A flower's season premiere

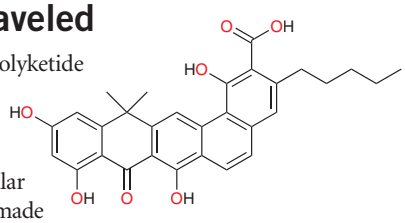
Plants regulate their flowering time based on seasonal changes in day length, with longer days signaling them to flower earlier. These day-length signals are transmitted by the vascular tissue of the leaves from plant shoots to the undifferentiated cells of apical meristems. In the laboratory, *Arabidopsis thaliana* plants shifted from short day length to long day length show an increase in expression of *FLOWERING LOCUS T* (*FT*) in leaves. Several models for the long-range signal exist, including one in which *FT* mRNA is the signal and another "relay" model in which the FT protein activates a second messenger but is not itself a mobile signal. Corbesier *et al.* now show that prolonged expression of *FT* in leaves is not required to induce sustained flowering at the shoot apical meristem (SAM), so it is likely that the protein product of *FT* is acting as part of the signal to the SAM. Indeed, the authors found that the FT protein (but not the mRNA) was distributed widely throughout the shoot apex and at the base of the SAM. A grafting technique that tests the long-range capacity of the FT protein supported movement of the protein as the model for the long-range signaling mechanism. They also ruled out the relay model and conclude that *FT* expression in leaves induces flowering because the FT protein itself moves to the SAM. Similarly, Tamaki *et al.* now show that the protein encoded by *Hd3a*, the rice *FT* gene, moves from the leaf to the SAM to induce flowering in rice plants in response to short days, which suggests a general flowering mechanism common to all seasonal plants. (*Science*, published online 19 April 2007, doi:10.1126/science.1141752 and 10.1126/science.1141753) *MB*

HIV-1 fusion peptide block

Although there is evidence that molecules in human blood can inhibit human immunodeficiency virus type 1 (HIV-1) infection, identifying natural inhibitors has proven difficult. Taking advantage of a recent technique for isolating low-molecular-weight circulating blood components from 10,000 liters of hemofiltrate, Munch *et al.* have isolated a biologically occurring peptide that inhibits HIV-1 infectivity. Starting with 322 chromatographic hemofiltrate fractions, the authors identified one fraction that had potent anti-HIV-1 activity but no apparent cytotoxicity. The active molecule from this fraction was determined to be VIRIP, a 20-residue peptide from human α1-antitrypsin, which is the most abundant circulating serine protease inhibitor. Chemically synthesized VIRIP had broad inhibitory activity, with an IC_{50} around 20 μM, against different viral subtypes and against strains resistant to protease, reverse transcriptase and fusion inhibitors. Alanine scanning demonstrated the importance of the C- and N-terminal regions of the peptide for inhibitory activity, and synthesis of approximately 600 peptide analogs resulted in an inhibitor that was two orders of magnitude more potent. The authors found that VIRIP binds to the fusion peptide region of HIV-1 gp41, a glycoprotein that is involved in mediating viral entry into target cells. These results suggest the HIV-1 gp41 fusion peptide as a new target for HIV-1 inhibitors and provide an important starting point for new drug discovery efforts. Further, the presence of VIRIP in serum suggests a potential role for this peptide in inhibiting HIV *in vivo*. (*Cell* **129**, 263–275, 2007) *JK*

Research Highlights written by Mirella Bucci, Catherine Goodman, Joanne Kotz and Terry L. Sheppard

Benastatins unraveled



Benastatins are a class of polyketide natural products that are produced by *Streptomyces* spp. Benastatin A and benastatin B are structurally similar to polyphenolic compounds made by actinomycetes, but each contains a distinctive five-carbon side chain and a geminal dimethyl modification. Recent studies by Xu *et al.* have uncovered the biosynthetic routes to benastatins and highlighted a new connection to related classes of natural products. The authors isolated a cluster of 17 genes encoding enzymes involved in benastatin biosynthesis, including the required type II polyketide synthase, cyclases and tailoring enzymes. The authors also identified two genes, *benF* and *benQ*, that are critical for benastatin synthesis. BenF is a methyltransferase that catalyzes the unusual dimethylation of the B-ring of benastatins using *S*-adenosylmethionine. The authors concluded that BenQ, which is similar to type III β-ketosynthase enzymes found in fatty acid biosynthesis, is essential for the incorporation of the pentyl side chain in benastatin because it selects the appropriate hexanoyl starter unit to initiate polyketide synthesis. In the absence of BenQ, shorter acyl initiators are used, which results in the production of several new hexacyclic compounds and branched benastatin analogs. These intermediates bear a structural resemblance to griseorhodin and fredericamycin, and suggest a possible biosynthetic link between these pathways. The observed intersection of the polyketide and fatty acid synthesis pathways in BenQ opens up the possibility of biosynthetic engineering of new benastatin analogs and encourages exploration of these related biosynthetic pathways. (*J. Am. Chem. Soc.*, published online 17 April 2007, doi:10.1021/ja069045b) *TLS*

RNA cuts in

Nucleolytic ribozymes cleave or ligate RNA backbones with outstanding rate accelerations, which is especially intriguing given the limited functionality available to accomplish the task. Previous work on the hairpin and hammerhead ribozymes has demonstrated that precise positioning of nucleotides provides substituents for general acid or base catalysis of the 2′-O-mediated rupture of the RNA backbone. In contrast to these studies, recent investigations of the VS ribozyme have been hampered by the lack of a crystal structure, but have identified A756 as one half of a general acid-base catalyst system. Now Wilson *et al.* have identified nucleotide G638 as the catalytic partner in the reaction. The authors observed that substitution of G638 drastically reduces ribozyme reactivity without altering the overall structure or interrupting substrate binding. Additionally, this effect could not be rescued by restoration of Watson-Crick hydrogen bonding with the substituted G638 base, meaning that the loss of activity is specifically due to the loss of a functional group necessary for the catalytic step. Though the specific role of each nucleotide remains to be determined, the cascade bears some similarity to the reaction pathway elucidated for the hairpin ribozyme, perhaps facilitated by their similar local architecture. However, the remaining differences in the reaction coordinate and the lack of significant homology between the two ribozymes suggest that this is an example of convergent evolution, thus implicating this pathway as a general mechanism for RNA catalysis. (*EMBO J.*, published online 26 April 2007, doi:10.1038/sj.emboj.7601698) *CG*