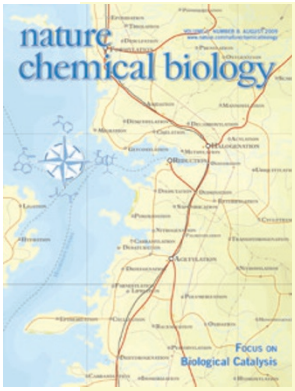


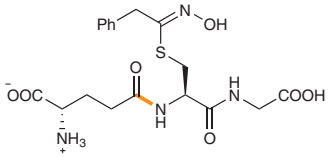
Focus on biological catalysis

Enzymes are central to cell biology, driving chemical reactions and regulating cellular conditions in response to a variety of external inputs. Now, increasing amounts of data and improved tools are yielding a wealth of information regarding these efficient machines. For example, newly sequenced genomes enable studies into biosynthetic and metabolic pathways [**Brief Communications, p. 575**], and integrating known pathways with new chemical measurements can provide unexpected insights into global cell metabolism [**Articles, p. 593**; **News & Views, p. 535**]. Genome sequences can also help to describe how enzymes are duplicated and evolve, either with the help of chaperones to stabilize protein function [**News & Views, p. 538**] or by optimizing promiscuous activities to detoxify anthropogenic compounds [**Reviews, p. 559**]. Along with this explosion of genome data, however, come new complications in organizing this information [**Commentaries, p. 521**].

Enzymes continue to provide inspiration in their ability to carry out complex chemical transformations. Cofactors in particular provide a rich source of mechanistic diversity, inspiring both discoveries of enzyme superfamilies and previously unknown classes of enzyme-catalyzed reactions [**Elements, p. 534**] and ongoing research on the sources and function of these natural products [**Meeting Report, p. 530**]. Exploitation and expansion of these reactions through enzyme engineering is leading to industrially relevant biocatalysts with improved or altered functions [**Reviews, p. 567**]. However, Kazlauskas and Bornscheuer argue that more rigorous analysis and comparison of current engineering methods are required for continued success in the field [**Commentaries, p. 526**].

Perhaps one limitation in creating novel catalysts is that we still do not fully understand how enzymes function. In this regard, Schwartz and Schramm propose that there is no stabilized transition state along the enzymatic reaction coordinate [**Perspectives, p. 551**], while Nagel and Klinman advocate that nuclear quantum tunneling must be included in our model for enzyme function [**Perspectives, p. 543**]. Both articles, however, highlight the importance of protein dynamics in catalysis. Indeed, new biochemical data about multisubunit and multidomain proteins are already blending our understanding of enzymology with that of protein assembly and dynamics [**Research Highlights, p. 540**]. Though many open questions remain, Zatalan and Herschlag remind us that basic chemical and physical principles can yield important insights into enzyme function [**Commentaries, p. 516**]. With so much yet to learn, we hope that this collection of articles encourages increased cross-talk between disciplines to inspire the next generation of enzyme research. *CG*

Searching for sulfur

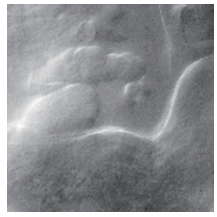


Glucosinolates, or amino acid–derived sulfated thioglucosides, are produced in vegetables and have been associated with cancer prevention. Use of these compounds, however, is limited by incomplete information about their biosynthesis, particularly as to how the reduced sulfur is incorporated. In an effort to increase access to these compounds, Geu-Flores *et al.* introduced five known biosynthetic genes for benzyl glucosinolate (BGLS) into *Nicotiana benthamiana*. Though some product was observed, the authors saw a preponderance of an expected intermediate in the pathway, suggestive of a metabolic roadblock. Further investigation revealed that GGP1, a putative glutamine amidotransferase, was the missing enzyme. Characterization of GGP1 confirmed that the enzyme hydrolyzed a γ-glutamyl peptide bond in the intermediate, a function previously described only for the γ-glutamyl transpeptidase family. The completion of this biosynthetic pathway and the successful synthesis of BGLS in this amenable host provide new opportunities to investigate and produce these interesting compounds. [**Brief Communications, p. 575**] *CG*

Chemical space branches out

There is a lack of intuitive methods for mapping the chemical relationships between a large collection of small molecules such as is found in a high-throughput screening library. Wetzel *et al.* now report user-friendly software for navigating chemical space. The program can start with biochemical data from a high-throughput screen and extract relevant scaffolds and activity data. The scaffolds are then simplified by removing one ring at a time to create tree branches. 'Virtual scaffolds', which are inserted as necessary to fill gaps between compounds within the library, provide leads for discovering new classes of ligands. In an accompanying paper, Renner *et al.* use this approach to analyze all the compounds in WOMBAT, a database that contains compound bioactivity data extracted from the literature. Beginning with approximately 170,000 ring-containing molecules, 46,000 unique scaffolds were identified and dissected into nearly 60,000 branches, of which approximately one-third had at least three consecutive scaffolds annotated with the same biological activity. As demonstrated, this approach and web tool can be used to identify new scaffolds with activity against desired targets. [Brief Communications, p. 581; Articles, p. 585; News & Views, p. 536] *JK*

Sweetening CLV3



The shoot apical meristem (SAM) is essential for organogenesis in flowering plants. In *Arabidopsis thaliana*, stem cell production and differentiation are controlled by the products of a set of CLAVATA (*CLV*) genes expressed in the SAM. Previous studies had suggested that CLV3 is a 12-mer peptide that regulates stem cell homeostasis by interacting with the CLV1 receptor. However, the chemical structure of active CLV3 has remained unresolved until now. Ohyama *et al.* isolated CLV3 peptide expressed from *A. thaliana* and established that CLV3 contains a hydroxyproline residue that is post-translationally modified with a trisaccharide comprised of β-1,2-linked L-arabinofuranose. Glycosylation is required for CLV3 binding to CLV1 and for *in vivo* activity of the CLV3 peptide. The authors also demonstrated that the trisaccharide occurs in several other plant peptides, suggesting that it may be a general motif involved in plant peptide hormone recognition. [**Brief Communications, p. 578**] *TLS*

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