Ten years reporting from the front line

American journalist wins award for her coverage

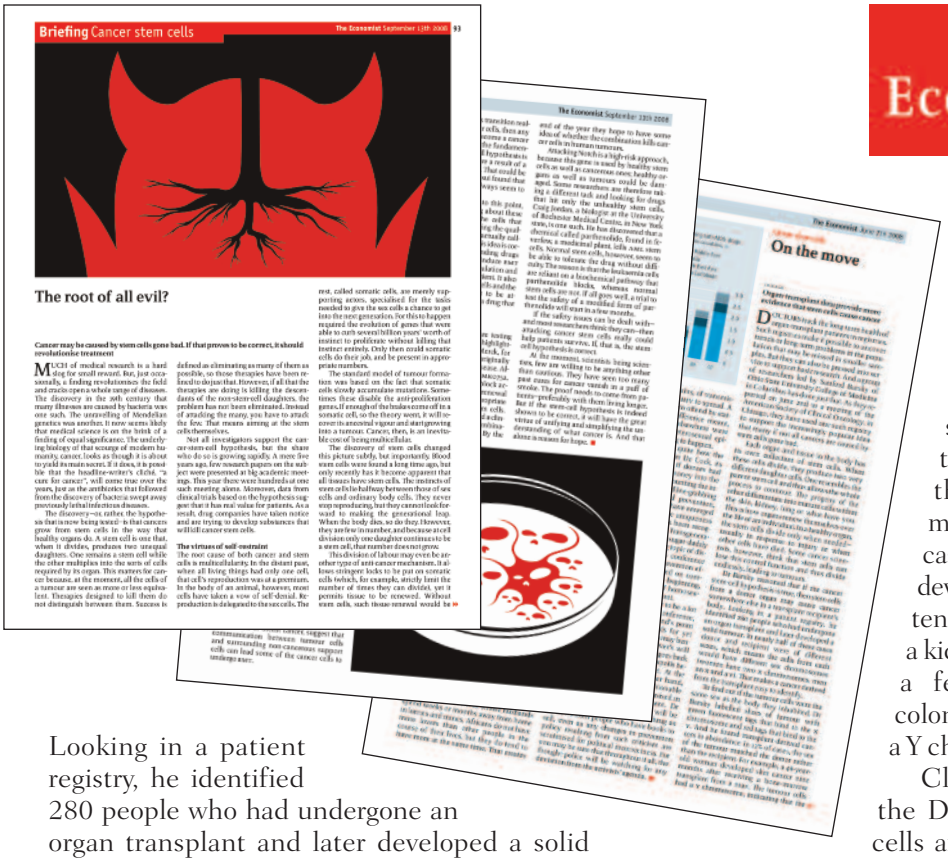
Reporting the unfolding story of the war against cancer is vital to building informed and critical public support for the research effort. **Rabiya Tuma** won a Best Cancer Reporter Award for her contributions to *The Economist* over the past 10 years. Below we reprint one of her articles, on how organ-transplant registries are being mined for evidence on the role of stem cells in cancer.

Doctors track the long-term health of organ-transplant patients in registries. Such registries make it possible to uncover trends or long-term problems in the population that may be missed in smaller samples. But they can also be pressed into service to support basic research. And a group of researchers led by Sanford Barsky of Ohio State University College of Medicine in Columbus has done just that. As they reported on June 2nd to a meeting of the American Society of Clinical Oncology, in Chicago, they have used one such registry to support the increasingly popular idea that many if not all cancers are caused by stem cells gone bad.

Each organ and tissue in the body has its own collection of stem cells. When these cells divide, they produce two very different daughter cells. One resembles the parent stem cell and thus allows the whole process to continue. The progeny of the other differentiate into mature cells within the skin, kidney, lung or what have you. This is how organs renew themselves over the life of an individual. In a healthy organ, the stem cells divide only when needed usually in response to injury or when other cells have died. Some cancer scientists, however, think that stem cells can lose this control function and thus divide endlessly, leading to tumours.

Rabiya Tuma

Dr Barsky reasoned that if the cancer stem-cell hypothesis is true, then stem cells from a donor organ may cause cancer somewhere else in a transplant recipient's body.



The Economist

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Looking in a patient registry, he identified 280 people who had undergone an organ transplant and later developed a solid tumour. In nearly half of these cases donor and recipient were of different sexes, which means the cells from each would have different sex chromosomes (women have two X chromosomes, men an X and a Y). That makes a cancer derived from the transplant easy to identify.

To find out if the tumour cells were the same sex as the body they inhabited, Dr Barsky labelled slices of tumour with green fluorescent tags that bind to the X chromosome and red tags that bind to the Y. And he found transplant-derived cancers in abundance: in 12% of cases, the sex of the tumour matched the donor rather than the recipient. For example, a 48-year old woman developed skin cancer nine months after receiving a bone-marrow transplant from a man. The tumour cells had a Y chromosome, indicating that the cancer arose from the donated bone marrow. In another case, a 62-year-old man developed colon cancer ten years after receiving a kidney transplant from a female donor. The colon-cancer cells lacked a Y chromosome.

Closer examination of the DNA in the tumour cells and surrounding tissue showed that the tumours definitely did originate from the donor organs, not the recipients. Dr Barsky also found that if a tumour formed in the transplanted organ, it could be derived from either recipient or donor cells.

In each of these cases, the tumour that formed resembled any other tumour that would form in that site. The 48-year-old woman's looked like skin cancer, not cancer of the bone marrow. The 62-year-old man's looked like colon cancer and not like a kidney tumour. Thus, once a cell migrated to a new site, it took on the behaviour and appearance appropriate to that location – losing the identity it had held in its organ of origin.

This observation does not absolutely prove

If the hypothesis is true, stem cells from a donor organ may cause cancer somewhere else in a recipient's body

The new data support the idea that tumours arise from stem cells that have gone wrong

that the migrating cells are stem cells, but it would be astonishing if fully differentiated cells from one tissue could up sticks to another organ and then take on the characteristics of that organ. Besides, biologists do know that stem cells in the bone marrow move into the blood stream. Thus the formation of donor-derived tumours in distant tissues after a bone-marrow transplant is not entirely unexpected. A few reports also exist in the medical literature of donor-derived tumours arising after a solid organ, such as a liver or a kidney, has been transplanted. Dr Barsky's data, though, show that this is not such a rare event after all. Stem cells in one organ thus seem malleable enough to adopt a whole new developmental programme in another organ, even late in a person's life.

More important, though, in Dr Barsky's opinion, is that the new data support the idea that tumours arise from stem cells that have gone wrong. It is not clear whether those stem cells are healthy when they migrate to a new site and mutate into cancer stem cells after they have taken up residence, or if they mutate first and then migrate. Either way, however, transplant registries may just have shed light on a fundamental question in cancer biology.

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