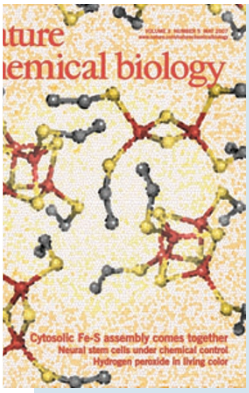
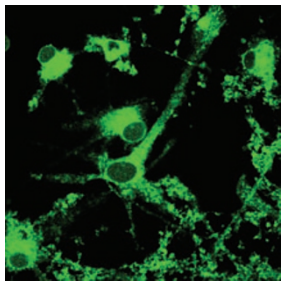


SUPPORT FOR FE-S IN THE CYTOSOL

Iron-sulfur clusters have important roles in catalyzing enzyme reactions, mediating electron transfer, and regulating gene expression. During biosynthesis in the mitochondria, iron-sulfur clusters are first assembled on scaffold proteins using sulfide ions donated by a cysteine desaturase; they are then transferred with the help of chaperones to [Fe-S] recipient proteins. Although much is known about the mitochondrial pathway, very little is known about how iron-sulfur clusters are inserted into cytosolic proteins in eukaryotes. Netz *et al.* have now identified the Cfd1–Nbp35 complex as a cytosolic scaffold for iron-sulfur cluster assembly. The Cfd1–Npb35 complex can bind up to three [4Fe-4S] clusters, which can then be transferred both *in vitro* and *in vivo* to physiological target apoproteins. Although many mechanistic details remain to be uncovered, the identification of the scaffold is a key step towards a molecular understanding of this pathway. [**Articles, p. 278; News & Views, p. 243**] *JK*

A glimpse at H_2O_2 signaling

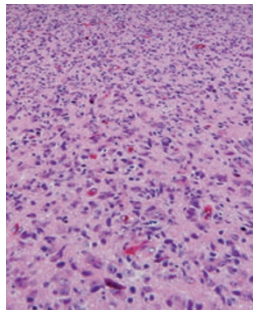


Hydrogen peroxide serves as an important mediator of cellular signaling. A molecular understanding of how this reactive molecule is directed toward specific pathways and post-translational modifications has been hampered by the lack of cellular methods for visualizing hydrogen peroxide. Current probes lack either specificity for hydrogen peroxide over other reactive oxygen species or the required sensitivity to detect endogenous concentrations of hydrogen peroxide. Miller *et al.* have developed monoboronated fluorophores that selectively fluoresce in response to hydrogen peroxide. The high sensitivity of the probes allowed visualization of endogenous peroxide produced in response to growth factor stimulation of mammalian cells and live hippocampal neurons. These probes provide an important new tool for investigating mammalian hydrogen peroxide signaling. [Letters, p. 263; News & Views, p. 244] *JK*

KCNQ channels get ZnPy

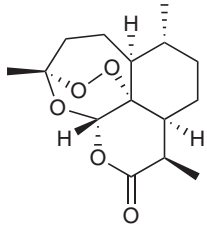
KCNQ channels are voltage-gated K^+ channels that are important for controlling electrical excitability in the central nervous system. Mutations in KCNQ2 and KCNQ3 cause benign familial neonatal convulsions (BFNC), and small-molecule activators of the channels are anticonvulsive. Xiong *et al.* used the functional recovery after chemobleaching assay, which exploits Rb^+ permeability of K^+ channels, to screen for new small-molecule effectors of KCNQ channels. One of the activators, zinc pyrithione (ZnPy), was shown to induce channel opening in both heterologously expressed and native channels. Biochemical evidence suggests that ZnPy may work by interacting directly with the gating machinery to stabilize the open conformation. ZnPy rescued the KCNQ channel currents that are reduced in BFNC neurons. [Articles, p. 287] *MB*

Neural stem cell chemical screen



Neural stem cells are a potentially important therapeutic target for neurological diseases and brain cancer. However, much remains to be learned about both the cellular signaling pathways that control neural stem cell proliferation and the potential for using small molecules to regulate this process. Using cultures of neural precursor cells, Diamandis *et al.* screened a chemical library for inhibitors of neural precursor proliferation. Within the 'hits' were a number of neuromodulatory compounds, including regulators of the serotonin, opioid, glutamate and vanilloid pathways, which suggests a role for neurotransmitters in governing neural stem cell self-renewal. Although additional mechanistic studies are needed to further investigate neural stem cell signaling pathways, this study suggests the possibility of using neuromodulatory compounds in the treatment of central nervous system tumors. [**Letters, p. 268; News & Views, p. 246**] *JK*

Putting P450s to work



Plant terpenes are an important class of biologically active small molecules, but they are challenging synthetic targets. Production of terpenes through metabolic engineering in *Escherichia coli* offers an alternative route for generating terpenes. However, the inability to heterologously express functional plant cytochrome P450 proteins, which are key terpene tailoring enzymes, has been a significant impediment toward the *in vivo* total synthesis of these natural products. Chang *et al.* have functionally expressed cytochrome P450 enzymes that catalyze oxidation reactions along the biosynthetic pathways of gossypol and artemisinin, which demonstrates the feasibility of *in vivo* production of functionalized terpenes in *E. coli*. [**Letters, p. 274**] *JK*

Beyond amino acids

Although α-amino acids are nature's building blocks of choice for proteins, synthetic chemists can access a wide range of monomeric units. Designing foldamers—sequence-specific oligomers that fold into discrete three-dimensional structures—provides fundamental information about folding and yields new frameworks for potential biological and nanotechnology applications. In a Review in this issue, Goodman *et al.* discuss the recent progress in designing foldamers from aliphatic and aromatic building blocks as well as current advances in engineering foldamers with biological function. They also highlight the potential for expanding the structural and functional space covered by foldamers. [Reviews, p. 252] *JK*

In This Issue written by Mirella Bucci and Joanne Kotz