IN THIS ISSUE

354 Sequence variation and structural conservation allows development of novel function and immune evasion in parasite surface protein families
Matthew K. Higgins and Mark Carrington

The surface proteins of parasitic organisms lie at the heart of the battle between the parasite and its host. They need to maintain ligand-binding phenotypes to allow them to perform essential roles in processes such as host cell invasion and nutrient uptake. However, they are also targeted by the human immune system, and are therefore under pressure to become more divergent to evade immune detection. Here the authors review how extensive sequence variation on a conserved molecular scaffold has allowed the development of novel functions in surface protein families from the parasites that cause sleeping sickness and malaria.

423 Crystal Structure of the transcriptional regulator Rv1219c of Mycobacterium tuberculosis
Nitin Kumar, Abhijith Radhakrishnan, Catherine C. Wright, Tsung-Han Chou, Hsiang-Ting Lei, Jani Reddy Bolla, Marios L. Tringides, Kanagalaghatta R. Rajashankar, Chih-Chia Su, Georgiana E. Purdy and Edward W. Yu

The TetR-family transcription regulators are capable of sensing and responding to various structurally dissimilar antimicrobials. Upon detecting these agents, the regulators allow transcription of an array of resistance markers to counteract these compounds. Mycobacterium tuberculosis Rv1219c is a multidrug efflux regulator, which represses the expression of the Rv1217c-Rv1218c efflux system. Here, the authors describe the structure of Rv1219c, revealing a dimeric two-domain molecule with an entirely helical architecture. The N-terminal domains of the Rv1219c dimer are separated by a large distance of 64 Å. The C-terminal domain of each protomer forms a large cavity, which binds drugs in the micromolar range.

344 Mechanisms for regulating deubiquitinating enzymes
Cynthia Wolberger

The attachment of the small protein, ubiquitin, to different proteins plays a dynamic signaling role in a broad array of processes in eukaryotic cells. Proteins can be modified by a single ubiquitin monomer or by one of eight types of polyubiquitin chains, each serving a distinct function. Deubiquitinating enzymes reverse these modifications, thereby playing a key role in ubiquitin signaling. Cells employ a variety of mechanisms to regulate the activity of deubiquitinating enzymes and thus ensure the appropriate biological response. Recent studies have shed light on the diverse mechanisms by which the activity of deubiquitinating enzymes is regulated.

508 Mispairs with Watson-Crick Base-pair Geometry Observed in Ternary Complexes of an RB69 DNA Polymerase Variant
Shuangluo Xia and William H. Konigsberg

Recent structures of DNA polymerase complexes with purine/pyrimidine mispairs have shown that they adopt Watson-Crick geometry indicating that the tautomeric or ionization state of the base has changed. To see whether the tautomeric or ionization state of base-pair could be affected by its microenvironment, we determined ten structures of an RB69 DNA polymerase variant with dG/dT or dT/dG mispairs at position n-1 to n-5 of the Primer/Template duplex. Different shapes of the mispairs, including those with Watson-Crick geometry, have been observed, strongly suggesting that the local environment of base-pairs plays an important role in their tautomeric or ionization states.