

Don't be deluded about "cancer breakthroughs"

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Don't be deluded that this is the cancer breakthrough

Last week's news of a melanoma 'cure' is the latest in a series of advances that lack staying power, says John Cornwell

It's been a heady fortnight for medical science. First there was thrilling news from the great stem cell bazaar. The boffins, it was claimed by the US biotech company Advanced Cell Technology, had got around a tricky ethical conundrum that would now allow researchers to experiment with human stem cells without actually killing off viable human embryos. Stem cell research could go full steam ahead to the final frontiers 'cures for everything from damaged spinal cords to blindness' free of George Bush's evangelical scruples.

Hot on the heels of this comes a revival of the fortunes of that other 'Next Big Thing' that never quite made it despite an ethical clean bill of health (save that the cure all too often turned out worse than the disease). The return of gene therapy.

Two dying men with malignant melanoma, it was announced on Friday in the American journal Science, had been cured after their genetically engineered white blood cells turned into 'cancer hunters' and mopped up proliferating malignant cells. If it works for this virulent form of skin cancer, argue the exultant scientists, then it could work for other cancers.

But before cracking open the champagne, there's more than a shiver of déjà vu about the news. Is this the same gene therapy that was promised in the dying days of the old century? The \$3 billion Human Genome Project, widely announced as the cracking of nature's code, was promoted through the 1990s as the beginning of the end of the 4,000 diseases that affect humankind: just find the faulty gene, send in a harmless carrier virus to knock it out or correct it, and Bob's your uncle.

Well, there was clearly no doubt genetic testing would reveal many of the

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secrets of the human body: including breakthroughs in isolating genes for specific cancers or who was likely to get Huntington's disease, or early heart disease, or diabetes ? if you really wanted to know. But gene ?therapy? was another matter.

On the eve of the millennium an Arizona teenager, Jesse Geslinger, suffering from a mild form of ornithine transcarbamylase deficiency, which affects the body's ability to process ammonia, volunteered for genetic therapy at the University of Pennsylvania. A gene correction aimed at curing him was attempted in the form of an engineered ?carrier? virus injected into his liver. He developed an infection and three days later he was dead.

It was a tragedy not only for Jesse's family but for the entire genetic medical science community. But genetic therapy researchers held their breath and tried again. The following year, 2000, two infants suffering from SCID (severe combined immunodeficiency disorder), causing them to live inside bacterium-free bubbles, were treated by a similar gene ?correction? strategy at Necker hospital in Paris.

In October 2002 one of the children was found to have leukaemia. When the second child developed leukaemia a year later the trials were halted. As James Watson, co-discoverer of the structure of DNA, remarked laconically: ?Gene therapy seems to have cured the children's SCID but caused leukaemia as a side effect.?

The record of gene therapy, so far, should give us pause before rejoicing over the melanoma cures in the US. In the first place they were just two claimed successes out of 17 similarly treated patients, and melanoma has a way of coming back after a patient has been declared free of it. In the second, scientists in the business of battling with cancer these past 40 years have given up on discovering anything like a magic bullet.

Winning the war against cancer, as the preponderance of the world's oncologists repeatedly stress, is a long hard slog on a great many fronts. The surest and longest-term successes appear to be in the middle ground of hormone and protein research rather than at the level of genes: the kind of strategies that have made Herceptin, the breast cancer drug, an apparent success.

As Professor Bruce Ponder, one of the British contributors to the discovery of the BRCA1 and BRCA2 breast cancer genes, tells me: ?We have come a long way in the past two decades and what we see is dauntingly complex. It's like walking on a waterbed: resolve one problem and five or six others pop up somewhere else. It is not one disease, it's hundreds.?

Ponder's belief in the multi-dimensional nature of cancer and its treatment is a crucial aspect of his direction of one of the largest cancer research sites in Europe at Cambridge, where 500 scientists will eventually be studying the disease in collaboration with clinicians. Genetic therapy is a crucial and continuing part of the war, he avers ? he

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is, after all, a geneticist.

But three years back, on the 50th anniversary of his great discovery with Francis Crick, Watson reflected sadly on the fact that genetic therapy had not lived up to anything like its great expectations. "Diagnostics," he declared, "are now our most powerful weapons . . . in the case of prenatal diagnosis it is the prospective mother who should make the decisions."

Which brings us, ironically, back to an ethical connection between genes and stem cells. The supposed breaking of the moral scruple of human embryonic research involves the discovery that it is possible to extract a single cell from the embryo at the 8-cell stage of development and to nurture that extracted cell into a stem-cell line for potential therapies. Such extractions are being done routinely in diagnostic testing of embryos for suspected genetic faults such as Down's syndrome; and objections persist.

Those who would quarrel with prenatal diagnostic testing as well as human embryonic experiment form, of course, a much wider constituency than George Bush and the Pope. Discovery of Down's syndrome in prospect, or cystic fibrosis, is one thing. But where, ask many ethicists, does it end? Choice of sex? Colour of eyes?

Furthermore, there are as yet no controlled experiments to prove that individuals who have grown from embryos deprived of a cell at the 8-cell stage will be normal. One can only speculate about the day when an accused villain in the dock cops the plea that his embryo was deprived of a crucial totipotent stem cell.

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