COMMENTARY

How to Search for Specific Markers of Cancer Stem Cells
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Abstract

According to cancer stem cell hypothesis, cancer stem cells with unlimited self-renewal and multi-differentiation properties such as adult stem cells are the root cause of cancer initiation and progression, and targeted therapy to cancer stem cells is to become the most efficient therapy of cancer. However, specific markers should be discovered to define cancer stem cells accurately before targeted therapy. Therefore, we propose a model of specific markers of cancer stem cells and how to search these markers.

Key Words: Cancer stem cells - markers - search and identification

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Introduction

Cancer is a type of tissue with different differentiated stage malignant cells which is termed heterogeneity (Dick, 2008). The traditional model of heterogeneity is the stochastic model which defines each cancer cell with the potential of initiation and progression of cancer. Another contrary one is the intrinsic model which defines cancer stem cell with unlimited self-renewal and multi-differentiation property such as adult stem cell is the root cause of cancer initiation and progression (Dalerba et al., 2007a). The second model is supported by more and more experimental evidence from 1997 (Bonnet and Dick, 1997). It shows good prospective in cancer early diagnosis and targeted therapy to cancer stem cells. Therefore, it is very important to understand signaling network, microenvironment, specific markers and other fields of cancer stem cells. In this paper, we mainly collect some literature about cancer stem cell markers and propose a model of specific markers of cancer stem cells.

Cancer Stem Cells with Markers

In 1997, Dick reported that CD34+CD38- cancer cells define stem cells present in leukemia patients. Since 2003, studies have shown that cancer stem cells with specific markers are present in solid tumors of the breast, brain, prostate, pancreas, colon, lung, liver, renal, ovary cancer and melanoma (Table 1). The cancer stem cell hypothesis is supported by more and more experimental evidence. Cancer stem cells with specific markers present in cancer are believed to be real by many cancer research scientists.

CD133 and other markers

At present, several markers such as CD24, CD34, CD38, CD44, CD90, CD105, CD117, CD133, CD166,
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Given these considerations, CD133 is a star marker in defining adult stem cells and cancer stem cells, but it is unlike to be an ideal marker of adult stem cells or cancer stem cells. Firstly, it is expressed in too many tissues and lack of tissue specificity to distinguish one tissue from another tissue. Secondly, it is both expressed in many cancer tissues and normal tissues and lack of cancer specificity to distinguish cancer from normal tissues. Thirdly, some study show that it is expressed in non-cancer stem cells and lack of stemness (Bidlingmaier et al., 2008). Therefore, it is improper to purify CD133 positive cancer cells as cancer stem cells and anti-CD133 targeted therapy will have many side effects. For example, the most important one is that harm will occur to normal stem cells of prostate, pancreas, intestinal, lung, liver, renal, ovary, skin and may make these normal stem cells mutate to cancer initiating cells.

A Model of Ideal Specific Markers

In our opinion, ideal specific markers of cancer stem cells should meet three criteria. First, stemness, which means that the specific markers are correlated with the ability of self-renewal and multi-differentiation, is to distinguish stem cells from non-stem cells (Glinsky, 2008); second, specificity of cancer, which means that the specific markers are only expressed in cancer tissues, is to distinguish cancer from normal tissues; third, specificity of tissue, which means that the specific markers are only expressed in one tissue like colon, is to distinguish colon from other tissues of body (Figure 1).

How to Search for Ideal Specific Markers

Does this kind of ideal specific marker exist in cancer stem cells? According to current limited literature, there is no research report discovering one ideal marker meeting all three criteria. Davidson said that each cell type in the human body, including normal stem cells and cancer stem cells, has a unique signaling network architecture that is maintained by cell-specific transcriptional regulatory states; this results in cell-specific expression of genes.
Searching the Mutated Stemness Genomic, Transcriptomic and Proteomic Data as an Enormous Project

It has been suggested that normal and cancer stem cells have potentially many common mechanisms for governing their populations (Reya et al., 2001). Such as adult stem cells, cancer stem cells have their own hierarchy: cancer stem cells (CSCs), cancer progenitor cells and cancer differentiated cells. Furthermore, Gao said “the CSC hypothesis covers the developing process of tumour-initiating cells (TICs), precancerous stem cells (pCSCs), migrating cancer stem cell (mCSCs), a cellular process that should parallel the histological process of hyperplasia (TICs), precancerous lesions (pCSCs), malignant cancer (CSCs) and metastasis (mCSCs)” (Brabletz et al., 2005; Chen et al., 2007; Gao, 2008; Jung et al., 2006; Shên et al., 2008). TICs, pCSCs, CSCs and mCSCs have their own specific genes, transcripts and proteins, because each cell type in the human body has a unique signaling network architecture (Davidson, 2006). The mutated stemness genomes, transcriptomes and proteomes of pCSC, CSC and mCSC may be also different. The approach of genomics, transcriptomics and proteomics is greatly progressing, but it still has some bottlenecks (Ghosh and Poisson, 2009; Polychronakos, 2008). Therefore, how to search the mutated stemness genome, transcriptome and proteome is an enormous project. However, with the development of technology the approach of genomics, transcriptomics and proteomics will have great progression and ideal specific markers will be discovered more and more in the future.

Conclusions

Recently, many studies showed cancer stem cells or cancer initiating cells with specific markers are present in many types of cancer. These markers are not specific enough according to our ideal marker criteria. Therefore, we propose a model and a candidate database of ideal specific markers for cancer stem cells. We wish the model will be useful to search specific markers of cancer stem cells, although a lot of hard work still needs to be done.

References


