpected finding has changed, yet again, our perception of the origin of cancer (or, at least stomach cancer). American scientists have discovered that stomach cancer originates from bone marrow-derived cells, rather than stomach cells!

Taken together with recent advances in the field, the above finding, which was reported in *Science* (26 November 2004), illuminates a new aspect of this multi-faceted disease. And while nobody is suggesting that we know everything about it, more often than not scientists are now expressing the belief that cancer will soon become a chronic disease.

It's been 15 years since scientists linked stomach cancer to infection with *Helicobacter pylori*, the ulcer-causing bacterium. Now, through ingenious experimentation, American scientists have shown that the cells that become cancerous do not belong to the stomach. Instead, they are bone marrow cells that "have been invited" to the stomach to help restore the damage caused by the *H. pylori* infection.

Working with mice, Jean Marie Houghton and Timothy Wang initially destroyed the animals' bone marrow. Subsequently they transplanted into the mouse bone marrow cells expressing a fluorescent protein. This enabled the scientists to follow those cells as well as their progeny through the body.

Infection of the animals with *Helicobacter felis* (which is the animal equivalent of *H. pylori*) resulted in the development of ulcers, as was expected. A few weeks after the infection, bone marrow cells started appearing in the area of the destroyed gastric epithelium and, while they tried to adopt the character of the traumatised cells, they exhibited some pre-cancerous alterations. When tumours were finally formed, their fluorescence betrayed their bone marrow origin.


ΙΑΤΡΙΚΗ/ΒΗΜΑSCIENCE

Ο καρκίνος; Μια... χρόνια νόσος

Αναστώνιας το φάρμακο...

BHMA Science

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According to Timothy Wang, "Bone marrow cells arrived at the stomach epithelium in order to heal the tissue. But chronic inflammation conditions prevented them from developing normally, so they progressed down the road to cancer." Indeed, Houghton and Wang's findings contribute to the notion that chronic inflammation favours tumour formation. True, the American scientists worked with mice, and their findings need to be confirmed in humans. But it is expected that the same principle will apply to a variety of human cancers that develop after chronic inflammation (such as colon cancer, lung cancer or liver cancer). A possible common mechanism for the formation of those tumours could lead to a common way of treating them.

Another finding that could lead to the development of a generalised strategy for the treatment of cancer concerns metastasis, the transport of cancerous cells and the subsequent development of tumours in tissues different from the tissue from which they originated.

Metastasis is not an easy process, because cancerous cells have to overcome a number of obstacles: they have to free themselves from the tumour, enter the circulatory system (by squeezing themselves through tiny blood vessels) and then exit again and establish new colonies in a different and hostile environment. The whole process is so complex that one wonders how cancerous cells are able to adopt all the different behaviours that are necessary for them to succeed.

Last summer, a team from the Whitehead Institute gave an answer (or at least part of the answer) to the above question. It seems that cancerous cells can resolve all their problems at once by re-activating a mechanism that normally operates only during embryogenesis (a period during which massive cell movement takes place).

According to their article (*Cell*, 25 June 2004), breast carcinoma cells "take as hostage" a protein named Twist. Under normal conditions, Twist is only functional during embryogenesis, controlling the movements of cells by activating the right genes at the right moment. The reactivated Twist works as a key to all doors for cancerous cells: it triggers the expression of genes that are needed for every stage of cell movement (entrance to and exit from the circulatory system, establishment of contact with new tissues etc).

The American scientists worked with mice and confirmed the activation of the protein in highly metastatic human breast carcinoma cells. Now they are looking for a molecule capable of inhibiting Twist. Such a molecule could prevent metastasis, rendering cancer a chronic disease. Their findings are also important for another reason: they have attracted the attention of other scientists to proteins with functions similar to that of Twist (which are known to scientists from developmental studies). In other words, a whole new variety of possible target molecules for anticancer medications have come to light.