Proportion of cancer stem cells can increase over the course of cancer treatment

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Stem cells in the bone marrow constantly give rise to new blood cells and are responsible for the maintenance of all vital blood components. However, errors during proliferation can change stem cell properties and cause tumours . Over the course of treatment, the number of these cancerous stem cells barely declines while the rest of the tumour shrinks. Scientists at the Max Planck Institute for Evolutionary Biology in Plön have developed a mathematical model with which they can calculate the proportion of cancer stem cells present over the course of treatment – those cells that maintain the supply of new tumour cells and thus promote tumour growth. While the number of tumour cells often declines during the treatment of certain types of leukaemia, the relative number of cancer stem cells remains more or less constant. The model developed by the Max Planck researchers could help doctors to predict tumour development in future and support them in the selection of suitable treatments.

Cancer cells are abnormal cells, which divide in an uncontrolled manner. Many tissues contain stem cells that form new cells over the entire life of a human. Blood cells, for example, are constantly formed from stem cells in the bone marrow. In the case of leukaemia, genetic changes in the stem cells can result in the uncontrolled proliferation of cells. "Although often stem cells only account for a small proportion of the tumour, we do not yet know exactly how big this proportion is in individual patients," says Benjamin Werner from the Centre for Evolution and Cancer at the Institute of Cancer Research in London and a former staff member at the Max Planck Institute for Evolutionary Biology.

The scientists have now developed a mathematical model that can utilise medical data from leukaemia patients. They analyzed growth and decline of leukemias over the course of treatment with the cancer drug Imatinib. Based on the change of disease burden during treatment, the computer model calculated the proportion of cancer stem cells in the patients' bodies. The results show that the number of cancer cells decreased by a factor of one hundred after a year of treatment, but the number of cancer stem cells remained approximately constant.. After 5 years of treatment, tumour burden decreased by a factor of 1000, but still the change in cancer stem cells was weak.

The number of cancer stem cells falls more slowly than that of the other cancer cells. The model also has the advantage that it does not incorporate any information about the cancer per se. This means that it can be applied to different forms of cancer.

"Cancer stem cells not only promote the growth of a tumour, they can also be resistant to radiotherapy and chemotherapy. If we can estimate the number of cancer stem cells at diagnosis and over the course of treatment, the treatment can be tailored accordingly," says Philipp Altrock, the study leader from the Dana Farber Cancer Institute in Harvard. This includes, for example, deciding how aggressive the treatment should be, how long it should last, and which combination of drugs would be most effective. "Patients with few cancer stem cells may be able to stop treatment, while those with a lot of cancer stem cells might benefit from a different therapeutic approach," explains Werner.

The model is not yet being used in clinical practice. "It will need to be developed further before this is possible," says Arne Traulsen from the Max Planck Institute for Evolutionary Biology, who was also involved in the study.

More information: B. Werner et al. The Cancer Stem Cell Fraction in Hierarchically Organized Tumors Can Be Estimated Using Mathematical

Modeling and Patient-Specific Treatment Trajectories, *Cancer Research* (2016). DOI: 10.1158/0008-5472.CAN-15-2069