



A Brief Review on Cancer Stem Cells

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Abstract

More than a decade ago, the existence of a rare population with both stem cell-like properties and tumor initiating capability was first identified in acute myeloid leukemia and, subsequently, in several solid tumors. These populations with stem cell-like properties were termed 'cancer stem cells (CSCs)', indicating that only a subset of cancer cells were tumorigenic and able to initiate and produce the bulk of tumors, thus also termed 'tumor initiating cells'. In this mini review on issues such as cancer stem cells markers, integrins, Matrix metallo-proteinases, chemokines and chemokine receptors are described to study the cancer stem cells associated metastasis. In this review article, several mechanisms and signaling pathways of cancer stem cells during self-renewal and differentiation were mentioned.

Keywords: Cancer stem cells; Matrix metallo-proteinases; Chemokines and integrins

Introduction

Many studies performed over the past 30 to 40 years, when viewed collectively, have shown that the characteristics of stem-cell systems, the specific stem-cell properties described above, or both, are relevant to some forms of human cancer [1]. A minor subpopulation of cells in tumor samples has the capacity to initiate clonal growth in *in vitro* cultures or in *in vivo* transplant models which has perplexed researchers in the past. Two theories were proposed to explain this paradox. The stochastic theory suggested that all cancer cells are equally malignant but only clones that randomly possess favorable biological properties will grow upon transplantation. An alternative theory predicted that tumors are hierarchical like normal tissues and only the rare subpopulation of cells at the pinnacle of that hierarchy have the unique biological properties necessary for tumor initiation. The role of stem cells is now being addressed in many solid tissue cancers. In 1990s Irving L. Weissman, coined these stem cells, "Cancer stem cell", stem cells arising through the malignant transformation of adult stem cells. These cancer stem cells are proposed to be the source of some or all tumors and cause metastasis/relapse of the disease state. Biologically distinct and relatively rare populations of "tumor-initiating" cells have been identified in cancers of the hematopoietic system, brain, and breast [2]. Cells of this type have the capacity for self-renewal, the potential to develop into any cell in the overall tumor population, and the proliferative ability to drive continued expansion of the population of malignant cells as shown in Figure 1. The discovery of cancer stem cells implores the question regarding the origin of these cells. Are they derived from normal stem cells with a cancerous phenotype? Or do previously differentiated progenitor cells with oncogenic mutations regain the ability to self-renew? A third theory hypothesizes that CSCs may come from a rare fusion event between stem cells and other cells. Figure 2 indicates the possible origin of cancer stem cells [3-5].

Markers for Cancer Stem Cells

They represent a tumour cell subpopulation, own typical stem cell properties as self-renewal and potential to differentiate and are possibly responsible for tumour growth. We have a lack of knowledge about the cells equipment of molecular markers that can be used for isolation and purification. One of the already established markers is the transmembrane-protein CD133. The role of CD133 as tumor stem cells marker is well depicted in the following Figure 3. All tested cancer cell lines possess minor populations of cells with highest expression of CD133, CD44 and CD166, whereas many cells are CD133-negative [6-8]. Several experimental approaches indicated a higher proportion of CD133-positive cells with increased *in vivo* tumorigenicity and the ability to produce

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