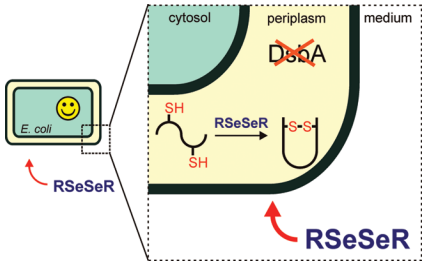
In this ISSUE

Selecting for Selenides

Formation of disulfide bonds is an important part of protein folding, and prokaryotic cells produce enzymes called oxidoreductases to help the process along. However, despite the presence of oxidoreductases in the bacterial periplasm, production of recombinant proteins often gets stuck at the protein folding stage. Agents capable of facilitating disulfide bond formation in such "folding-challenged" proteins could greatly improve the production of recombinant proteins with interesting biotechnological applications. Beld *et al.* (DOI: 10.1021/cb9002688) report that small-molecule diselenides are efficient catalysts for the conversion of dithiols to disulfides in the oxidative folding of diverse proteins.

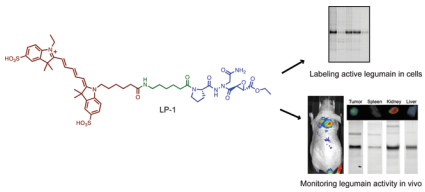
Using a redox sensor engineered into cells deficient in the oxidoreductase DsbA, numerous diselenides were screened for their ability to restore oxidative activity to the cells. The diselenide selenocystamine was found to facilitate the folding of diverse proteins, and the low concentrations needed suggest that it functions catalytically. The authors propose that numerous properties of selenocystamine, such as its efficient oxidation of thiols and rapid reoxidation by atmospheric oxygen, contribute to its protein-folding prowess.



A Closer Look at Legumain

Emerging evidence over the past decade has implicated a lysosomal cysteine protease known as asparaginyl endopeptidase, or legumain, in fundamental processes such as antigen presentation and matrix degradation, as well as in pathological conditions including cancer and atherosclerosis. Investigation of legumain function, however, has been hampered by the lack of potent small molecule probes that selectively target the enzyme. Now, Lee and Bogyo (DOI: 10.1021/cb900232a) report the design and activity of a new class of legumain inhibitors that enable imaging of legumain in normal and diseased tissue.

The legumain probes are built around an aza-asparagine epoxide group and function as irreversible inhibitors, forming a covalent bond in the active site of the enzyme. Incorporation of a fluorescent tag and cell-permeabilizing groups facilitated use of the probes for monitoring legumain activity in cells as well as in tumors in mice. These potent and selective compounds are valuable new tools for further investigation of legumain function in normal and pathological processes.



Sialic Acids: Challenging Chemistry, Intriguing Biology

Sialic acids are nine-carbon α-keto aldonic acids whose structural diversity has long challenged chemists and whose important roles in biological and pathological processes have long fascinated biologists. Chen and Varki (DOI: 10.1021/cb900266r) review the chemistry and biology of sialic acids, highlighting recent advances in synthetic, analytical, and bioengineering methods that have contributed to our understanding of these intriguing compounds.

The review touches on the numerous aspects of sialic acid chemistry and biology. Progress in our understanding of the chemistry of sialic acids, including characterization of the natural structural diversity both within sialic acid itself and as a component of larger glycoconjugates, chemical and chemoenzymatic approaches to their synthesis, and new analytical methods for their characterization, is reviewed. From a biological standpoint, a discussion of the production of sialic acid containing glycoconjugates, exploration of sialic acid binding receptors, and the development of sialoglycan arrays is provided. Together, the review illustrates the tremendous progress that research at the chemistry–biology interface has offered to this rich area of investigation.

Published online February 19, 2010 • 10.1021/cb1000235 CCC: $
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