The chemogenomics grand challenge

The Chemogenomics Laboratory, Research Unit on Biomedical Informatics, IMIM…

In recent years, the implementation of important technological advances in chemistry and pharmacology, both in academia and industry, has dramatically increased our capacity for synthesising molecules and testing them in biochemical assays. The result has been a significant rise in the number of biological activity data being generated and made available for a growing amount of molecules. However, we are still far from fully mapping the chemical space on the human proteome. In this respect, one of the greatest challenges in chemical biology for the coming decades will be to identify a small molecule modulator for all potential human protein targets.

The completion of this 'human chemome' would ideally require global co-ordinated efforts to assemble chemical libraries containing millions of compounds and their systematic screening of a panel of thousands of targets. However, even in the utopic scenario of putting together such an initiative, achieving a decent level of completeness would still not be realistic experimentally. The chemical space would always be too vast to be covered extensively. The current ability to construct virtual chemical libraries containing hundreds of millions of compounds and to develop in silico pharmacology methods able to profile those compounds on thousands of protein targets emerge as strategic alternatives to focus experimental campaigns on the most promising regions of chemical space.

It was this vision that led to the creation of the Chemogenomics Laboratory in September 2003, with the help of Dr Jordi Mestres of the Municipal Institute of Medical Research (IMIM), who had seven years' experience in the pharmaceutical industry (one year at Pharmacia & Upjohn in Kalamazoo, the USA, and six years at Organon, first in Oss, the Netherlands, and then in Newhouse, Scotland, the UK). Today, it is an established laboratory in chemogenomics and molecular informatics, and has contributed over 25 articles published in internationally recognised journals in these fields.

Research at the Chemogenomics Laboratory (http://cgl.imim.es) is carried out at the interface between chemistry, biology, and informatics, which requires a multidisciplinary team of skilled individuals in the different areas. The ultimate aim is to develop and apply novel integrative biochemoinformatic tools for the systematic annotation of molecules to entire target families of therapeutic relevance. This information can then be used either upstream to identify chemical probes for target validation or downstream to identify novel hits for the generation of the drug discovery process.

Research Unit on Biomedical Informatics

The Chemogenomics Laboratory is part of the Research Unit on Biomedical Informatics (GRIB), one of the research units of the Municipal Institute of Medical Research (IMIM), a research institute appointed to the University Pompeu Fabra (UPF).

GRIB (http://grib.imim.es) brings together a team of about 80 scientists, as well as technical and management staff. GRIB has wide experience in the participation and co-ordination of research projects funded by the European Commission. In the last years, the unit has participated in more than 20 European projects, most of them funded by the European Commission. Seven of these projects, including the FP6 Network of Excellence on Biomedical Informatics INFOBIOMED, were co-ordinated by GRIB. It is also involved in many other research projects funded by national research funding agencies. Moreover, GRIB has a long tradition of collaboration with industry in R&D projects.

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GRIB is currently organised into seven laboratories: Computational Genomics, devoted to the computational analysis of genomic sequences and information, led by Mar Albà, Robert Castelo, Núria Lòpez-Bigas, and Eduardo Eyras; Complex Systems, focused on the understanding and modelling of the synthesis and evolution of complex biosystems, led by Ricard V Solé; Structural Bioinformatics, dedicated to the analysis and modelling of proteins and their interactions, led by Baldomero Oliva; Computational Biochemistry and Biophysics, interested in the development and

The impressive premises of the Barcelona Biomedical Research Park, right in front of the Barceloneta beach

use of modelling and simulation methods to understand biochemical and biophysical phenomena at the molecular and systemic levels, led by Jordi Villà-Freixa and Gianni de Fabritiis; Chemogenomics, dedicated to the development of novel integrative biochemoinformatic methods and its application to the annotation of large chemical libraries to entire protein families of therapeutic interest, led by Jordi Mestres; Computer-Assisted Drug Design, devoted to the development and application of computational methods oriented to the discovery and optimisation of new drugs, led by Manuel Pastor; and Integrative Biomedical Informatics, a singular group particularly dedicated to the generation and execution of research initiatives that aim at contributing to the development of projects connecting bioinformatics and medical informatics, led by Ferran Sanz.

Chemotargets S.L.

Chemotargets S.L. was created in March 2006 as a spin-off initiative from the Chemogenomics Laboratory under the auspices of the Municipal Institute of Medical Research (IMIM – Hospital del Mar). The company is currently located within the impressive new premises of the Barcelona Biomedical Research Park, right in front of Barceloneta beach, in an area that is called the 'San Diego of the Mediterranean'.

Chemotargets' core in silico pharmacology platform currently provides an affinity alert when profiling small molecules on 1,497 targets organised in the main protein families of therapeutic relevance, including 837 enzymes, 233 GPCRs, 198 ion channels and transporters, and 32 nuclear receptors. This platform is being exploited through collaboration agreements with drug discovery and chemical partners aiming at: designing chemical libraries directed to particular sets of disease related targets or entire protein families; identifying new chemical entities with customised affinity profiles (hit identification); and identifying potential off-targets at which compounds designed for a particular target may have residual affinity (target fishing).

The company has also developed proprietary software for the construction of medchem isosteric libraries around known bioactive ligands, which, when combined with target profiling, provide a unique means for synthesis planning as well as anticipating all protein targets worth considering in hit and lead optimisation programmes.

For further information on Chemotargets S.L., visit the website: www.chemotargets.com or email: infochemo@chemotargets.com.

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