Warhead

This year marks the 40th anniversary of President Nixon's declaration of war on cancer. For all his faults, Richard Milhous Nixon and his advisers were foresighted enough to pump public funding into a long-term research project, aiming to amass the knowledge needed to defeat this scourge of contemporary society. They probably believed that victory would take no more than a decade. After all, John F. Kennedy's superficially more ambitious technological feat of landing men safely on the Moon had been achieved in comfortably less time. The Cold War had provided the impetus for Kennedy's Moon programme. Nixon dreamed of bettering his historic rival—and the Soviets—by affixing his name to a therapeutic warhead that he believed would bring him far more glory than planting the Stars and Stripes on an arid dust plain in outer space.

Nixon's war on cancer has outlasted both his Presidency and his lifetime. Yet, 40 years on, we are still waiting for substantial progress in actual therapy, even if the amount of published knowledge in the intervening period seems voluminous enough to stretch to the Moon.

In public forums in which I have voiced this inconvenient truth, distinguished colleagues have fervently rebutted my remarks, eager to explain to the public just how close we are to understanding and conquering the disease in the near future. In particular, it is frequently claimed that the new generation of 'targeted' therapies being trialled at many centres offer a real prospect of breakthroughs in treatment very soon.

While the hope remains that this might come to pass, the truth is that most of the—rather modest—improvement in cancer survival rates since 1971 has been achieved by earlier and more accurate diagnosis, paid for by public healthcare systems or private insurance companies. Apart from this, the greatest advances have come from public-health measures, such as the campaign against smoking. Despite all that we know

about oncogenes, tumour suppression mechanisms and metastatic progression—plus the underlying derangement of cell signalling, genome fidelity, transcription, cell adhesion, epigenetic regulation and apoptosis—we have not yet succeeded in widely applying this knowledge in the clinic.

There is now a danger that cancer mortality rates might actually start to nudge upwards again as quality healthcare becomes less affordable in the wake of the debt crisis. There is an equal danger that public policy-makers, quoting comments such as those in this editorial out of context, will decrease spending on the very type of basic research that we know is required to make real, long-term progress. This is not only a result of spending cuts. It is also partly due to the increasing fashion for 'translational research', nurtured by governments oblivious to the fact that lack of progress towards goals such as cancer cures is not due to a structural defect in the university system, but to insufficient basic understanding. Translational research is meaningless without something to translate. True, we do not lack anonymous biomarkers for disease, but the mechanistic framework needed to interpret those biomarkers and devise workable strategies to intervene in aberrant processes is still missing. The idea that tens of thousands of scientists are sitting on secret knowledge that could be applied today, if only they were provided with the simple tools and incentives that are needed to create a start-up company, is simply absurd.

The war continues. I believe its next phase must be a vigilant battle against public misperceptions and the cynical, almost wilful misunderstanding of reality by politicians seeking to shave a few more dollars off our tax bills. Despite the anthropomorphism, cancer is smarter than we are: put more scientifically, natural selection at the cellular level has so far defeated all our ingenuity. More positively, new concepts have emerged in the past decade that offer fresh

possibilities for eventually reducing cancer to a manageable, albeit chronic disease: the cancer stem-cell theory, the rediscovery of the Warburg hypothesis and the increasing recognition of the crucial importance of the cancer-cell milieu. But translating these ideas into effective therapies could take another 40 years or more, and certainly cannot be achieved without unrelenting efforts in basic molecular biology.

We must therefore fight against the defeatist proposition that medical research has failed to win the war on cancer. Instead, we need to convince politicians and the public that the war is winnable, but only by much greater scientific effort. Western policy-makers have accepted that the so far limited success of the war against Islamist terrorism calls for a change in tactics, not abandonment of the struggle. Exactly the same applies to cancer. We need to broaden the fight to include areas such as metabolism, immunity and neuroendocrinology, as well as the more traditional focus on signalling and cell differentiation.

We cannot fight thermonuclear weapons with tanks and battleships any more than with sticks and stones. In scientific terms, cancer therapy is still in the era of tanks and battleships, even if they are the best tanks and battleships ever designed and sometimes succeed in penetrating the enemy's superficial defences and distracting it for a while. But more effective surgery, better-targeted radiotherapy and smarter cytotoxic drugs and antibodies will not win the war. We need to figure out exactly how the enemy's warhead works, in order to devise a way of disabling it. This requires not only massive and sustained funding, but also for us to free up every drop of audacious ingenuity we can muster. Any country faced with a real, existential military crisis mobilizes its best brains. This war requires no less.

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