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Thematic Issue: Ion Channels and Cancer
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Foreword

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Introduction

Almost ten years ago, Wonderlin and Strobel summarized in their excellent topical review in the *Journal of Membrane Biology* the role of potassium channels in proliferation and G1 progression.[1] Since this illuminating review, there is an ever increasing number of studies reporting the role of a broad spectrum of ion channels in proliferation and carcinogenesis. This provides sufficient reason to devote a special issue of the *Journal of Membrane Biology* to the role of ion channels in cancer. The general hypothesis is easily conceivable: At some stage during development from a mutated cell to cancer, "pathological" ion channels are expressed, which are essential for or at least support tumor development (Fig. 1). After all, this is a relatively new field of research, which, however, has a large potential for future drug development and therapeutic intervention. This series of reviews and original articles gives an overview over the present knowledge and provides recent experimental results. In the first paper, Pardo and coworkers will discuss the role of voltage-gated potassium (Kv) channels in cancer. The group was among the first who discovered the importance of Kv channels for cancer development. They will focus on the role of ether à go-go (EAG) potassium channels and the related HERG channel in cell proliferation and development of cancer. Pardo and collaborators will discuss the possible mechanism by which these voltage-gated K^+ channels may affect cell proliferation. They also will present preliminary data on a new infrared technique, which allows the study of ion channel expression in vivo. Surprisingly, neuronal ion channels, such as voltage-gated K^+ channels, promote proliferation of non-excitable epithelial cells and support cancer growth. It will be interesting to learn in the second paper about the role of the N-methyl-D-aspartate (NMDA) receptor in human prostate cancer. Abdul and Hoosein will report that the NMDA receptor, which is well known for its contribution to proliferation of neuronal tissue and development of glioma and neuroblastoma, is also expressed in cancer tissues from prostate, breast and colon. Thus, their results demonstrate that yet another neuronal ion channel has a role in cancer.

Membrane ion channels belong to the basic equipment required by any cell to maintain cellular homeostasis and to survive the harsh conditions during proliferation and cell division. Fundamental cellular parameters are challenged during cell cycling, such as intracellular pH and Ca^{2+} signaling. It is well known that intracellular Ca^{2+} levels rise and fall during the cell cycle and previous work also discovered the importance of cytosolic pH in proliferating cells. In the fourth paper, Schreiber will update on Ca^{2+} signaling, intracellular pH and cell volume in cell proliferation. Regulatory volume decrease is essential to maintain proper cell volume and is due to parallel activation of Cl^- and K^+ channels. However, large inward Cl^- currents (Cl^- efflux out of the cell) induce cell shrinkage and induce programmed cell death, called apoptosis. The team of Okada will report that a volume-sensitive Cl^- current is activated by the common anti-cancer drug cisplatin, which leads to apoptotic volume decrease, activation of caspases, and apoptosis. Apoptosis will also be the topic of the contribution by Lang and coworkers, in which they compare cellular processes during apoptosis and proliferation. This review will focus on the role of K^+, Cl^- and Ca^{2+} channels in both processes and will illuminate common or distinct aspects of both.

This special issue will conclude with two further reviews on the role of ion channels in cancer. I will review the various channels that may be related to

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[1]Wonderlin, W. F., Strobl, J.S. 1996. Potassium channels, proliferation and G1 progression. *J. Membrane Biol.* **154**:91–107

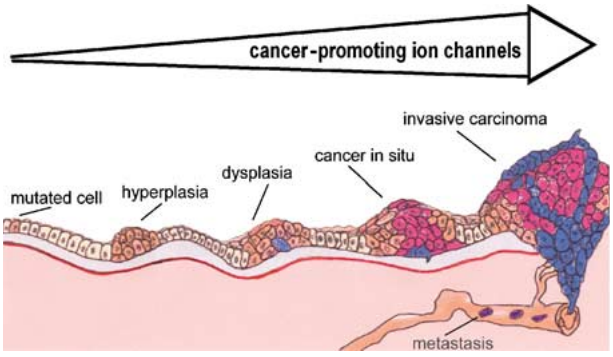

Fig. 1. Schematic drawing of the development of a single mutant cell towards an invasive cancer and a possible contribution of ion channels.

cancer and try to analyze the possible impact of these channels on essential cellular physiological parameters. The article by Schönherr reviews the topic from a more clinical point of view. Various types of cancer are analyzed in regard to their ion channel expression. Also the clinical relevance of these data is discussed, such as ion channel expression as new diagnostic parameter or as a target for a novel cancer therapy. Thus, this collection of papers presents an up-to-date overview of this new area of research. It may contribute to the understanding of the very complex process of tumor development and cancer growth. Therefore this issue should be of interest for a wider audience of cell physiologists, pharmacologists and medical doctors.