Preface

The idea of assembling a *Methods in Enzymology* book on cell death at first struck us as not very different from assembling a *Methods* book on Biology. There are so many aspects to cover and such a diversity of techniques that it seemed impossible to put together a manual of direct laboratory use such as one might do by offering a volume on, for instance, the isolation and study of mitochondria. After some reflection, we realized that the complexity was the point: it would be useful to compile a work that would, first, clearly define the types of cell death; second, indicate that not all forms of death were apoptosis; third, indicate the major means of documenting apoptosis; and fourth, explain how to document forms of cell death that are not apoptosis. In this manner we would provide a guide for the junior investigator and define criteria in a manner that would help readers recognize and avoid the confusion that exists in the literature because of the lack of clear definitions.

There are many means of organizing these overlapping topics. We have chosen to group the more biologic and general topics into the first volume, with the more clinical and specific topics in the second volume. A particular reader will find it useful to pick and choose information, perhaps in several chapters. Nevertheless, readers can expect to find in the first volume: comparisons of the characteristics of apoptosis, necrosis, autophagy, and other forms of cell death (Chapters 1, 12, 13, 19, and 20); means of studying the often unusual forms of cell death in nonmammalian organisms (Chapters 21 and 22); more general and commonly used methods for studying apoptosis in mammalian cells (Chapters 2, 3, 10); and means for studying specific events or components of apoptosis: The CD95 DISC (Chapter 4); the TNF receptosome (Chapter 5); the apoptosome (Chapter 6); and four types of enzymes active in apoptosis and other forms of cell death: caspases (Chapter 7); lysosomal cathepsins (Chapter 8); granzymes (Chapter 9); and nucleases (Chapter 11). In addition, we include discussions of the metabolic components of apoptosis such as mitochondrial membrane permeabilization (Chapter 14); oxidative lipidomics (Chapter 15); endoplasmic reticulum stress-induced apoptosis (Chapter 16); membrane scrambling (Chapter 17); and glucose metabolism (Chapter 18). In the second volume, readers can find chapters on studying apoptosis in different model systems (Chapters 1, 2, 3, 4, 5), investigation of several of the key promoters and signaling pathways that regulate programmed cell death (Chapters 6, 7, 8, 9, 10,11, and 21), analysis of several mechanisms by which apoptotic pathways are

regulated (Chapters 12, 13, 14), analysis of programmed cell death in different tissue and organ systems (Chapters 15, 16, and 17), methods for generation and analysis of death ligands (Chapters 18 and 19), methods for identifying caspase activity and substrates (Chapter 21), generation and analysis of BCL-2 stabilized peptides (Chapters 22 and 23), and, finally, methods for a genetic screening strategy that could be potentially be used in identifying novel factors regulating programmed cell death (Chapter 24).

Although each reader will undoubtedly identify particular items that he or she would have preferred to see, or a different order of presentation, we were very pleased that almost all of the contributors that we originally invited accepted our invitation and delivered to us manuscripts conforming to our goals. Thus, this work represents what we intended—a broad spectrum of approaches to apoptosis and programmed cell death by recognized leaders in their respective fields. Thus, we hope that it will contribute by serving as a guide and a means of helping researchers to ask the most meaningful questions and to design their experiments for the highest clarity.