MEDICINE-HEALTH

Inside Story

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ONCOGENES, ANEUPLOIDY AND AIDS
A Scientific Life & Times of Peter H. Duesberg

Harvey Bialy
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Harvey Bialy is a microbiologist, and a poet. He brings a love for words as well as a love for science to this amazing book. It gives an entertaining and penetrating insight into the lumbering ways of human beings, as we struggle to understand our world whilst encumbered with desires and agendas that often obscure our vision.

The book opens a door towards new ways of thinking about cancer and AIDS. For both diseases the challenges presented are mind-rattling, as Bialy puts it, with far-reaching implications for research and treatment. But he writes so well that the scientific controversies themselves seem almost like side scenes compared with the human behaviours surrounding them.

Peter Duesberg, whose scientific life and times are chronicled, is an eminent molecular biologist who became notorious for persistently questioning the hypothesis that HIV is the cause of AIDS. He was labelled a "pariah of his profession" by those who felt such questioning would cost lives by damaging the public's sense of urgency over the disease. (Similar criticisms accompanied my own reports on Duesberg's critique, published in The Sunday Times in the early 90s.) But some degree of rehabilitation is now under way for this brilliant American scientist, who has worked at the leading edge of microbiology for 35 years.

Duesberg's extraordinary role has been to help give birth to two powerful and related ideas, and then vainly attempt to curb them as, like Frankenstein's monster, they grew out of control, eventually turning on their creator. In trying to persuade his scientific colleagues to reappraise those concepts, he became extremely unpopular. Yet the work he has done and discoveries he has made in seeking to counter the dogmas

he helped bring into being may prove to be his best contribution to science.

It was in the early 1970s that Duesberg came to prominence, defining biochemically what came to be known as the first retroviral oncogene: a gene that causes cancer, carried by a retrovirus. (Retroviruses, so-called, are short stretches of genetic material that bud out of cells as RNA-containing particles, then copy themselves back into the DNA of other cells).

The work was timely; the idea that genes could cause cancer was just what a substantial section of the scientific community wanted to hear. New tools for examining the workings of microbes and cells in ever greater detail were coming on line, and billions of taxpayer dollars were available as part of the "war on cancer" for microbiologists holding out the hope that examination of these inner workings could lead to a cure. As all this money and energy poured into the field, science journals enjoyed a phenomenal increase in advertisements for the reagents, test kits and other research equipment involved.

Since retroviruses spring from the DNA of their hosts, as well as reimplant themselves there, Duesberg's work helped to fuel the belief that normal cells harbour genes that can cause them to become cancerous. Thus began a long, enormously expensive and so far fruitless search for "cancer genes". Although a number of human genes have been nominated as suspects associated with the disease, none has been shown to cause it.

As far back as 1983, Duesberg published a review in which he sought to make it clear that the vast majority of animal retroviruses do not carry a cancer-causing gene. Furthermore, in the very rare instances where a retrovirus does have such a gene, the gene's structure and function is such that it does not have an equivalent in the host cell. In some cases, for example, elements from several cellular genes are needed to generate a cancer-causing retrovirus. Duesberg has shown that some highly touted examples of "oncogenes" are no more than experimental artefacts generated by the protocols used.

Even the term retrovirus is considered by some to be misleading, since it implies a "virulent" capacity to harm. Yet retroviruses are ubiquitous – there at least 50-100 in the human germ line. Rather than being pathogens, their presence and activity may represent a natural form of genetic engineering, helping cells to adapt to immunological challenge.

The concept of a viral cause for cancer fell into disrepute by the early 1980s. But the oncogene concept was to survive for another two decades; and in 1984, the belief that human retroviruses can kill received a massive boost when American government researchers claimed to have identified HIV as the cause of the devastating collapse of the immune system seen in AIDS.

For the past 20 years, Duesberg has questioned both ideas with increasing urgency. The further he went down this path, the more he became excluded from the company of colleagues with whom he had previously been riding high, and from the journals that used to publish him without question. Once voted California's Scientist of the Year, a member of the prestigious US National Academy of Sciences, and recipient of a $350,000 Outstanding Investigator Award from the National Institutes of Health, he gradually became excluded from mainstream scientific discourse.

Bialy is particularly scathing about the behaviour of "Sir John Maddox OBE", the former editor of Nature, who took it upon himself to reject numerous submissions from Duesberg on the subject of HIV and AIDS. His starting point was not scientific, but rather, concern for the public health and the reputation of science. On November 17, 1988, he wrote to Duesberg:

I am glad you correctly infer from my letter that I am in many ways sympathetic to what you say. I did not ask you to revise the manuscript, however. The danger, as it seems to me, is that the dispute between you and what you call the HIV community will mislead and distress the public in the following way. You point to a number of ways in which the HIV hypothesis may be deficient. It would be a rash person who said that you are wrong, but...if we were to publish your paper, we would find ourselves asking people to believe that what has been said so far about the cause of AIDS is a pack of lies.

With this letter, Bialy writes, Maddox became the slave rather than the foil of scientific fashion, putting "the weight of his journal (which, along with *Science*, shapes the thinking of the vast majority of working biologists) irrevocably behind the virus-AIDS hypothesis." From that point on, no matter what holes were punched in the fabric of HIV-AIDS, "it would magically heal itself and continue to wrap the entire globe in its satisfying warmth, a kind of medical Linus' blanket for everybody."

This magical construct has proved enduring, and Duesberg has made little progress in his efforts to dissolve it. On the cancer front, however, the last few years have been more fruitful for him.

Today's orthodoxy holds that carcinogens alter the genes of ordinary body cells, activating or disabling genes linked with cell proliferation mechanisms. Bialy says animal studies have tended to disprove this hypothesis, which in any case has been unproductive.

He describes a pivotal role Duesberg has played in winning greater acceptance for the idea that aneuploidy – gross imbalances in the number of genes, caused when chromosomes are severely damaged, or present in abnormal numbers - plays an essential part in cancer. Cancer, from this perspective, involves an alteration in the function of thousands of genes and their products and roles, not just changed activity of a small group of genes. It isn't so much a disease caused by unbridled cell growth, but one arising from the fact that the cancerous cell becomes like a species of its own, destructive of the healthy functioning of the body in a variety of ways and eventually consuming the organism from which it evolved.

Bialy, a friend of Duesberg for more than 35 years, unveils these radical, stimulating and potentially therapeutically important ideas with the excitement and enthusiasm of a genuinely inquiring scientific mind, as well as with wit and intelligence. It is clear that Duesberg mirrors these same qualities, and that a kind of love is involved, a meeting of like minds, in the saga of their shared experiences. There is no hint of a recognition in the book that Duesberg may have his own blind spots, and for this reason, the reader would do well to stay open-minded over where the truth may lie on cancer and AIDS. But as an eye-opening and absorbing insider's account of nearly three decades of controversy involving one of the leading players on the scientific stage, the book is uniquely informative.

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