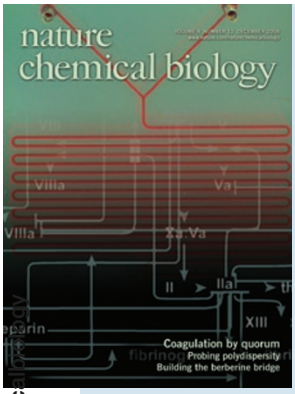


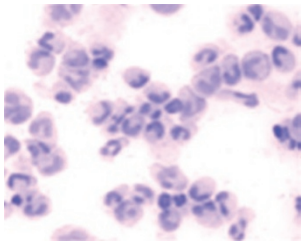
Coagulation via clustering

Blood coagulation is a complex process involving many protein factors that act in a cascade to initiate clot formation. Bacteria are known to activate individual coagulation factors but were not thought to be able to trigger the full coagulation cascade. Kastrup *et al.* now use microfluidics and micropatterned surfaces to demonstrate that sufficiently dense clusters of *Bacillus* spp. can directly and rapidly initiate the coagulation cascade in human blood and plasma by activating prothrombin and factor X. They propose a mechanism, called 'quorum acting', in which a high local density of bacteria releases sufficient amounts of soluble factors to successfully initiate coagulation; for *B. anthracis*, this factor appears to be InhA1. In contrast to quorum sensing, neither interbacterial interactions nor changes in bacterial gene expression are necessary for quorum acting. [**Articles, p. 742; News & Views, p. 718**] *KS*

SAMe chemistry, different motif?

Thiamine pyrophosphate is synthesized in several steps *in vivo*, with the penultimate conversion being the coupling of thiazole phosphate (TMP) and the pyrophosphate analog of thiamine pyrimidine (HMP-PP). A mechanistic understanding of HMP-PP synthesis is lacking, although HMP-P synthase (from the *ThiC* gene) is known to perform a particularly elaborate rearrangement *en route* to HMP-PP. The successful reconstitution and investigation of HMP-P synthase by Chatterjee *et al.* now provides definitive proof that the enzyme uses radical SAM chemistry and an iron-sulfur cluster to perform the reaction. This activity confirms that the unusual CX_2CX_4C motif is supportive of radical SAM chemistry, and thus expands the search criteria for radical SAM family members. Analysis of the protein structure further shows similarities to adenosylcobalamin radical enzymes, highlighting a functional link between these proteins and radical SAM enzymes. [**Articles, p. 758**] *CG*

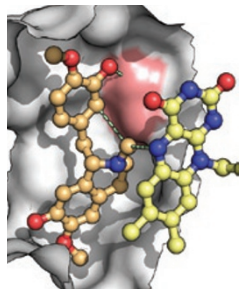
Sialidase redecorates cells



The CD15 antigen is a cell-surface glycan that mediates adhesion of neutrophils to dendritic cells and has been used as a marker for differentiation of granulocyte-series cells. Although expression of most cell-surface glycans is determined by glycosyltransferase activity in the endoplasmic reticulum or Golgi apparatus, the molecular mechanisms regulating CD15 expression have not been fully characterized. Through biochemical analysis and flow cytometry, Gadhoum and Sackstein now show that, unexpectedly, CD15 expression is upregulated in differentiating myeloid cells not by glycosyltransferase-mediated *de novo* synthesis but via increased sialidase activity, which converts sialyl-CD15 to CD15 on the cell surface. Further analysis showed that the increased CD15 comes mainly from sialyl-CD15 displayed on glycoproteins rather than sialyl-CD15 on glycolipids. The study demonstrates post-Golgi enzymatic glycoside hydrolysis as the molecular mechanism for modulating display of an important cell-surface glycan. [**Articles, p. 751; News & Views, p. 721**] *KS*

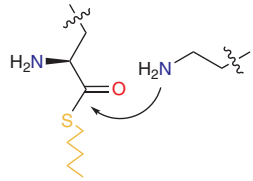
Written by Catherine Goodman & Kenneth Sercy

Bridge under construction



The biosynthesis of many alkaloids relies on the formation of a carbon-carbon bond, or the 'berberine bridge', as (*S*)-reticuline is transformed into (*S*)-scoulerine. The transformation, which has no equivalent in synthetic chemistry, is performed by berberine bridge enzyme (BBE) and has been proposed to operate by a two-step mechanism. Winkler *et al.* now provide structural and biochemical evidence that the reaction instead proceeds in a single step. The authors identify Glu417 as key to initiating the reaction cascade by removing a proton from a hydroxy group in (*S*)-reticuline. The resultant formation of a carbonyl causes an S_N2-type attack on a neighboring carbon to create the berberine bridge, with the ejected hydride ion being absorbed by BBE's flavin cofactor. The full description of this unusual reaction may also have implications for other synthases known to be similar to BBE. [Brief Communication, p. 739; News & Views, p. 719] *CG*

Biosynthetic polydispersity



ε-Poly-L-lysine (ε-PL), one of only a few natural homopolymers, consists of variable-chain-length lysine sequences connected via isopeptide linkages. The chain-length diversity in ε-PL is significant for function, as longer sequences are more effective antimicrobial agents than shorter polymers, but the origin of this polydispersity was not clear. The recent discovery of ε-PL–degrading enzymes also suggested that dispersity could be generated by cleaving a unique long-chain precursor at variable positions. By isolating and characterizing an ε-PL synthetase (Pls), Yamanaka *et al.* now demonstrate that an unusual NRPS hybrid directly generates the full complement of ε-PL sequences. The synthetase combines A domains and T domains typical of NRPS machinery with three tandem, membrane-bound, peptide ligase–like domains, and uses two distinct substrate binding sites to initiate polymerization, both of which are shown to accommodate substrate analogs. These results set the stage for the creation of non-natural polymers and pose further questions regarding the structure and function of Pls. [**Articles, p. 766**] *CG*

Transcription deconstructed

Intrinsically disordered proteins (IDPs) continue to challenge our understanding of the structure-function relationships of proteins. In a review in this issue, Fuxreiter *et al.* argue that IDPs are particularly well suited to participate in transcription, as the promiscuity and low binding affinities of IDPs allow the interactions with a multitude of potential biological partners on the fast timescales that are necessary to coordinate this fundamental biological process. Specific proteins that serve as IDPs, as well as future experimental and conceptual challenges in the field, are explored. [Review, p. 728] *CG*