



Press Release

FOR IMMEDIATE RELEASE

Cellzome Publishes Novel Approach For The Systematic Use Of Protein Interaction Maps In Drug Discovery In Nature

HEIDELBERG, Germany, January 10, 2002

Cellzome AG today announced the publication of a pioneering study in the proteomics field in the January 10 issue of the journal Nature describing the first draft of a functional map of the yeast proteome. The map visualizes an entire network of protein complexes and their interactions in yeast *Saccharomyces cerevisiae*, forming a basis for the operative organization underlying a cell's activity under different conditions, thereby making the map a first of its kind.

"These maps will enable researchers to more fully assess the roles of individual proteins in biology and provide for a more comprehensive approach in choosing targets for drug discovery," said Dr. Giulio Superti-Furga, Vice President of Biology of Cellzome. "By knowing the molecular context in which targets act, investigators can better predict the effect of drug candidates on the parameters that influence safety and efficacy, while protein interaction maps provide the framework on which to add data mined from the literature and from other experimental approaches. Taken together, this information can be used to improve the efficiency of the drug discovery process."

The paper entitled "Functional Organization of the Yeast Proteome by Systematic Analysis of Protein Complexes," appears on the cover of Nature (Vol. 415, No. 6868), and portrays a functional proteomic map for the yeast *Saccharomyces cerevisiae*, a commonly used eukaryotic model in pharmaceutical development. The map characterizes the function and interactions of 1,440 yeast proteins comprising 232 multi-protein assemblies, or complexes, which directly affect biological activity. An interdisciplinary team at Cellzome used a proprietary protein complex assembly and retrieval technology that was originally developed at the European Molecular Biology Laboratory (EMBL) to isolate multi-protein assemblies directly from cells under near physiological conditions.

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"After decades of deconstructing biological complexity through the process of creating catalogues of molecular biological information, the new aim is to reconstruct and integrate the information so as to uncover a real depiction of cellular behaviour," said Dr. Superti-Furga. "The yeast genome was sequenced in 1996, yet as many as half the genes still await functional assignment. Our goal was to decipher the functional architecture of the proteome so that gene function could be interpreted within the molecular environment of the corresponding gene product, and that the cellular processes can be understood in terms of the concerted action on molecular machines."

The team employed homologous recombination to individually modify 1,700 yeast genes within the genome with a molecular double-tag. The resulting proteins expressed by the gene could then be efficiently isolated using the tags successively as retrieval hooks. Because proteins form molecular assemblies with other proteins, retrieval of the tagged protein typically led to the recovery of a protein complex, comprising the interacting proteins. Expression under the control of the endogenous promoters guaranteed that the natural cellular physiology was largely maintained throughout the assembly and retrieval process. Matrix-assisted-laser-desorption-ionisation-time-of-flight mass spectrometry was used to identify the proteins and bioinformatics tools were developed to analyse the network. By applying Cellzome's bioinformatics tools, visualization of the yeast proteome at the protein complex level and then at the protein-protein level allows the navigation of the "proteome space" along functionally meaningful pathways. To encourage the widest use of this rich data set, Cellzome has made the data publicly available at <http://yeast.cellzome.com>

Benefits of Cellzome's approach include:

- Identifying novel entry points for drug discovery that are based on the in vivo isolation of molecular machines under various experimental conditions

- Providing a platform on which to load other data and information to power an in-silico based approach to experimental design
- Using differential assembly of complexes in the presence of drug candidate as the basis to anticipate safety and efficacy and optimise lead selection
- Building a comprehensive intellectual property estate based on complex composition, medical use, and methods for screening and identifying lead compounds
- Discovering novel proteins and their functions through the assessment of their interaction with known proteins

“Cellzome is going beyond conventional drug target discovery and is applying its technology to determine the precise physiological context of drug targets that will better direct our experimental efforts and decrease the risks associated with drug development,” said Dr. Charles Cohen, Chief Executive Officer of Cellzome. “We are currently using this approach with human cells to establish the molecular context involved in the onset and progression of various chronic degenerative diseases. The pharmaceutical expertise gained through our recently acquired facilities in the UK will enable us to rapidly transform this functional map into drug development programs.”

Cellzome's technology is a flexible platform that can be systematically applied to human samples. The high degree of similarity between yeast and human orthologous complexes suggest basic mechanisms that drive cellular function. By understanding the basic mechanisms underlying cellular function, and identifying and characterizing protein complexes that play a critical role, Cellzome's technology has the capability to effectively improve and speed the drug discovery process by focusing on the molecular targets that really matter.

About Cellzome

Cellzome AG, with laboratories and operations in Heidelberg, Germany and Elstree, just north of London, UK, is a biopharmaceutical company that uses its proprietary functional proteomics technology for target discovery, validation, and drug development. The Company was founded in May 2000 with a team of scientists from the European Molecular Biology Laboratory (EMBL), including pioneers in the fields of protein mass spectrometry, bioinformatics, structural biology and signal transduction. The company currently has 105 employees.

Learn more at www.cellzome.com