

Cancer Stem Cells: Getting to the Root of Cancer

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An emerging concept in cancer biology is that a rare population of Cancer Stem Cells (CSC) exists among the heterogeneous cell mass that constitutes the tumour. Based on this notion, tumours are thought to be driven by a cellular subpopulation that retains key stem cell features. Yet, despite their critical importance, much remains to be learned about the developmental origin of cancer stem cells and the mechanisms responsible for their emergence in the course of the disease. We will focus more specifically on the blood-related cancer leukemia, which was the first disease where human CSCs, or leukemic stem cells (LSCs), were isolated. Acute myeloid leukaemia (AML) is a clonal disorder defined by the accumulation of abnormally differentiated myeloid blasts. Because leukemic blasts have very limited proliferative capacity, it is believed that leukemic clone is maintained by a rare population of leukemic stem cells (LSC) that have extensive proliferation and self-renewal capacities. Elucidating the nature of the target cell that undergoes leukemic transformation and characterising the LSC is essential for both the understanding of the leukemogenic process and for the design of effective therapies. The development of an *in vivo* model that replicates many aspects of human AML had provide a mean to identify LSCs. LSC is defined by the ability of that cell to initiate AML in NOD/SCID mice. This *in vivo* assay provides the foundation of an assay to define the biological and molecular properties of such LSCs. Despite the clear importance of the LSC in the genesis and perpetuation of leukemic disease, little is currently known about the biological and molecular properties that make LSCs distinct from normal haematopoietic stem cells.

Existing therapies have been developed largely against the bulk population. The lack of durable response in most cases, suggests that the treatment used may not effectively target the LSC population. Indeed, the failure of the current therapeutic regimens is likely related to the resistance and persistence of LSC. Thus, the identification of LSC has important implications for future research as well as for the development of novel therapies. Research focused on identifying and characterizing the rare cancer-initiating cells, should allow the identification of specific targets for CSCs, which if specific should provide effective cure and prevent disease relapse.