

Stem Cells

The in vivo function of normal stem cells is repair of tissue damage and stem cells are present in tissues undergoing rapid turnover of cells such as the haematological system, skin and the intestine. The hallmarks of normal stem cell biology are the ability to self-renew throughout the lifespan of the individual as well as the ability to differentiate into the cell type of the tissue in question.

Cancer stem cells

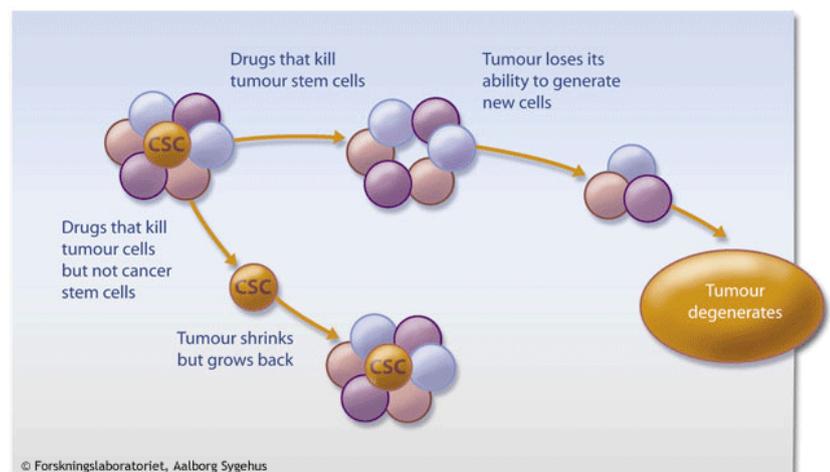
In recent years the concept of a "cancer stem cell" has gained acceptance as a model for explaining aspects of cancer biology in particular within the field of haematology. The hypothesis is that an undifferentiated cell is present that has stem cell-like qualities. But what is the evidence in favour of this hypothesis? It is necessary to show that a cancer stem cell (CSC) is able to self-renew as well as differentiate into the different cell types of the cancer (see figure).

Evidence for a cancer stem cell originated from the haematological disease acute myelogenous leukaemia (AML). John Dick and co-workers have isolated a fraction of AML cells based on surface markers that were able to initiate a tumour of similar phenotype in the recipient mice. Furthermore, they have shown that this fraction is able to cause cancer in new mice after serial transplantation. This indicates that this fraction of AML cells is able to self-renew as well as giving rise to differentiated cells, and therefore has stem cell qualities.

Other fractions of AML cells were only able to cause cancer in the initial mouse, but not to be serially transplanted. This indicates that these cells are progenitors and not true stem cells. Furthermore it was shown that AML blasts were unable to divide and represent the differentiated cell type.

Since these initial studies, the presence of CSC in other types of cancer has been demonstrated for example human breast carcinomas and brain tumours. In current clinical practice, anticancer agents are used to kill the bulk of the tumour mass. However, as the stem cell model of cancer gains acceptance it introduced another possible way of treatment, namely to target the CSC specifically. In this way the root of the cancer – so to speak – is removed and patient relapse may be avoided (see figure).

In the figure the influence of a drug targeting cancer cells (A) or the CSC (B) is shown, if the hypothesis of cancer stem cells in tumours is confirmed. Drugs targeting the CSC directly are thought to completely remove the tumour long-term whereas with drugs targeting cells in general, relapse is possible because the CSC can reform the tumour.



References and further reading

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