

## Potential Biomarkers and Therapeutic Targets in Cancer Stem Cells

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Major advances in basic and applied fields of the oncology in the last few years have led to an earlier diagnosis and more effective therapeutic treatment of patients with localized cancers in the clinics. Although this, the rapid progression of localized cancers to invasive, advanced and metastatic disease states that are resistant to current anti-hormonal, radiation and/or chemotherapies typically culminates to disease relapse. In fact, the rapid spread of cancer cells to distant tissues and organs and metastases remain the leading cause of the death of cancer patients. Consequently, many efforts have been made to identify and validate novel molecular biomarkers and therapeutic targets in cancer cells at primary and secondary tumors to prevent cancer progression and metastases and optimize the genetic- or proteomic-based individualized treatment of cancer patients.

Importantly, a growing body of experimental evidence has revealed that the accumulation of genetic and/or epigenetic alterations in tissue-resident adult stem/progenitor cells may result in their malignant transformation into cancer stem/progenitor cells endowed with stem cell-like properties. Cancer stem/progenitor cells, also designated as cancer-, tumor- or metastasis-initiating cells, can provide critical functions for the tumor growth, metastases at distant tissues, treatment resistance and disease relapse. In support with this, the subpopulations of highly tumorigenic cancer stem/progenitor cells have been identified and isolated from different primary cancers, peripheral circulation and metastases at near and distant tissues. The cancer types harboring immature cancer stem/progenitor cells include leukemias, melanomas, brain tumors and the majority of epithelial cancers such as skin, lung, liver, gastrointestinal, pancreatic, breast, ovarian and prostate cancers. It has been shown that cancer stem/progenitor cells with a high self-renewal ability and aberrant differentiation potential were able to give

rise to the total mass of cancer cells and form primary or secondary tumors with histological features resembling those of the original patients' tumors.

Of great interest, multiple gene products that are frequently deregulated in cancer stem/progenitor cells and their progenies during cancer initiation and progression to locally invasive and metastatic cancers have also been identified. The deregulated signaling elements include distinct stem cell-like markers such as telomerase, aldehyde dehydrogenase (ADLH), CD133, CD44 and/or CXC chemokine receptor-4 (CXCR4) and epithelial-mesenchymal transition (EMT)-associated molecules (vimentin, snail and twist). Moreover, it has also been shown that cancer stem/progenitor cells typically show high expression levels and/or activities of diverse growth factor signaling elements such as hedgehog, EGFR, Wnt/ $\beta$ -catenin and/or NOTCH, anti-apoptotic factors, multidrug ATP-binding cassette (ABC) multidrug transporters and DNA repair and detoxifying enzymes. Consequently, these gene products altered in cancer stem/progenitor cells and their progenies may constitute potential molecular biomarkers for improving screening tests and current diagnosis and prognostic methods and therapeutic targets for optimizing the personalized treatment of cancer patients in the clinics. In this matter, the **scientific researchers with an expertise in the field of cancer stem/progenitor cell biology reviewed for us.....** The emphasis is on .... The potential therapeutic targets in cancer- and metastasis-initiating cells and their progenies as well as their local microenvironment are also discussed. The provided information should help researchers to develop novel multiplex biomarker approaches and multi targeted therapies for improving the current anti-hormonal, radiation and chemotherapeutic treatments against aggressive, recurrent and lethal cancers.

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