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Thematic Issue

Ion Channel Roles in Cell Death Induction

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Foreword

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Cell death occurs in both physiological and pathological conditions in response to a number of signals and stresses. Alterations in membrane transport can be not only the result of but also the cause of cell death. Some ion channels act as sensors or receptors for the cell death-related signals or stresses. Persistent cell shrinkage and swelling are major hallmarks of the early phase of apoptotic and necrotic cell death, respectively, as schematically depicted in Fig. 1. The early-phase shrinkage of cells undergoing apoptosis, termed apoptotic volume decrease (AVD), is accomplished by release of cell water driven mainly by efflux of K^+ and Cl^-, whereas the early-phase swelling of necrotic cells, termed necrotic volume increase (NVI), is induced by water uptake driven mainly by influx of Na^+ and Cl^-. Therefore, it appears that both AVD and NVI involve activities of a number of ion channels and/or transporters. On the other hand, it is well known that most animal cells after shrinkage and swelling exhibit volume regulation, called regulatory

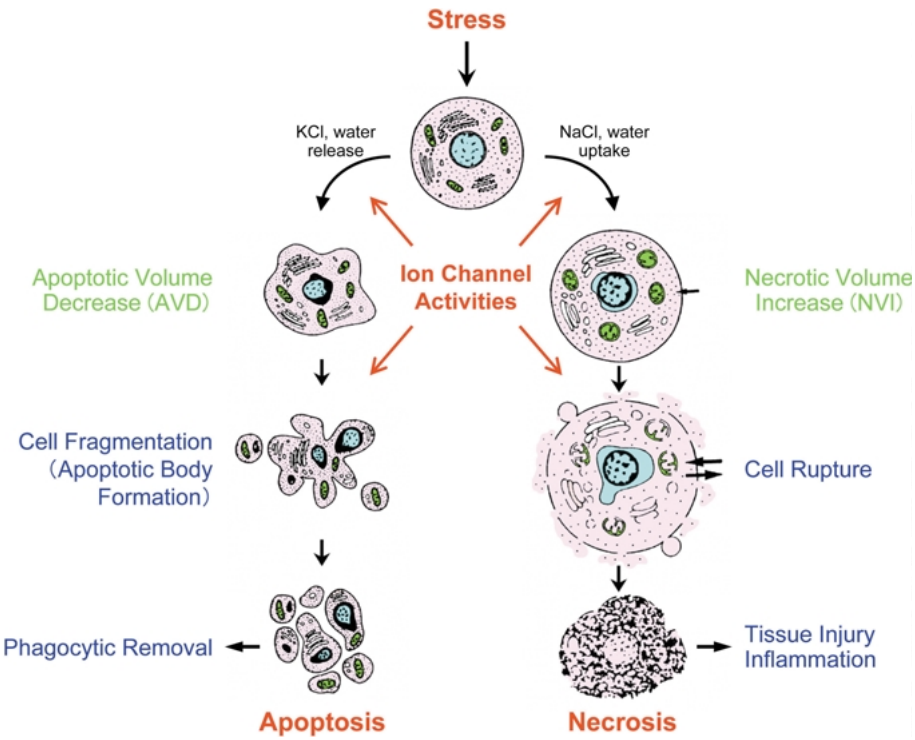

Fig. 1. Schematic illustration of the roles of ion channels and cell volume changes in cell death processes.

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volume increase (RVI) and regulatory volume decrease (RVD), respectively, in which a variety of ion channels and transporters are involved. Thus, it is likely that volume-regulatory activities of ion channels and transporters are impaired or disregulated during cell death processes. Altered membrane permeability plays a central role in cell death, and mitochondrial ion channels, too, are relevant to the regulation of apoptosis and necrosis. Thus, activation or inhibition of ion channels should be involved in multiple steps of the cell death process (Fig. 1). In fact, recent studies have demonstrated that altered activities of a variety of ion channels play roles in apoptotic, necrotic or ischemic cell death.

This special issue comprised of five review articles gives several representative examples of ion channel roles in cell death. I and my collaborators will review a prerequisite role of the volume-sensitive outwardly rectifying (VSOR) Cl^- channel in AVD and apoptotic cell death. The team of Cidlowski will report potential roles of electrogenic ion transport, including Na^+-permeable channels, and resultant membrane depolarization in apoptosis. The contribution by Yuan and coworkers will describe roles of different types of K^+ channels in controlling the different phases of apoptosis including AVD, cytochrome *c* release, caspase activation and DNA fragmentation. Miller will discuss roles of several members of the TRP channel family in oxidative stress-induced and anoxic cell death. Xiong et al. will report the role of acid-sensing ion channels (ASIC) in acidosis-mediated, glutamate receptor-independent, neuronal cell death under ischemic brain injury.

These studies as well as many other recent investigations have made it clear that animal cells co-opt ion channels and transporters that serve as cell survival machinery under ordinary conditions, to trigger and achieve the cell death events. Thus, a novel field of membrane biology of cell death is now wide open.