Chemical biology is a scientific discipline spanning the fields of chemistry and biology

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DESCRIPTION

Chemical biology is a scientific discipline spanning the fields of chemistry and biology. The discipline involves the application of chemical techniques, analysis, and often small molecules produced through synthetic chemistry, to the study and manipulation of biological systems. In contrast to biochemistry, which involves the study of the chemistry of biomolecules and regulation of biochemical pathways within and between cells, chemical biology deals with chemistry applied to biology (synthesis of biomolecules, simulation of biological systems etc.). Some forms of chemical biology attempt to answer biological questions by studying biological systems at the chemical level. In contrast to research using biochemistry, genetics, or molecular biology, where mutagenesis can provide a new version of the organism, cell, or biomolecule of interest, chemical biology probes systems *in vitro* and *in vivo* with small molecules that have been designed for a specific purpose or identified on the basis of biochemical or cell-based screening (see chemical genetics).Chemical biology is one of several interdisciplinary sciences that tend to differ from older, reductionist fields and whose goals are to achieve a description of scientific holism. Chemical biology has scientific, historical and philosophical roots in medicinal chemistry, supra molecular chemistry, bioorganic chemistry, pharmacology, genetics, biochemistry, and metabolic engineering.

ENRICHMENT TECHNIQUES FOR PROTEOMICS

Chemical biologists work to improve proteomics through the development of enrichment strategies, chemical affinity tags, and new probes. Samples for proteomics often contain many peptide sequences and the sequence of interest may be highly represented or of low abundance, which creates a barrier for their detection. Chemical biology methods can reduce sample complexity by selective enrichment using affinity chromatography. This involves targeting a peptide with a distinguishing feature like a biotin label or a post translational modification. Methods have been developed that include the use of antibodies, lectins to capture glycoproteins, and immobilized metal ions to capture phosphorylated peptides and enzyme substrates to capture select enzymes. Enzyme probes to investigate enzymatic activity as opposed to total protein, activity-based reagents have been developed to label the enzymatically active form of proteins (see Activity- based proteomics). For example, serine hydrolase- and cysteine protease- inhibitors have been converted to suicide inhibitors. This strategy enhances the ability to selectively analyze low abundance constituents through direct targeting. Enzyme activity can also be monitored through converted substrate. Identification of enzyme substrates is a problem of significant difficulty in proteomics and is vital to the understanding of signal transduction pathways in cells. A method that has been developed uses "analog-sensitive" kinases to label substrates using an unnatural ATP analog, facilitating visualization and identification through a unique handle. While DNA, RNA and proteins are all encoded at the genetic level, glycans (sugar polymers) are not encoded directly from the genome and fewer tools are available for their study. Glycobiology is therefore an area of active research for chemical biologists. For example, cells can be supplied. With synthetic variants of natural sugars to probe their function. Carolyn Bertozzi's research group has developed methods for site-specifically reacting molecules at the surface of cells *via* synthetic sugars. Chemical biologists used automated synthesis of diverse small molecule libraries in order to perform high-throughput analysis of biological processes. Such experiments may lead to discovery of small molecules with antibiotic or chemotherapeutic properties. These combinatorial chemistry approaches are identical to those employed in the discipline of pharmacology. Many research programs are also focused on employing natural biomolecules to perform biological tasks or to support a new chemical method. In this regard, chemical biology researchers have shown that DNA can serve as a template for synthetic chemistry, self-assembling proteins can serve as a structural scaffold for new materials, and RNA can be evolved *in vitro* to produce new catalytic function. Additionally, hetero bi-functional (two-sided) synthetic small molecules such as dimerizers or PROTACs bring two proteins together inside cells, which can synthetically induce important new biological functions such as targeted protein degradation. Chemical synthesis of proteins is a valuable tool in chemical biology as it allows for the introduction of non-natural amino acids as well as residue specific incorporation of "posttranslational modifications" such as phosphorylation, glycosylation, acetylation, and even ubiquitination. These capabilities are valuable for chemical biologists as non-natural amino acids can be used to probe and alter the functionality of proteins, while post translational modifications are widely known to regulate the structure and activity of proteins. Although strictly biological techniques have been developed to achieve these ends, the chemical synthesis of peptides often has a lower technical and practical barrier to obtaining small amounts of the desired protein. In order to make protein-sized polypeptide chains *via* the small peptide fragments made by synthesis, chemical biologists use the process of native chemical ligation. Native chemical ligation involves the coupling of a C-terminal thioester and an N-terminal cysteine residue, ultimately resulting in formation of a "native" amide bond. Other strategies that have been used for the ligation of peptide fragments using the acyl transfer chemistry first introduced protein ligation allows for the biotechnological installation of a C-terminal thioester using inteins, thereby allowing the appendage of a synthetic N-terminal peptide to the recombinant-produced C-terminal portion. Both sulfurization/desulfurization techniques and the use of removable thiol auxiliaries involve the installation of a synthetic thiol moiety to carry out the standard native chemical ligation chemistry, followed by removal of the auxiliary primary goal of protein engineering is the design of novel peptides or proteins with a desired structure and chemical activity. Because our knowledge of the relationship between primary sequence, structure, and function of proteins is limited, rational design of new proteins with engineered activities is extremely challenging. In directed evolution, repeated cycles of genetic diversification followed by a screening or selection process, can be used to mimic natural selection in the laboratory to design new proteins with a desired activity. Several methods exist for creating large libraries of sequence variants. Among the most widely used are subjecting DNA to UV radiation or chemical mutagens, error-prone PCR, degenerate codons, or recombination.

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