IAPSAP/MPSA 2008 Pehr Edman Awards

The 2008 IAPSAP/MPSA Pehr Edman Awards will be presented to Dr. Richard Perham, Department of Biochemistry, University of Cambridge, and to Dr. Ettore Appella, Laboratory of Cell Biology, National Cancer Institute, NIH. The awards are supported by Applied Biosystems and The Waters Corporation.

Dr. Richard Perham received his Ph.D. at the MRC Laboratory of Molecular Biology in Cambridge, in the laboratory of Drs. F. Sanger and J. I. Harris. He was a Helen Hay Whitney Fellow in Molecular Biophysics at Yale University with Professor F. Richards, before returning to Cambridge. He has been

an EMBO Fellow in the Max-Planck-Institut für Medizinische Forschung in Heidelberg, a visiting Professor at the University of New South Wales in Sydney, Australia, and a Fogarty International Scholar at the National Institutes of Health, Bethesda, Maryland, USA. Dr. Perham began his work at Cambridge on structural and mechanistic studies of glyceraldehyde 3-phosphate dehydrogenase. He and Ieuan Harris held the world record in the mid-1960s for determining the longest amino acid sequence (over 330 residues) of a protein, and they elucidated much of the mechanism associated with the thioester intermediate. In the late 1960s he uncovered the importance of charge-charge interaction between protein subunits in the self-assembly of tobacco mosaic virus capsids and later elucidated the novel mechanism of protein-DNA charge interaction that governs the assembly of filamentous bacteriophage virions. He introduced a number of important techniques in chemical modification of proteins, in particular based on reversible amidination and trifluoroacetylation of lysine residues. After some 30 years of effort, he and his colleagues have recently produced the first essentially complete description of the structure and assembly pathway of a multienzyme complex, the pyruvate dehydrogenase complex (molecular mass 10 MDa). In studying its dihydrolipoamide dehydrogenase component, he and his group were the first to demonstrate how to change the coenzyme specificity (NAD/NADP) and the kinetic mechanisms (ordered and allosteric) of an enzyme by rational mutagenesis and uncovered a new mechanism of active site cooperativity, distinct from allostery, that operates through a buried proton wire in the thiamine-dependent pyruvate decarboxylase. In parallel studies, he and his colleagues have demonstrated how to use filamentous bacteriophage capsids and the icosahedral cores of pyruvate dehydrogenase complexes as molecular scaffolds for the multiple display of foreign peptides and proteins, which has led to important insights on antigen recognition and the immune response in vaccine design.

Dr. Ettore Appella received his M.D. from the University Medical School, in Rome, Italy and then became a Research associate at Johns Hopkins University. After a post-doctoral fellowship at the Centre de Recherches sur les Macromolecules in Strasbourg, France, he began his research at the National Institutes of Health, in 1963. In 1979, he and his colleagues identified the p53 tumor suppressor protein, and they have continued p53 studies since that time. For more than 15 years they have contributed to deciphering the code through which posttranslational modifications to p53, including phosphorylations, acetylations, and methylations, modulate p53 activity and stability in response to cellular stresses including DNA damage induced by ionizing radiation, UV light, or chemical agents used in cancer chemotherapy. His recent work includes analysis of the functional effects of single or multiple knock-in mutations at sites of posttranslational modifications, especially in those tissues that show increased tumor development. In 1997, his group discovered a wild-type p53-induced phosphatase, Wip1 (PP2Cdelta or PPM1D), which functions as a negative regulator of the p38 MAP kinase- and ATM-p53 signaling pathways, essential for p53 activation. Another of his long time interests has been

the interaction between CD8+ T cells and their cellular targets. His group has focused on how the T cell receptor (TCR) of CTL interacts with class I molecules of the Major Histocompatibility Complex (MHC). Using a model system they have developed to examine cross-recognition of different MHC/peptide complexes by a single TCR, they have been probing the structural, functional, and biochemical features of ligand engagement.

The Pehr Edman Award is given to individuals whose efforts have significantly advanced the fields of protein chemistry, protein structure analysis, or proteomics. The award honors and commemorates the work of Pehr Edman, the Swedish chemist principally responsible for developing the chemistry for sequencing proteins by removing amino acids from the amino terminus one at a time. The Award is given in conjunction with Methods in Protein Structure Analysis (MPSA) meetings, which are sponsored by the International Association for Protein Structure Analysis and Proteomics (www.iapsap.bnl.gov).