Cancer research – can the entity be bigger than the sum of its parts?

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ABSTRACT

Cancer Research has benefitted from substantial expenditures by federal and nonprofit organizations. The resulting success in patient care has been uneven. Two lessons from the 20th century history of science suggest infrastructural changes that can boost success. We need to better organize big science, explicitly aiming for expedient clinical translation. In parallel, resource allocation should enable investigator-initiated exploration on the basis of productivity per research dollars spent.

The War on Cancer, Personalized Medicine, Moonshot: Since the signing of the National Cancer Act of 1971, we have believed that we are finally close to ending the scourge of this disease for good, with each of these initiatives having triggered a phase of elevated confidence. Certainly, there has been progress since the dark ages before 1946, when trial and error approaches – mostly based on metal tinctures and herb extracts – dominated drug treatment. Three epochs have ensued [1]. Monotherapy with the first efficacious agents1 demonstrated that remission is principally achievable under chemotherapy. In 1956, Min Chiu Li, Roy Hertz and Donald B. Spencer reported their success with the methotrexate treatment of choriocarcinoma [2]. From 1965 through the close of the 20th century, clinical trials were crowded with countless permutations of combination chemotherapy, designed to spread out the horrendous adverse effects of this treatment modality, while doing the utmost to reach efficacy, thus manifesting in hard-earned remission at best. Molecular biology research into cancer flourished in parallel and – starting with the FDA approvals of rituximab (Rituxan, 1997) and imatinib mesylate (Gleevec, 2000) – ushered in the third phase. We have come a long way by pushing back the administration of non-specific DNA-damaging or anti-proliferative agents and replacing them in first line treatment with drug molecules that exploit tumor-specific changes (mutations). In addition, the targeting of tumor-host interactions has come of age with hormone treatment, anti-angiogenesis agents, and recently spectacular (albeit spotty) results with immunotherapy.

Nonetheless, the intense investment of resources and resulting high expectations have come to less than full fruition. A few years ago, a much-noticed analysis stated: “More than 40 years after the war on cancer was declared, we have spent billions fighting the good fight. The National Cancer Institute has spent some $90 billion on research and treatment during that time. Some 260 nonprofit organizations in the United States have dedicated themselves to cancer […]. Together, these 260 organizations have budgets that top $2.2 billion” [3]. Today, cancer mortality in the United States is around 163.5 per 100,000 (men and women per year, based on 2011-2015 deaths). The underlying cancer mortality rates decreased by 1.8% per year among men (2006 to 2015), 1.4% per year among women (2006 to 2015), and 1.4% per year among children (2011 to 2015) [4]. Intertwined in oncology are countless stories of either remarkable success or disturbing lack thereof.

Where have we fallen short of the noble goals? Big problems require big efforts. Prima facie, the need for coordination, collaboration, and large-scale science to aid patient care appears to have been addressed with the establishment of NCI-Designated Cancer Centers.

1 Nitrogen mustards, originating from chemical warfare in World War I, were introduced as drugs after World War II. Independently developed, aminopterin was the first rationally designed anti-cancer agent, soon to be replaced by methotrexate.
organize large science with the explicit goal of rapid clinical translation. This structuring can be modeled from the Human Genome Project (HGP), the National Aeronautics and Space Administration (NASA), the European Organization for Nuclear Research (CERN) and similar organizations. Resource allocation needs to be judiciously balanced to also enable investigator-initiated exploration across all cancer-active academic institutes. In striving to best utilize public funds, past productivity per research dollars spent impresses as the most accurate predictor for future contributions.

CONFLICTS OF INTEREST

The author declares no potential conflicts of interest.

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