Preface

Serpins comprise a family of proteins that has fascinated investigators for over 60 years. Besides highlighting the importance of the homeostatic regulation of proteolysis, serpin research has yielded precious insights into protein–protein interactions and protein conformational change, and the relationship between protein misfolding and disease. Further, the family contains striking examples of the use of a common protein fold for different biological purposes: besides protease inhibition, serpins are used as hormone precursors, hormone carriers, and protein folding chaperones. Insights into the flexibility of the serpin fold are pointing the way toward development of therapeutics that will ameliorate some common human afflictions.

At the time of writing, there are more than 1000 serpins, mostly appearing as predicted proteins derived from genome sequencing projects. The majority of these are anticipated to be protease inhibitors, based upon the presence of conserved motifs in the crucial reactive center loop region. It is, however, evident that serpins occur in all kingdoms of life and perform a wide array of evolutionary and biological roles (including important functions outside the inhibition of proteases). This diversity is reflected in the broad scope and multiple systems covered by chapters in these volumes. The challenge for the field is to elucidate the role of each particular serpin in its own niche, and this will typically require examination of structure, tissue distribution and cellular localization, identification of partners or targets, and assessment of physiological significance via forward or reverse genetics. Examples of these approaches will be found within these pages.

What then are the "big questions" or achievements remaining in serpin research? We would nominate (in no particular order) the precise physiological mechanism of serpin polymerization and associated cytotoxicity, the roles of noninhibitory serpins and the contribution of conformational change to their function, and the development of additional targeted antiserpin therapeutics. Finally, as we move into the era of the 1000 genomes project and the routine sequencing of human genomes for medical purposes, we expect that a greater number of serpin mutations will be associated with a wide range of human diseases. The next generation of serpin researchers will make great inroads into all these problems.

We acknowledge and thank all the authors for contributing chapters that neatly illustrate the state of play in our understanding of serpins and the cutting-edge approaches from a variety of disciplines that are being used to expand the frontiers of our knowledge. We hope that these

chapters in these two volumes will prove a very useful resource for both seasoned serpinologists and new hands.

In closing, we dedicate these volumes to our teachers, mentors, colleagues, and students, who continue to inspire us in our personal journeys of discovery.

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