

Conclusions: Pleural infiltrating T-cells represent an attractive source of T cells for immunotherapy. They are numerous, readily expandable without protracted passage and can be induced to secrete immunostimulatory and effector cytokines and specifically kill autologous tumor.

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SP 18

Are there really cancer stem cells and how do they operate?



Robert Gale

Some but not all data suggest within a cancer not all cancer cells are the same, namely, there are diverse cell types. The *stem cell* theory of cancer proposes amongst all cancer cells a very few act as *stem cells*. These cells reproduce themselves and sustain the cancer much like normal stem cells renew and replenish organs and tissues like the haematopoietic system. There are important therapy implications if cancers are really driven by a few *stem cells*. For instance, many anti-cancer therapies are evaluated based on their ability to make a cancer smaller. This can happen without killing cancer *stem cells*. If so, the cancer is likely to recur, perhaps in a more dangerous form such as metastases. In fact, most people with cancer die from metastases, not the primary cancer. The analogy is selecting a more virulent microbe by indiscriminate use of antibiotics.

One component of the cancer *stem cell* theory concerns how cancers arise. Typically, for a cell to become cancerous it must accumulate substantial numbers of mutations. A leukaemia such as chronic myeloid leukaemia (CML) is an exception caused by 1 mutation (*BCRABL1*). Conventional cancer theory is that any cell has the potential to become a cancer. However, other data suggest only some cells, those with *stem cell* potential, can develop into a cancer. This may explain why some normal people can have cancer-related mutations without having cancer, for example normals with *BCRABL1* or normals with *t(14;18)* without CML or without a lymphoma. The hypothesis is the cell(s) in which these mutations occur are not *stem cells* and therefore lack the potential to cause cancer. However, we must also consider the possibility some mutations can re-programme a cell without *stem cell* potentially to become a *stem cell*. An example of this are induced pluripotent stem cells (iPSC) which are adult (non-stem) cells reverted to an *embryonic stem cell* state by introducing 4 genes. Another notion is only cells with *stem cell* like features survive sufficiently long to accumulate the typically large number of mutations required for cancer development. The theory, therefore, is cancer *stem cells* arise from normal *stem cells* or precursor cells produced by normal *stem cells*.

Another important implication of the cancer *stem cell* theory is cancer *stem cells* are closely related to normal *stem cells* and share many properties. Cancer cells produced by cancer *stem cells* should follow many of the rules observed by normal daughter cells. In this regard cancer cells can be considered a caricature of normal cells with similar but distorted features. If so, it may be possible to use knowledge about normal *stem cells* to identify and attack cancer *stem cells*.

Lastly, it may not be necessary to eradicate all cancer stem cells to cure a cancer. For example, in CML, therapy with tyrosine kinase-inhibitors (TKIs) markedly reduces numbers of mature leukaemia cells but not any and certainly not all CML *stem cells*. Regardless, in a substantial proportion of people with CML responding favorably to TKI-therapy it is possible to stop therapy without leukaemia returning. In sum, increasing knowledge of cancer stem cells should improve our understanding of and ability to treat diverse cancers.

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Challenges in treating solid tumors in developing countries



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There is an increasing number of cancers worldwide due to epidemiological transition. Longer life spans resulting in aging population is among some of the reasons for growing burden in cancer worldwide. The number of new cancer cases is expected to increase by nearly 75% by 2030 (107,000 additional cases per annum), with 60% of cases in the elderly (aged ≥ 65). The extent of cancer related morbidity and mortality is directly linked to the effectiveness of efforts to prevent, control and treat cancer, particularly in the developing world. In 2012, almost 57% of all cancer cases and 65% of cancer deaths occurred in low-and middle-income countries. If the current trend continues, the burden of cancer will increase to 22 million new cases annually by 2030, with 81% of new cases and almost 88% of mortality occurring in less developed countries. Cancer care in a country like Pakistan is challenging because of lack of strategic information and national planning for cancer control. Cancer registry provides important information that helps in directing and planning cancer prevention and care. Lack of national cancer registry limits estimation of true burden, identification of areas that require special need and thereby proper treatment strategy. Health systems required to deliver comprehensive life-saving treatments are limited in the country. Out of pocket payments and private health care usage remains high. A number of patients are not covered by insurance and individuals face catastrophic expenditure in seeking treatment. As a result, there is disparity in access to quality care. High incidence of later stage disease is very common due to social stigma associated with cancer treatment, myths, lack of awareness and preference for alternative treatment options. Drugs that have lately revolutionized cancer management are either not available in the country and if present, are extremely expensive for a common person to afford. Palliative care and access to supportive care medicines is almost nonexistent. Pain management is restricted to analgesics without narcotics. With cancer rates steadily rising in low- and middle-income countries, the disease will inevitably