

Cancer stem cells : what if stemness is a systemic property?

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According to the cancer stem cell (CSC) model, cancers, like healthy tissues, contain a sub-population of cancer cells with stemness properties—the CSCs. The CSCs are defined by the unique ability to long-term self-renew and to produce all the other cancer cells. The other cancer cells are doomed to disappear through exhaustion of their proliferation ability. Since the rise of this model at the turn of the century, CSCs became a target of particular interest for cancer treatment. However, the very nature of CSCs remains unclear and debated. Accumulating data have highlighted that cancer cells' phenotype can be plastic. In some cancers, especially solid tumors, cancer non-stem cells can return to a stem cell state. These observations have led to skepticism toward the CSC model. The current view is thus that in some cancers, like myeloid leukemias, the CSC model applies, while in others, like melanoma, colon cancers, or some breast cancers, it does not.

I will argue that this binary view of the CSC model is a poor approximation, and that a more complex and pluralist view of the CSC model can be more productive. First, I will show that the stemness property can be of four different types (categorical, dispositional, relational, systemic). It depends on cancers. I will draw the consequences of these different views for cancer treatments: different treatments will be efficient depending on what stemness is. This will lead me to the observation that there are currently no approaches developed to treat cancer in cases where stemness is a systemic property. I will thus spend more time on this notion of stemness as a systemic property, argue that rather than abandoning the CSC model, we should instead better understand how stemness is regulated in this case, and suggest various avenues that could be investigated for the development of new therapeutic strategies.