

MEDICINE

Cancer's magic bullet returns

Tumour immunology has travelled a long and bumpy road. **Gerard Evan** examines an uneven treatment of it.

I confess: back in the 1970s, I was a tumour immunologist, entranced by the idea that incipient cancers are constantly erupting in our bodies and routinely culled by our own immune systems. But in the 1980s, it became clear that people with suppressed immune systems (such as people with HIV, or those taking immunosuppressive drugs after transplants) remained stubbornly — and happily — free of the commonest cancers. So I lost faith and retreated to the more immediately fruitful research areas of cancer-causing genes and tumour suppressors.

Now, decades on, I am enjoying an emotion peculiar to academics. Let's call it reverse *schadenfreude*: a combination of excitement, optimism, admiration, delicious irony and humility that comes with the realization that I got it wrong. Big time.

The past decade has seen key cancer treatments — surgery, chemotherapy and radiotherapy — augmented and even supplanted by a host of drugs engineered to hit specific targets in cancer cells. Leading the pack is a revolutionary development: our emerging ability to coerce our immune systems to



The End of the Beginning: Cancer, Immunity, and the Future of a Cure
MICHAEL S. KINCH
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treat cancer. Cancer immunotherapies are curing some people for whom all other treatments have failed, engendering excitement. But in truth, the field's trajectory has been long and stumbling, from its nineteenth-century roots as a theoretical concept through to that twenty-first-century status at the cutting edge of cancer care. Michael

Kinch's *The End of the Beginning* gives an account both personal and compendious.

Kinch, now at Washington University in St. Louis, Missouri, co-developed an early antibody-based cancer immunotherapy in the 2000s, and he writes with passion and authority. He deftly describes how each immune system is unique, shaped in part by individual histories of infection. Our newborn immunity starts off relatively non-specific, and is ▶

nature's giant web, whether a species or a local climate, will have knock-on effects, he argued. He presciently warned, for example, that deforestation could harm the climate and environment, because forests moisten and cool the atmosphere and prevent soil erosion.

He was friends with other intellectual giants of his time, including polymath Johann Wolfgang von Goethe, and Charles Darwin acknowledged the intellectual debt he owed Humboldt. Many phenomena are named after him, from the Humboldt Current that flows along the western coast of South America to the stately Humboldt Peak in Colorado's Rocky Mountains. Numerous plant and animal species bear his name, too — and many German cities have a Humboldtstrasse.

Humboldt was a liberal who vocally opposed slavery. He was a driven and highly focused scientist. He was a man of near-infinite self-confidence. *The Adventures of Alexander von Humboldt* offers a splendid way to begin to know him. ■

Alison Abbott writes from Munich, Germany.

See go.nature.com/2ykzd9c for more images from *The Adventures of Alexander von Humboldt*.



A build-up of white blood cells (shown in purple) in chronic lymphocytic leukaemia.



MARTIN DIVISEK/BLOOMBERG VIA GETTY

Researchers in the Czech Republic test cells involved in the manufacture of cancer vaccines.

► meticulously trained to recognize non-self and self, attacking the former and ignoring the latter. All this is held in equilibrium by tier after tier of checks and balances whose operations are still incompletely understood.

Kinch covers all the key advances in cancer immune therapy. He discusses courageous attempts in the early 1990s by Ronald Levy and his colleagues to use monoclonal antibodies — industrially designed to target specific cell-surface molecules — to treat lymphomas. He delves into the past half-century of growing understanding and manipulation of the signals that flash between the diverse components of the immune system and govern its actions. He also describes the often messy territory of drug development in which academic and commercial interests collide, and the courage and brilliance of those who took risks and worked hard for their patients. And he details the latest dazzling, Nobel-prizewinning technologies, fruits of insights by James Allison and Tasuku Honjo, that redirect the immune system to eradicate a cancer.

Kinch starts securely on a personal note, citing his early interest in canine models of prostate cancer. This proceeds logically to a consideration of the long latency of such cancers in humans; many asymptomatic young and older men have early-stage prostate lesions, which usually don't progress. This is, of course, intriguing, but is it intended to foreshadow how the immune system acts to keep cancers at bay? Or is it merely part of his

personal epiphany? It's not clear.

Kinch follows with a brief introduction to cancer, then a discussion of whether cancers are diseases of “accelerated cell growth”; he says that such a view is “not entirely accurate”. But instead of explaining this, he sidesteps into the etymology of the word tumour. Then it's cell-cycle checkpoints. Then apoptosis. Then the stigma and self-blame some people with cancer experience. Then a digression on badger hair, loosely presaging the key discovery of the tumour-causing Rous sarcoma virus. This higgledy-piggledy narrative is ultimately bewildering and often seems laboured.

For example, Kinch gives pages of background detail on Queen Victoria's eldest daughter, just so he can segue into nineteenth-century German immunologist Paul Ehrlich's concept of the “magic bullet”, a treatment that exclusively targets a specific pathogen or cancer cell. Such excursions are not helped by Kinch's gesture towards the likes of US businessman James Graham, who suggested that cancers might drive evolution, serving as organismal quality control. This dubious concept confuses types of mutation and is hard to square with cancer as a disease whose principal victims are beyond reproductive age. And in a book from an author fascinated by dog cancers, it is ironic to see no mention of canine transmissible venereal tumour. This bizarre disease is caused by a cancer clone that spreads from dog to dog through sex. Originating some 11,000 years ago in a husky-like

canine, the clone is now a global parasite whose very existence depends on its ability to evade its host's immune system.

All in all, those interested in human stories of research might relish the biographies and historical snippets. However, to me, they were distracting; those looking for a more focused, technical account might find the book slow, rambling and frequently frustrating.

Misleading anthropomorphisms are another, all too familiar, bugbear. Too many writers imbue cancers with baleful intent and strategy, and it is disappointing to see Kinch do the same. Cancers have no brain, no plan, no free will; they bear neither virtue nor malice. Cancer cells do not exhibit “carelessness” and are not “audacious”; there are no “choices by a cell not to perform its regular house-keeping chores” or to use T cells as “human shields”. Cancer cells are automatons that act because of corrupted software, not evil purpose. We must never forget that people with cancer are patients — not contestants locked in some epic struggle with their disease.

The End of the Beginning is a timely reminder of the bright future in cancer treatment that seems to lie ahead. If only Kinch had made it easier for us to see the hoped-for forest for the trees. ■

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