Why the CBI Society Organized This Meeting?

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History of the CBI Society and new wave

The Chem-Bio Informatics (CBI) Society, initially named the CBI Association, was established in 1981 to "support the research and develop of an informational and computing environment for researching useful materials and using them safely." On the basis of this mission, the Society has focused not only on the traditional natural science fields of Physics, Chemistry, Biology, Pharmacology, Toxicology, and Medicine, but also on such interdisciplinary fields as Information Technology (IT), Computer Science, Artificial Intelligence (AI), and Bioinformatics. During the past 27 years, the Society has sponsored more than three hundred meetings including lectures, seminars, and symposia on chemical computing, chemical informatics, bioinformatics, biological computing, and drug discovery.

Completion of the Human Genome Project, however, followed by rapid advances of its associated -omics and other related technologies are forcing us to reform the scope and structure of the Society. The eventual goal of this reformation is to accelerate medical and pharmaceutical research and catalyze collaborations between basic (bench) researchers and clinical (bedside) researchers by focusing on informational and computing methodologies. The Society is presently interested in the following areas of interest: (1) Molecular Computing, (2) Molecular Recognition, (3) Bioinformatics and Bio Computing, (4) Genome Wide Experimental Data Analysis, (5) Information and Computing Infrastructure for Drug Design and Toxicology, (6) Disease Mechanisms and Control Models, and (7) Emerging New Technologies. Areas (4) and (6) have been added in keeping with our reformation.

Pathway/Network to Disease and Drug Discovery

In the history of the Society, structure-based or rational drug design has always been the holy grail of the society members. This goal is unchanged, but targeted gene/protein-based drug design should be extended to also target pathway-based drug design. Such an approach had already been proposed to the CBI Society in the mid 1990s by one of the authors [1]. In this so-called post genomic era, understanding diseases and discovering new drugs from pathways and networks have become emerging key concepts in the biomedical and pharmaceutical sciences [2]. Mechanisms of diseases are being reinterpreted in molecular, i.e., genome-omics-pathway/network, language. Already many graduate level standard textbooks have been revised or written adapting to such a change [3], [4]. Yet our present pathway/network knowledge is largely limited to the level of single cells. It is still very difficult to describe tissue models in pathway/network language. The task becomes formidable if one wants to describe physiological phenomena at the same resolution by using the same language. Many of the so-called multi-scale models and physiological pathway/network models so far proposed are anecdotal and episodic. At these levels, the spirit of omics, whereby all possible cases are listed and counted, can not be applied in a straightforward manner. Here the effective role of computers is not for computing in a mathematical sense but for handling and processing scattered data and knowledge for

experts to interpret more meaningfully. Here, it may be useful to consider so-called knowledge engineering, which first arose for modeling human expert judgmental processes such as the diagnosis of certain diseases, in the early 1980s in the medical informatics field [5].

Emerging New Strategy

The key for approaching the above complex problem domains is not to fit uniform models or frames but to assemble and integrate many tools, models, and resources in parallel. In fact, the focusing of a wide range of informatics and computing resources and manpower on a particular area in biomedical research seems to be an emerging strategy for combating such important health problems as cancer. The NIH-supported caBIG™ (https://cabig.nci.nih.gov/) is one such example. Quite independently, one of the authors has proposed that the CBI Society approach the study of nuclear receptors and the "metabolic syndrome" by assembling and integrating the appropriate informatics and computational resources and workforce [6].

Informatics and Computing in Nuclear Receptor and Metabolic Syndrome Research

Nuclear receptors and the metabolic syndrome, or so-called life-style related diseases, are two of the most important and rapidly advancing interdisciplinary biomedical research areas, where not only experimental methods but also informatics and computing methods are essential. Some of these research areas are as follows:

1. Identification of candidate genes for Metabolic Syndrome and related diseases
2. Computational chemistry for selective nuclear receptor modulators (SNRM)
3. Comparative genomics for nuclear receptors, their cofactors, and their target genes
4. Identification of all the target genes of nuclear receptors
5. Comprehensive network of nuclear receptors and their related transcription factors, their target genes, and their product proteins.
6. Models for digital physiology: Pathway/network to disease
   - ・Data and knowledge base for adipocytes
   - ・Insulin/IGF receptor pathways and Longevity pathway
   - ・Pathway/network for food intake control
7. Metabolic process models of the liver
8. Insulin secretion models of pancreatic beta cells
9. Knowledge engineering for elucidating complex experimental data and biomedical expertise
10. Infrastructure for network-linked research community.

Many of these are new challenges for both wet-bench researchers and theoretical and computational specialists. For example, regarding the fourth problem, the identification of all target genes of nuclear receptors, implies the problem of predicting promoter regions of the nuclear receptors and related transcriptional factors. Both ChIP-on-Chip technology and computational technology have been used to approach this problem, which is one of the most important genomic problems in the post-genomic era. Identification of a pathway/network for a specific physiological or patho-physiological phenomenon is another example where wet-bench researchers and computer-oriented researchers must collaborate closely. Undoubtedly there are many new uncultivated yet attractive research themes for chemical computing, chemical informatics, bioinformatics, and biological computing.

In the case of nuclear receptors, for example, there have been efforts were make relevant data and information available on the Internet. A few of such sources are listed below.

・NURSA (http://www.nursa.org/index.cfm)
・NucleaRDB (http://www.receptors.org/NR/)
・NuReBase (http://www.ens-lyon.fr/LBMC/laudet/nurebase/nurebase.html)
・NRR (http://nrr.georgetown.edu/nrr/nrr1.html.)

Unfortunately, except for NURSA these sites have not been updated regularly, and there are not so many links from these sites to Metabolic Syndrome and other related disease sites.

New Style of Collaboration

When the human genome project was attaining its goal, C. Leo and others wrote in their paper published in Endocrine Reviews [7], "・・・In this way, new metapatterns can be discovered, and pathways spanning the scope of different methods can be understood ranging from regulatory DNA sequences to gene transcript expression to protein function." They continued, "This phase relies heavily on collaboration within the biomedical community because no single laboratory is likely to have the expertise, time, and resources to generate such large datasets using different high-throughput methods. This transition of hormonal research from a single laboratory approach to an integrated community effort will pose an important challenge for the next generation of endocrine researchers." Now The Endocrine Society of America has a unique partnership with the NURSA project, in that some articles of the Endocrine Society's journal, Molecular Endocrinology and NURSA's Molecule Pages are hyperlinked to each other.

Web Portal as an Infrastructure

Since smooth and active communication among researchers in different fields may be the key for such collaborations, we are providing an Internet portal for that purpose. This infrastructure portal is designed to share the rich resources of informatics and computing research that are relevant to researchers in experimental and clinical fields, facilitate the entry of researchers in informatics and computing into fields of nuclear receptors and Metabolic Syndrome research, and offer opportunities for researchers of both fields to collaborate and exchange ideas. Although at present the text is only in Japanese, the prototype pages are nearly completed and are put onto one of the CBI Society's Internet web servers [8]. We intend to extend this portal to provide (1) computational chemistry environments for docking studies on selective nuclear receptor modulators (SNRMs), and (2) a knowledge environment on the key pathways and network models of MS and related diseases. The participation of wet and clinical researchers is the key to success of this project. We are also intending to provide such tools as blogs and wikis for more active collaborations [9], [10].

Next Goal

This meeting is a rare opportunity for informatics and computational specialists who are interested in biomedicine and drug discovery to meet with cutting-edge wet research scientists on the topics of nuclear receptors, metabolic syndrome, and related diseases. Conversely there may be chances for wet researchers to encounter theoretical or computational specialists who are interested in collaborating with wet researchers. Our hope is that the meeting should not be a goal but rather a new start for the

CBI Society to serve as the catalyst for a new style of collaboration between wet and dry researchers in biomedicine. In the near future, such an approach will be extended to include other vitally important health problems such as cancer, depression, neurodegenerative diseases, and immune diseases.

References

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