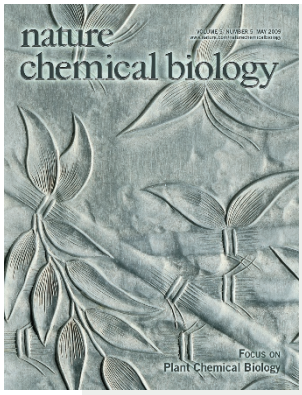


Focus on plant chemical biology

In this special issue, we highlight several emerging areas of plant chemical biology where the molecular details of plant biology are coming into focus.

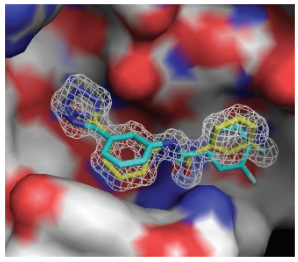
Plants have evolved signaling and transport mechanisms that enable them to thrive in a fixed location. Recent research has provided new insights into small-molecule plant hormones, which serve as the key signaling molecules within plants. Santner *et al.* [**Reviews, p. 301**] provide an overview of the major classes of plant hormones, discuss how they are biosynthesized and sensed, and outline their involvement in plant growth regulation. To act at the proper site and time, plant hormones and other essential molecules must be transported efficiently within plant tissue and directed to target cells. Robert and Friml [**Reviews, p. 325**] discuss mechanisms for long distance and cellular transport in plants. Metal ions are essential in plants, and Palmer and Guerinot [**Reviews, p. 333**] take an integrated look at the mechanisms of mobilization, uptake and transport of copper, iron and zinc ions within plants.

Plants must also be adept at responding to hostile environmental conditions. Pieterse *et al.* [**Reviews, p. 308**] discuss the basics of plant-pathogen interactions and examine how crosstalk among plant hormone pathways is able to fine-tune plant immune responses to microbial insults. Dicke *et al.* [**Reviews, p. 317**] outline how plants emit cocktails of herbivore-induced plant volatiles (HIPVs) in response to attacks from insects and explore how HIPV profiles are affected by and regulate plant-herbivore interactions. Finally, Vickers *et al.* [**Perspectives, p. 283**] put forward a new hypothesis about how volatile isoprenoid compounds protect plants from abiotic stressors by enhancing their ability to remediate imbalances in reactive oxygen species.

The tools and mechanistic approaches of chemical biology have much to contribute to plant biology. Hicks and Raikhel [**Commentary, p. 268**] discuss how chemical probes have provided important mechanistic insights into plant biology and call for enhanced interactions between chemical biologists and plant biologists. Fonseca *et al.* [**Articles, p. 344; News & Views, p. 273**] illustrate this point, as they identify the key jasmonate signaling hormone in plants and propose a mechanism for its metabolic inactivation. Chemical biology also provides tools with wide-ranging impact—for example, to identify new components of plant circadian clocks [**News & Views, p. 277**], investigate the mechanisms of RNA interference [**News & Views, p. 278**] and understand complex plant pathways such as pollen tube growth [**Research Highlights, p. 281**]. Finally, Leonard *et al.* [**Perspectives, p. 292**] offer insight into metabolic engineering strategies that enable the large-scale production of natural and non-natural plant alkaloids for drug discovery applications.

We hope that these articles will provide an overview of key areas in current plant biology—particularly those where crosstalk between plant and chemical biologists will be strongly rooted in molecular details.

Finding fragments virtually

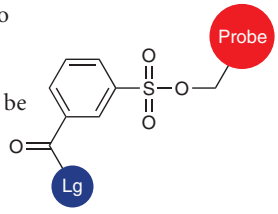


Fragment-based drug discovery (FBDD), in which weakly binding drug 'fragments' are identified and then developed into more potent drug leads, has emerged as a powerful alternative to high-throughput screening of large drug-like libraries. However, current screening methods for FBDD rely on low-throughput biophysical techniques such as NMR, X-ray crystallography and surface plasmon resonance. To test the potential for *in silico* screening in FBDD, Chen and Shoichet screened a large library of virtual fragments by computational docking and successfully identified fragments that bind to β-lactamase. Subsequent crystal structures revealed that the docking accurately predicted the fragment binding modes. The computationally identified fragments were then developed into potent β-lactamase inhibitors. This approach opens up a high-throughput route to FBDD. [**Articles, p. 359; News & Views, p. 274**] *JK*

Shining a light on a ribozyme pK_a

Hairpin ribozymes are a class of small RNAs that catalyze site-specific RNA cleavage. Biochemical and structural analysis of hairpin ribozymes has led to a model in which two active site purines—guanine 8 (G8) and adenosine 38—act as general acid–general base catalysts for the cleavage reaction. Liu *et al.* now use site-specific incorporation of a base analog to probe this mechanism directly. The authors substituted G8 with 8-azaguanine and used its fluorescence properties to directly measure the pK_a of this residue. The observed pK_a of ~9.5 was approximately 3 units higher than the apparent pK_a derived from kinetic measurements, which indicates that G8 is largely protonated in the active site. Because the reaction's pH-rate profile cannot be explained as being dependent on G8 deprotonation, the role of this nucleotide and A38 in the catalytic cycle of the hairpin ribozymes will need to be reexamined. The investigation also offers a useful chemical probe that will aid future studies of acid-base catalysis by other ribozymes. [**Articles, p. 352**] *TLS*

Silent protein labeling



The use of chemical reporters or tags to interrogate protein targets can provide important information about enzyme activity or protein localization but can be misleading if they interfere with protein function. Tsukiji *et al.* now utilize tosyl chemistry to introduce 'traceless' tags suitable for *in vitro* and *in vivo* labeling. By inserting a labile tosyl group between a known protein ligand and a desired probe, the authors were able to target several molecules to the corresponding protein. A reactive group on the protein surface then attacks the tosyl functionality, covalently linking the probe to the protein and releasing the ligand. Labeling was demonstrated with several disparate proteins, and was effective and selective in red blood cells and mice. Attachment of an ^{19}F probe further allowed quantification of carbonic anhydrase inhibitor function in intact cells. This robust methodology should enable a variety of experiments examining protein activity. [**Brief Communication, p. 341; News & Views, p. 275**] *CG*

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