

Ernst Schering Foundation Symposium
Proceedings 2006-5
Cancer Stem Cells

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Cancer Stem Cells

Novel Concepts and Prospects
for Tumor Therapy

O.D. Wiestler, B. Haendler, D. Mumberg
Editors

With 42 Figures

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Preface

The concept that cancer stem cells play an important role in malignant tumors is gaining more and more support due to recent advances in the field. The latest progress in this area is increasingly reported and commented on in the lay press, documenting the high excitement and hopes it generates.

An intricate relationship between stem cells and cancer cells was originally identified in leukemia, and evidence has now accumulated that cancer stem cells are also found in many solid tumor types including breast, prostate, and colon carcinomas. They are closely related to normal stem cells, a very small number of which are found in most tissues. Normal stem cells divide asymmetrically and have the unique capacity to produce an identical daughter cell and one that can differentiate. These progenitor cells have the ability to give rise to all the specialized cells of a given tissue. This process is strictly controlled by the niche microenvironment in which these cells reside, so that the number of stem cells remains constant. Mutations in normal stem cells and failure of the control mechanisms provided by the niche may both play essential roles in the formation of cancer stem cells and in the development of tumors.

The exciting new findings in this field were made possible mainly through the development of novel techniques such as high-speed cell sorting and by the identification of specific cell surface markers. This allowed the purification of the very rare cancer stem cells present in

tumors (often less than 1%). Some of the markers are shared by cancer stem cells of various origins, but others are specific for the tumor type. The establishment of culture conditions appropriate for maintaining the stem cell phenotype will be instrumental in the study of cancer stem cells.

Importantly, cancer stem cells have properties very different from those of the rest of the tumor cell population. They divide much more slowly, which allows them to escape from traditional radio- and chemotherapies that hit fast-multiplying cells. Also, they have very efficient systems to pump out drugs, making them highly resistant to most conventional therapies. Current treatments might therefore only hit the bulk of the tumor but spare cancer stem cells, thus leading to recurrence and metastasis.

Both the origin and the precise impact of cancer stem cells on tumor pathogenesis are still debated. Normal stem cells may over time accumulate genetic and epigenetic changes that disturb the control of self-renewal. An arrest of progenitor cell differentiation and the recovery of unlimited proliferation properties may also be responsible for the initiation and progress of cancer.

On the other hand, some experts in the field consider cancer stem cells to represent the bad seeds of tumors and suggest that eliminating them has the potential to eradicate the disease. The targeting of cancer stem cells, however, represents a shift in focus and will probably require the identification of novel drugs. This is an enormous challenge because of the paucity of cancer stem cells, the technical difficulties of keeping them in culture, and their unusual drug resistance. However, the identification of proliferation and differentiation pathways that are active in cancer stem cells but not in normal, differentiated cells may offer interesting new opportunities for selective therapies.

The Cancer Stem Cell Workshop was organized to discuss recent advances and controversies in this fast-moving research area. We have tried to bring together many of the internationally highly recognized experts in this relatively young field who, through a variety of approaches, have made seminal contributions, thus leading to major strides forward. We are grateful to all of them for their excellent presentations and lively discussions, and also for their contributions to this book. We are convinced that the proceedings of the workshop will allow a better understanding

of the important role that cancer stem cells play in tumors and help in the future development of more effective and selective cancer treatments.

Finally, we would like to express our gratitude to the Ernst Schering Foundation for its generous support and perfect organization, which allowed us to hold this workshop under the best possible conditions. Our grateful thanks to the Berlin-Brandenburg Academy of Sciences and Humanities and to Prof. G. Stock for hosting the meeting on their premises.

Berlin, March 2007

Otmar D. Wiestler
Dominik Mumberg
Bernard Haendler

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