

## Preface

Posttranslational modification of proteins is now recognized as a key means of functional regulation. In fact, protein phosphorylation can be regarded as one of the most critical mechanisms of modulating cell function. The enzymes that catalyze this process are known as protein kinases, and it goes without saying that this class of enzymes represents a very large and diverse family. The protein kinases thus play a role in countless physiological and pathological processes. One member of this large family of enzymes is the protein kinase CK2 (formerly known as casein kinase 2 which is not an accurate name since casein is not its physiological substrate). CK2 is a multi-functional protein kinase which plays a role in numerous functions including control of cell growth and proliferation, cell differentiation and cell survival. CK2 is a highly conserved and ubiquitous protein serine/threonine kinase, localized in the cytoplasmic and nuclear compartments where its multiple functional activities may occur in the cell. In accord with its localization to many distinct sub-cellular sites is the recognition of an extensive list of protein substrates localized in various compartments of the cell. Evidence continues to mount implicating CK2 in many cellular functions several of which highlight its critical role in transformation and tumorigenesis. Despite significant progress in our knowledge of CK2 many of its features remain intriguing.

Over the last decade, scientists interested in the subject of CK2 have made an effort to gather at specially organized international meetings held every 3 years to discuss the emerging developments in our understanding of the various aspects of CK2 such as its structure, regulation and functions. Three previous meetings on CK2 were held in Heidelberg, Germany (1994), Villard de Lans near Grenoble, France (1997), and San Esteban, Chile (2001). The Fourth International Meeting on this subject entitled “Protein Kinase CK2: From Structure to Function and Regulation” was held at the beautiful campus of the University of Western Ontario, London, Ontario, Canada, from July 29 to August 1, 2004. This meeting was a Symposium of the International Union of Biochemistry & Molecular Biology (IUBMB). Initially scheduled in conjunction with the International Congress of Biochemistry and Molecular Biology that was to be held in Toronto, Ontario, in 2003, the meeting was postponed until 2004 because of the unfortunate circumstances associated with the SARS outbreak. Status as a Symposium of the IUBMB was retained as was financial support from the IUBMB. The meeting in

London, Ontario, brought together most of the major investigators engaged in research in this area and followed a similar pattern as the previous meetings on CK2, with the goal of providing a venue to discuss the new progress on the subject. The present compilation of the papers is based on the presentations made at the various sessions of the meeting.

The overall organization of the meeting involved eight sessions for invited talks, followed by a general discussion at the end of the meeting, and a Poster Session for young investigators that was highlighted by a Young Investigator Poster Award from the *Biochemical Journal*. The following is a brief description of the talks in the various sessions highlighting the recent developments covering aspects of the structure, function and regulation of CK2.

The meeting was opened with a welcome address by the organizer of the meeting Dr. David W. Litchfield (London, Canada) who presented a historic evolution of the international meetings on CK2. Session I entitled “Historical Introduction and Emerging Views of CK2” chaired by David Litchfield (London, Canada) opened with a talk by Lorenzo Pinna (Padova, Italy) discussing the historical development of CK2 during the past 50 years. The second talk, by Karsten Niefind (Cologne, Germany), presented a detailed discussion of the current understanding of CK2 based on detailed examination at the atomic level of its crystal structures. The third talk in the session was by Odile Filhol (Grenoble, France) who presented elegant studies highlighting the dynamic nature of the CK2 subunits in the living cells, a feature that may participate in the still enigmatic control of this protein kinase.

Session II, chaired by Lorenzo Pinna (Padova, Italy), was dedicated to “Structure/function Analysis of CK2”. In this session, Flavio Meggio (Padova, Italy) gave a talk on the role of autophosphorylation of the  $\beta$  subunit of CK2 holoenzyme as probe of the supramolecular structure. This was followed by a talk by Claude Cochet (Grenoble, France) discussing the structure and function of the CK2 $\beta$  regulatory subunit. The final talk in this session was by Brigitte Boldyreff (Odense, Denmark) presenting studies on characterization of the essential nature of the CK2 $\beta$  subunit on the basis of CK2 $\beta$  gene disruptions in embryonic stem cells and in mice.

Session III, chaired by Khalil Ahmed (Minneapolis, USA) dealt with “Physiological Targets of CK2”. In this session, the presentation by Jorge Allende (Santiago, Chile) recounted the current studies on CK2 functions under investigation in his

laboratory. The second talk by Miwako Homma (Fukushima, Japan) focused on the intriguing observations on the regulatory role of CK2 during progression of cell cycle. The final talk in the session was by Emilio Itarte (Barcelona, Spain) analyzing the function of CK2 in the activity of eukaryotic translation initiation factor eIF2 $\beta$  subunit.

Session IV, chaired by Olaf-George Issinger (Odense, Denmark) dealt with the theme of "CK2 in Cancer and Prospects for Therapy". In this session, the first talk presented by David Seldin (Boston, USA) linked CK2 and Wnt signaling to tumorigenesis. The second talk was by Lorenzo Pinna (Padova, Italy) that described the design of CK2 inhibitors and discussed their potential usefulness in cancer therapy. This theme was continued in the third talk in the session presented by Khalil Ahmed (Minneapolis, USA) describing the induction of potent apoptosis by molecular downregulation of CK2 in xenograft models of cancer. An interesting feature was the observation that the normal cells compared with cancer cells appeared to be somewhat resistant to the effects of antisense CK2 $\alpha$  oligonucleotides which suggested the feasibility of targeting CK2 signal for cancer therapy. The final talk in the session by David Meek (Dundee, UK) was focused on a discussion on aspects of regulation of p53 by CK2.

Session V, chaired by Claude Cochet (Grenoble, France), considered the "Regulatory Mechanisms Controlling CK2 Activity". The first talk presented by Walter Pyerin (representing Karin Ackermann) (Heidelberg, Germany) discussed the evidence showing that Ets family members are key regulators of human CK2 genes. The second talk by Katherine Lawson (Omaha, USA) provided additional evidence on the regulation of CK2 by polyamines. The final talk by David Litchfield (London, Canada) was devoted to the functional role of CK2 interacting proteins as modulators of its regulation.

Session VI, chaired by Claiborne Glover (Athens, USA), was entitled "CK2 in Model Systems and Development". In this session, Isabel Dominguez (Boston, USA) presented interesting data on the role of CK2 and Wnt signaling in dorsal axis formation in *Xenopus embryos*. Along the same lines, Ashok Bidwai (Morgantown, USA) discussed the mechanism of CK2-mediated regulation of eye development in *Drosophila*. The final talk by Ravi Allada (Evanston, USA) brought forth the intriguing data regarding the role of CK2 in circadian behavior that has emerged from elegant genetic and biochemical studies in *Drosophila*.

Session VII, chaired by David Seldin (Boston, USA) was on the topic of "CK2 in Conserved Physiological Processes". The first talk by Olaf-Georg Issinger (Odense, Denmark) presented new studies on the biochemical characterization of the

human homologues of the *andante* and *timekeeper* proteins of *Drosophila* with respect to CK2. Claiborne Glover (Athens, USA) presented a detailed discussion of the complex roles of CK2 that have emerged from genetic and biochemical studies in *Saccharomyces cerevisiae*. The final talk by Yoshihiko Miyata (Kyoto, Japan) implicated CK2 in phosphorylation of Cdc37 thereby controlling multiple signaling kinases.

Session VIII, chaired by Jorge Allende (Santiago, Chile) was devoted to "CK2 in Cell Cycle Control and Apoptosis". The first talk by Mathias Montenarh (Homburg/Saar, Germany) recounted the role of CK2 in life and death decisions in the cells. Walter Pyerin (Heidelberg, Germany) discussed the role of CK2 in gene control at cell cycle entry. The final talk of the session by Khalil Ahmed (Minneapolis, USA) discussed the new data showing that CK2 can suppress the receptor-mediated apoptosis. These studies expanded on the previous observations in this laboratory, and brought forth the notion that CK2, besides its function in cell growth and proliferation, may also have a global role as a suppressor of apoptosis.

The meeting ended with a brief general discussion and a general feeling of satisfaction on the excellence and success of the meeting. The 23 papers in this *Focused Issue* of the *Molecular and Cellular Biochemistry* are based on the materials presented by the authors at the meeting. We believe they provide a view of the latest progress on protein kinase CK2. To that end, we express our sincere gratitude to all the participants in the meeting for their efforts.

The major credit for the organization of the meeting goes to David W. Litchfield and his laboratory at the University of Western Ontario (particularly Melanie Bailey, Ashley Bibby, David Canton, James Duncan, Mary Ellen Olsten, Jane Weber, Victoria Wraw and Piotr Zien) as well as Aneta Zien. The meeting was generously sponsored by The International Union of Biochemistry and Molecular Biology (Symposium and Interest Group Committee), The University of Western Ontario (Office of the Vice President (Research), Faculty of Medicine and Dentistry, and Department of Biochemistry), GE Healthcare (Amersham Biosciences Division), and *Biochemical Journal* (Sponsorship of the Biochemical Journal Young Investigator Award). We are deeply appreciative of their support for making possible the Fourth International Meeting on CK2.

Guest Editor: Khalil Ahmed, Minneapolis, USA  
 Guest Co-editors: Claude Cochet, Grenoble, France  
 Olaf-Georg Issinger, Odense, Denmark  
 David W. Litchfield, London, Canada