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Commentary: Could cancer stem cells be considered as alpha and omega in cancer progression?

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Did we start our fight against cancer from the beginning?

Revealing the origin of cancer has been one of the main efforts of our century, in order to find a treatment able to definitively eradicate malignancies.

Emerging theories about the correlation between stem cells and cancer have to be considered as an update of the embryonal rest theory. The very first hypothesis on the role of undifferentiated cells in promoting cancer development was advanced in the 1870s by Rudolf Virchow and Julius Cohnheim. In 1877, Cohnheim[1] extensively formulated his theory of the embryonic origin of cancer, which postulates that the origin of cancer must be attributed to the existence in the body of "embryonic rests" that remained unused during development.

From the mid-19th, many steps have been taken leading to the current cancer stem cell theory postulating that tumor growth is supported by a small fraction of the tumoral cells that have stem-like properties (cancer stem-like cells or CSCs)[2].

In 1997, researchers[3] observed that certain types of leukemia originated from a subpopulation of stem cells by searching for stemness markers.

Al-Hajj et al[4], in 2003, identified cancer stem-like cells (CSCs) in breast tumors and demonstrated that most tumor cells were unable to self-renew and presented limited proliferative and differentiation potential. Similar findings were observed in brain cancer, colon cancer, bone cancer, and melanoma[5].

Therefore, the hypothesis emerging from the whole literature was that tumoral growth was directed and supported by CSCs. If the growth of solid cancers was driven by cancer stem cells, what kind of implication does it have for cancer therapy?

Ideally, if solid CSCs were prospectively identified and isolated according to specific biomarkers on their surface and therapeutic targets were identified, CSCs population could be detected and eliminated permanently.

Although currently available drugs can shrink metastatic tumors, these effects are usually fleeting and often do not appreciably improve patients' survival.

Chemo-resistance acquired by cancer cells and failure of existing therapies in eliminating CSCs are the main assumptions explaining the lack of control in disease progression.

Existing therapies have been developed largely against the bulk population of tumor cells because they are often identified by their ability to shrink tumors[6]. Since most cells with cancer have limited proliferative potential, the ability to shrink a tumor mainly reflects an ability to kill these cells. It seems that normal stem cells from various tissues tend to be more resistant to chemotherapeutics than mature cell types from the same tissues[7] but these issues are still debated[8].

Hence, CSCs would be more resistant to chemotherapeutics than tumor cells with limited proliferative potential. Even therapies that cause complete regression of tumors might spare enough CSCs to allow tumor regrowth. Therapies that are more precisely directed against CSCs might determine long-lasting responses and even cure advanced tumors.

Immunohistochemical analysis of malignant tumors has shown different patterns of molecular expression that can be used to group tumors into different categories, often reflecting different mutations and tumors behavior[9].

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As a result, tumor types that cannot be distinguished pathologically, but differentiated on the basis of the molecular-expression profile, can reflect a proper treatment sensitivity. Thus, a tailored treatment protocol could be offered to each patient.

CSCs identification cannot be easily made, because highly proliferative cells that drive tumorigenesis often represent a small cluster of cancer cells. To address this issue, microdissection could help generating profiles that reflect more homogeneous collections of cells[10].

The next frontier could be purifying CSCs from tumor cells with limited proliferative potential and performing gene-expression profiling on those cells.

New therapeutic and diagnostic targets discovered by CSCs profiling will ultimately yield new approaches to fight tumor growth.

According to this view, as CSCs seem to initiate and maintain cancer progression, could they be effectively recognized as both the beginning and the end of cancer progression, hence the final objective of targeted therapy?

Conflict of Interest

The Authors declare that they have no conflict of interests.

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