Preface

An overarching challenge in the field of proteomics is the assignment of the molecular, cellular and physiological functions to the proteome - the entire compliment of proteins encoded by an organism's genome. As protein functions are governed by a vast array of post-translational modifications, methods to directly investigate native protein activity against a background of high biological complexity have been developed. At the forefront of these techniques is the use of small molecule probes that display selective interaction with active proteins, labelling them and allowing a fractionation of the proteome based on activity. This method, named Activity Based Protein Profiling (ABPP), is emerging as a mature discipline in the field of proteomics, and allows for the identification, classification and biochemical characterization of low abundance proteins that would otherwise remain undetected.

In this special volume of Topics of Current Chemistry, we have assembled review articles from various experts in the field of ABPP. Topics covered include the use of natural products and photoaffinity labels in ABPP, the use of metabolomic approaches for functional protein characterization and the use of ABPP in mapping microbial pathogenesis.

The first article by Nodwell and Sieber provides a general introduction, surveying analytical platforms for ABPP, enzymatic classes addressable by ABPP probes, and biological applications of ABPP.

The term "activity-based protein profiling" implies mechanism-based probe/target reactivity. Photoaffinity labelling approaches represent a complementary technique to mechanism based APBB probes. The use of these photoreactive "affinity-based protein profiling" probes in proteomic studies are reviewed by Overkleeft et al.

Natural products, by virtue of their co-evolution with protein systems, possess integrated biointeractvity. The unique properties of natural products render them ideal scaffolds for activity-based protein probes. Krysiak and Breinbauer cover the use of natural products in ABPP.

With the development of antibiotic resistant bacterial strains such as methicillin-resistant *Staphylococcus aureus* (MRSA), infectious diseases have become again a life-threatening problem, raising concerns of a return to a "pre-antibiotic" era. A key approach to arresting the spread of resistant bacteria is the understanding of pathogenesis. Heal and Tate focus on the use of ABPP to discovering and mapping pathways of pathogenesis in bacteria.

Many enzymes that are identified via ABPP are uncharacterized and many of them play crucial roles in pathogenesis. In order to understand the function of these enzymes in more detail their substrates have to be investigated via metabolomic procedures. Kim and Saghatelian highlight this important technology.

We, the volume editors, hope that this book will prove to be a helpful reference for students as well as the advanced researcher. We have attempted to provide a background to ABPP as well as review some of the more intriguing applications of this emerging technology. At the time of writing, this field is far from being comprehensively explored, and novel innovations and applications of ABPP will undoubtedly provide insight into protein function for many years to come.

Stephan Sieber and Matthew Nodwell