ACCADEMIA NAZIONALE DEI LINCEI

FONDAZIONE «GUIDO DONEGANI»

PROTEIN STRUCTURE AND DYNAMICS

1-3 DICEMBRE 2010

COMITATO ORDINATORE

IVANO BERTINI (I), MAURIZIO BRUNORI (I), WILLIAM A. EATON (USA), GIOVANNI GIACOMETTI (I), HARRY B. GRAY (USA)

COMITATO ORGANIZZATORE

MAURIZIO BRUNORI (I), STEFANO GIANNI (I), CARLO TRAVAGLINI-ALLOCATELLI (I), BEATRICE VALLONE (I) (Dipartimento di Scienze Biochimiche, Sapienza Università di Roma)

Il Convegno è stato organizzato con il contributo di: Società Italiana di Biochimica e Biologia Molecolare, Istituto Pasteur - Fondazione Cenci Bolognetti, Roma

In February 1960, when the 3D structure of myoglobin and hemoglobin was solved, J. C. Kendrew and M. F. Perutz allegedly said that "looking into the structure was like seeing for the first time ever a new world". Their discovery opened new perspectives on fundamental aspects of protein science. The availability of many genomes has been capitalized by progress in computational methods to predict the 3D structure of a protein from its amino acid sequence. At the same time, it became clear that (i) the total number of functionally competent proteins is far greater than what presumed from the number of genes, because epigenetic events lead to a multiplication of structures and functions; (ii) proteins are dynamic objects that populate a number of inter-converting conformational states, exploring a dynamic range extending from picoseconds to seconds and above; (iii) an unexpected fraction of proteins exists in the cell in a partially unfolded, inherently disordered state, adding a new dimension to the multiplicity of structures and revealing a link between protein folding and the *repertoire* of states involved in functional control and molecular recognition.

Given the huge complexity of the protein universe, we badly need novel informative experimental results and theoretical understanding. The concepts of general significance to unveil the essentials of such a complex ensemble of structures and functions need to be carefully scrutinized and confronted with experiments on paradigmatic models. The aim of this meeting is to discuss in depth structures and dynamics of proteins, and whenever possible their significance for physiopathology.

Wednesday December 1st, 15 to 19

FOLDING AND BINDING

The emergence of the function of a protein along its folding pathway is an important and challenging issue. Understanding folding pathways has improved considerably over the last ten years, attention being focused on the structure of folding intermediates and transition states. Moreover the nature of the denatured state, the role of inherently disordered domains in native proteins and their significance for medicine have acquired relevance to patho-physiology.

Chair: MIKAEL OLIVEBERG (SE) and CARLO TRAVAGLINI-ALLOCATELLI (I)

Introduction by M. OLIVEBERG (SE)

JOEL L. SUSSMAN (IL): *Function and structure of inherently disordered proteins*
ALAN R. FERSHT (UK): *Ultra-fast folding of homeodomains on a rough energy landscape*
PHILIP N. BRYAN (USA): *A minimal folding code for switching protein structure and function*
STEFANO GIANNI (I): *The folding problem simplified: protein families, circular permutants and heteromorphic pairs*

Thursday December 2nd, 8.30 to 13

DYNAMICS AND COMPLEXITY OF THE CONFORMATIONAL LANDSCAPE

Advances in the field of protein dynamics led to the concept of energy landscape postulating a multiplicity of conformational states accessible to a protein; the experimental results by transient spectroscopy, time-resolved Laue crystallography and molecular dynamics simulations have been illuminating. Where do we move from here, and what are the most challenging aspects to tackle?

Chair: HANS FRAUENFELDER (USA) AND MICHELE VENDRUSCOLO (UK)
Introduction by H. FRAUENFELDER (USA)

PETER G. WOLYNES (USA): *Energy Landscapes and Free Energy Spectra: the Overlap of Folding and Function*
PHILIP A. ANFINRUD (USA): *Watching proteins function with 100-ps time-resolved x-ray diffraction and solution scattering*
PAOLO CARLONI (I): *Targeting protein flexibility with metadynamics*
CLAUDIO LUCHINAT (I): *Exploring the conformational space of flexible multi-domain proteins*
MARTINO BOLOGNESI (I): *Recognition of the CCAAT box by the histone-like NF-Y heterotrimeric transcription factor*

Thursday December 2nd, 15 to 18.30

SINGLE MOLECULE BIOPHYSICS

The importance of investigating complex biochemical reactions by following events in single molecules cannot be overemphasized. Intriguing results on catalysis, folding and recognition have been reported; the technologies are quickly improving, but pitfalls and potentialities are hidden in the details. Nevertheless this experimental approach is so promising that an in-depth discussion devoted to this theme seems in order.

Chair: JANE CLARKE (UK) AND GIOVANNI GIACOMETTI (I)

Introduction by J. CLARKE (UK)

XIAOLIANG SUNNEY XIE (USA): *Single molecule enzymology*
WILLIAM A. EATON (USA): *Watching single protein molecules fold and unfold using FRET*
General discussion

Friday December 3rd, 8.30 to 13

METALLOPROTEINS IN HOMEOSTASIS AND ELECTRON TRANSFER

In view of their interest for pathology and bioenergetics, the role of metals as cofactors is nowadays tackled by a proteomic approach of metalloproteins comparing structure and dynamics, *in vitro* and *in vivo*. Principles of electron transfer and theoretical approaches, based on structural analysis of productive pathways, are a framework for application of general concepts to complex membrane proteins and their regulation.

Chair: MICHAEL T. WILSON (UK) and IVANO BERTINI (I)

Introduction by M. T. WILSON (UK)

THOMAS V. O'HALLORAN (USA): *Transition metal-receptor interactions in control of inorganic physiology*
LUCIA BANCI (I): *Maturation of proteins essential for cytochrome c oxidase assembly and copper incorporation*
HARRY B. GRAY (USA): *Electron flow through proteins*
SERGIO PAPA (I): *Cooperative coupling in mitochondrial protonmotive respiratory chain complexes*

Friday December 3rd, 15 to 18.30

CELLULAR STRUCTURAL BIOLOGY

Of primary interest for cellular regulation is the knowledge of the structure of large multi-component assemblies. These huge multi-protein complexes have been tackled by molecular biology, crystallography, NMR, electron-microscopy, mass-spectroscopy and sophisticated computational methods. The goal is to unveil a path to understand the control of integrated functions and the emergence of general concepts governing stability and dynamics of these huge machines.

Chair: MAURIZIO BRUNORI (I) and BEATRICE VALLONE (I)

JEAN-PIERRE CHANGEUX (F): *Structure and dynamics of nicotinic receptors channel gating and its allosteric modulations*
CAROL V. ROBINSON (UK): *Mass spectrometry of protein complexes - A new phase for structural biology*
PETER B. MOORE (USA): *And yet it moves: Ribosomal structure, dynamics and function*
DAVID I. STUART (UK): *pending*

La REGISTRAZIONE è obbligatoria:
http://arianna.bio.uniroma1.it/folding

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Fino alle ore 10 è possibile l'accesso per le automobili da Lungotevere della Farnesina, 10