

PREFACE FOR THE SPECIAL ISSUE OF THE *IUBMB LIFE* JOURNAL ENTITLED:

BIOINTERACTOMICS

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Communication is instrumental for complex organizations, from human societies to living cells. In the latter context, communication is established through biomolecules that physically and specifically contact each other to transmit messages in an efficient way.

A comprehensive characterization of complex molecular interacting networks between all molecules within a cell provides a framework for understanding biological systems as a whole. Binding events between macromolecules are acutely orchestrated to sustain the life-death balance. The systematic screening of specific molecular recognition patterns between macromolecules (such as protein–protein, protein–nucleic acid, protein–carbohydrate, protein–membranes, and protein–metabolite) will, therefore, expand knowledge of mechanisms underlying biological functions; and the generated knowledge will enable the development and design of novel drugs that may prevent cellular dysfunctions or the onset of illnesses.

Unveiling the complete set of interconnected biomolecules and its implications for a given organism is the goal of Biointeractomics, which is a fusion science of biology, informatics and engineering to determine molecular and cellular level interactions. This emerging supradisciplinary field relies on a combination of experimental and computational approaches to find evidence of interactions, and benefits from the biophysical and atomic details, allowing the assessment of their functional relevance. Compilations of high-throughput methods — mainly based on Yeast-Two-Hybrid assays and Affinity Chromatography coupled to Mass Spectrometry techniques — shed valuable

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3 light on the complexity of biointeractomes, although still produce high rates of false
4 positives and miss potential contacts. Independent orthogonal low-through put and high-
5 resolution interaction methods — such as Isothermal Titration Calorimetry, Surface
6 Plasmon Resonance and X-ray/NMR techniques — are required to complement and
7 verify all interacting pairs obtained from previous screens. At that point, differentiation
8 between sets of biomolecules pairs that can interact (biophysical interactions) and do
9 interact (biological interactions), because they are present within the same subcellular
10 compartment at the same time, is only possible by means of a multidisciplinary
11 methodology. Novel approaches include these available structural features about binding
12 surfaces and evolutionary conservation in large-scale computational assays, with which
13 predict interacting partners and assemble reliable biointeractome scaffolds.
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25 The global picture becomes even more complicated for macromolecules having
26 multiple functions and multiple interacting partners, named moonlighting counterparts,
27 so determining the whole biointeractome maps may be elusive. For those protein-
28 involving interactions, post-translational modifications can drastically alter the binding
29 network and, therefore, regulate cell signaling mechanisms which, in turn, form the so-
30 called signalosome. This suggests that the biointeractome is inherently plastic and that it
31 evolves during cell lifespan and strongly varies from cell to cell.
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39 If genome sequencing contributed the starting material to perform global analyses
40 of structures and dynamics of networks where gene products mediate their function, the
41 recent Encyclopedia of DNA Elements (ENCODE) project, which provides a detailed map of
42 additional functional non-coding units in the human genome, opens new insights into the
43 transcriptional biointeractome that controls gene regulation mechanisms. ENCODE offers
44 a novel roadmap in the Biointeractomics field, uncovering both the magnitude of the task
45 ahead as well as the potential roadblocks on the way.
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55 Keeping this in mind, this Mini-theme Issue of *IUBMB Life* Journal, entitled
56 “Biointeractomics”, aims to bring together the most exciting research from top scientists
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3 in the this emerging field. All of them are invited speakers at the *International Symposium*
4 *on Biointeractomics* (Seville, 2012) held under the auspice of the Ramon Areces
5 Foundation. Being impossible to cover all aspects of "Biointeractomics" into a single
6 volume, we sincerely hope that the selection of themes herein presented will help IUBMB
7 Life readers learn the state-of-the-art and the exciting and fast development of current
8 research in biosciences.
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18 manuscripts for their helpful criticisms and comments, as well as to the Editorial Office of
19 IUBMB Life for their excellent technical assistance and support.
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