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# Cancer Stem Cells

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Three customs of cancer research are shared together to provide increasing precision to the causal mechanisms of tumor heterogeneity and recognition how these are linked to therapy resistance, tumor progression, and recurrence. Advanced genome sequencing has established that cancer within a single patient is a heterogeneous mixture of genetically distinctive subclones that arise through branching evolution [1,2] . The exclusive driver mutations within each subclone can impact the cancer hallmarks in a different way, thus contributing to functional heterogeneity. Correspondingly, strong confirmation is emerging that nongenetic determinants, principally connected to developmental pathways and epigenetic modifications (DNA methylation, histone modification, chromatin openness, microRNA [miRNA], and other noncoding RNA) contribute to functional heterogeneity [3-5] .These determinants are commonly attributed to the continuation of normal tissue stem cell hierarchies. Equally, nongenetic determinants create hierarchically ordered tumor tissues where a subpopulation of cancer stem cells (CSCs) sustains the long-term clonal maintenance of the neoplasm. Proof from both experimental models and clinical studies indicate that CSCs survive many generally employed cancer therapeutics. Furthermore, the properties and transcriptional signatures specific to CSC are highly predictive of overall patient survival pointing to their clinical importance [6].

CSC is a general term referring to the cancer cells talented of differentiation and self-renewal which is the role of CSCs chemotherapy resistance. The description of CSCs does not decide their origin and the term "Cancer Stem Cell" does not denote that cancer begins from stem cell. CSCs are more differentiated than stem cells together with a more restricted spectrum of the cells existing in a tissue [7]. In 1994, CSCs were isolated for the first time. In 1855, German pathologist stated that cancers arise from the activation of dormant, embryonic- like cells present in mature tissue and argued that cancer does not simply appear spontaneously [8].

The initial cell that develops cancer is not essentially a cancer stem cell, despite the fact that cancer-initiating cell and cancer stem cell are occasionally used interchangeably. The existence of CSCs was initially projected 40 years ago, though analysis of its details leftovers a mystery until the development of advanced investigation tools [9]. The most excellent evidence to support the existence of CSCs arose from the study of hematological malignancies [10]. Taking into consideration the task of embryonic stem cells and self-renewal in mature cells like blood cells, the definition of CSCs was discovered [11].

In addition to developing tumors, CSCs direct to the migration and propagation of tumors in new sites that take place in metastasis. Although the role of CSCs in the renewal and initiation of tumors has been exposed, the correlation between CSCs and metastasis is yet

to be found out [12]. Hermann *et al* [13] used pancreatic cancer as a model to investigate the relationship between CSCs and metastasis. They analyzed the initial tumors and established that a chief part of the tumor has the aptitude to form tumor after implantation. They comprise a sub-category of CD133+ cells which have the tumorigenesis and high resistance features of Gemcitabine. These tumorigenic CD133+ cells were channeled serially, signifying their capability for self-renewal, and that they were capable to create tumor heterogeneity by manufacturing differentiated, non-tumorigenic progeny [14].

Long term cell culture, FACS (fluorescence-activated cell sorting), and MACS (magnetic cell sorting) are the chief techniques used to isolate CSCs. CSCs enrichment can be completed by means of the FACS technique. Cells are as well isolated based on the expression of special proteins of cellular-level, cell culture, epigenetic changes and expression pattern of such cellular-level markers as CD 24, CD133, ALDH1 and CD44. CSC characteristics can be determined through mRNA and miRNA expression analysis, copy number variation, etc. Subsequently phenotypic and genotypic characteristics can be linked with in vitro and in vivo clinical data [15].

In spite of advances in radiation therapy and chemotherapy, the prognosis of patients with advanced malignant tumors remains poor. Unproductive targeting of CSCs has been suggested as one explanation for present treatment failure [16]. CSCs have been recognized to be resistant to a variety of chemotherapeutic agents and radiotherapy [17]. The resistance of CSCs to chemotherapy may engage augmented expression of drug efflux pumps, more efficient DNA repair [18], and interactions of CSCs with their microenvironment [19]. With reference to CSC resistance to conventional therapeutic agents, development of alternative/novel therapeutic strategies that can specifically and efficiently target CSCs is needed to improve the efficacy of other therapeutic agents. There are a number of hypothetical reasons which give a rationale for rising immune approaches to target CSCs. It is clear that CSCs and their more differentiated progeny exhibit distinct gene expression profiles and consequently express diverse antigens. Immunologic approaches directed against whole tumors are principally biased toward more differentiated tumor cells which form the bulk of the tumor and which express "differentiation" antigens. This suggests that effective immune targeting of CSC may necessitate the specific targeting of this cell population. Additionally, within a tumor, CSCs may themselves exhibit heterogeneity resultant from both genetic and epigenetic regulation related to tumor progression and metastasis. For case in point, breast CSCs uphold that flexibility to transition between mesenchymal (EMT) and epithelia (MET) states in a process regulated by the tumor microenvironment. The capability of immunotherapies to target multiple antigens makes these approaches right to the targeting of these heterogenous CSC populations [20].

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