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Welcome Address

Cell death, the clinical way

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The concept that cells could commit suicide was first realized by Richard Lockshin, John Kerr, AR Currie and Andrew Wyllie about 35 years ago, and since then great headway has been made in understanding the molecular mechanisms behind cell death. Over a dozen caspases, 20 BCL2 family members and numerous regulatory proteins and adaptors have been identified. They have also been biochemically characterized and their function has been finely dissected. In several cases, pharmacological tools have been developed. However, as cell death is involved in many pathological processes, it is logical that the next phase in cell-death research will be its manipulation to treat disease. Indeed, translational research is ongoing in this area, and more efficient drugs are being developed to interfere with the process. To understand how these potential drugs could be used, we first need to elucidate the precise role of cell death in human diseases. For these reasons, we bring you the first translational issue of *Cell Death and Differentiation*.

In this, we focus particularly on four areas in which recent developments have been made – atherosclerosis, erythropoietin, bone remodelling and resistance to cancer therapy – and cover the subjects with a range of content types, from editorials to interviews and reviews to research.

Atherosclerosis and cancer are the two most significant causes of death in the Western world, and cell death plays an important role in both diseases. In atherosclerosis, the unfolded protein response is thought to trigger apoptosis in endothelial cells, which can initiate the process; however, it can also induce cell death of macrophages, which signals the final stage of plaque rupture. In cancer cells, the role of apoptosis is a little different, as most cancer therapies aim to activate an apoptotic response to kill the cells. Resistance to apoptosis, and hence therapy, is a hallmark of cancer, but strategies are being developed to circumvent this problem.

Erythropoietin was traditionally known as a cytokine that induced proliferation and differentiation of the haematopoietic system, but recent work has uncovered a new function for it as an anti-apoptotic factor. This role seems to be particularly important in the brain, so it could be used therapeutically for neuroprotection. Finally, the regulation of osteoclasts – involved in bone resorption – is discussed. Alterations in the balance between these cells and their counterparts, osteoblasts, can lead to diseases such as osteoporosis and osteopetrosis, so the mechanisms involved in their formation, function and survival are important to determine.

We hope to follow the success of this issue with other translational issues that both expand on the topics covered here and explore new ground, such as the role of apoptosis in diseases caused by retroviruses such as HIV and cardiovascular pathology. So do look out for these issues – we hope you enjoy them.