

Targeting Cancer Stem Cells: Therapeutic Strategies and Pipeline Developments (2010)

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Description

Cancer Stem Cell (CSC) research has accelerated in the last two years and considerable efforts are now being made to identify drug molecules that selectively target and destroy these cells. Today, more than 50 developmental molecules or classes are being evaluated in the hope of targeting this subset of cancer cells. More than 40 companies and commercial groups are progressing these activities and around 20 drug-targeting strategies are being evaluated. Efforts are being made to target CSCs using novel single agents as well as combinations, based on new and established classes. This 2010 report gives a comprehensive update on current therapeutic and diagnostic development in this field, on the drug development pipeline and on the most promising research areas in CSC characterisation. New therapeutic and diagnostic opportunities in this field are also presented.

Background: Many cancers contain a subset of stem-like cells believed to play a critical role in the development and progression of the disease. These cells, named Cancer Stem Cells (CSCs), have been found in leukaemia, myeloma, breast, prostate, pancreatic, colon, brain, lung and other cancers. Findings suggest that CSCs are able to “seed” new tumour formation and drive metastasis. CSCs also show resistance to a number of chemotherapy drug classes and radiotherapy – which may explain why it is difficult to completely eradicate cancer cells from the body, and why recurrence remains an ever-present threat. If these findings are confirmed in the clinic, the targeting of CSCs alongside the bulk of other cancer cells will offer a new paradigm in cancer therapeutics. Currently, there are more than 50 CSC R&D programmes in progress, around 50% of which are at Phases I-III. Patient data from the first clinical trials on CSC-targeting drugs are now being reported. More than two thirds of CSC R&D programmes are being taken forward by SME's, and >90% of the patents in this field have been filed by Universities. Substantial opportunity for collaboration exists in this field, and this has led to agreements between SMEs and number of international pharmaceutical companies.

Drug Pipeline: Approximately 20 different strategies, which are described in this report, are being pursued in the hope of discovering ways of selectively targeting CSCs. Recently for example, at the CTRC-AACR San Antonio Breast Cancer Symposium in December 2009, data were presented on the targeting of chemotherapy-resistant breast CSCs with the Merck compound MK-0752, a gamma-secretase inhibitor that targets the Notch pathway. In a study involving 35 women with advanced breast cancer, biopsies revealed reduced numbers of breast CSCs. In this particular case, it was suggested that combination therapies involving agents that also target the Notch pathway (believed to be important in CSC renewal) may offer more powerful strategies for killing resistant CSC populations.

Cancer Diagnostics: CSCs are believed to be causally linked to the development and metastatic spread of cancer. If this is confirmed in the clinic, this will place CSCs at the heart of cancer diagnostics and biomarkers. Scientists have identified a number of surface proteins, such as CD44, CD133 and many others, that may have important utility in both of these areas. A number of intracellular markers found in CSCs may also have diagnostic utility. These developments are described in this report. For example, CD133 mRNA levels in peripheral blood, measured using RT-PCR, have been found to predict colon cancer recurrence. There is a need for new methodologies that isolate and characterise circulating tumour cells (CTCs) in the blood, and can be applied to CSCs. CTC technologies using the EpCam marker to isolate these cells are able to predict breast and colon cancer recurrence. The adaptation of these techniques, based on specific CSC phenotypes, may provide sensitive new methods for identifying CSCs in the body. If this is achieved, it will have important implications in therapeutic decision-making and monitoring.

This 2010 report gives a comprehensive and up-to-date review of global R&D on CSCs, and strategies to target them. This includes around 40 companies or commercially based research organisations (including 27 SMEs and 8 international pharmaceutical companies) that are progressing drug discovery activities, including drug pipeline (pre-clinical to Phase III), discovery strategy, candidate molecules, drug targets, clinical trials and related areas.

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