In This Issue

Fitting into the Catalytic Pocket

PAGE 615

The enzyme activation induced cytidine deaminase (AID) mutates antibody genes in B lymphocytes, leading to enhanced immunity; however, off-target AID activity can lead to cancer. The structure of AID is not known. King et al. use a combination of computer simulations and functional experiments to uncover how AID activity is regulated.

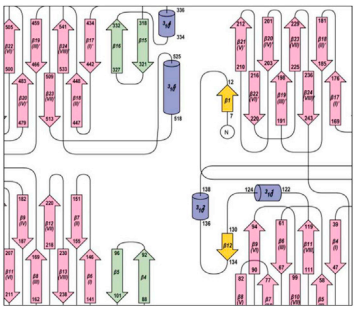
Seeing Is Believing: Rhodopsins All in a Row

PAGE 628

Gunkel et al. show by cryo-EM that rhodopsin in intact photoreceptors is hierarchically organized in dimers, rows, and parallel tracks. Simulations suggest that tracks form a kinetic trap for the preassembled G protein transducin.

Regio- and Stereoselectivity of Prolyl-Hydroxylases

PAGE 639



Horita et al. present structures of the first prolyl-3-hydroxylase from humans, OGFOD1, in complex with small molecule inhibitors. The results shed light on the catalytic mechanisms and evolution of the OGFOD1 subfamily and the related "oxygen sensing" hypoxia-inducible factor trans-P4Hs (PHDs).

Substrate Specificity and Plasticity in FERM Hands

PAGE 653

Eps15 is a newly identified substrate of PTPN3 known to be involved in the regulation of EGFR trafficking. Chen et al. reveal the molecular insights into the specific recognition of Eps15 by PTPN3 and members in the FERM domain containing the PTP subfamily, which is comprised of PTPN4, N13, N14, and N21.

Flu Season: pH-Dependent Conformational Change of Hemagglutinin

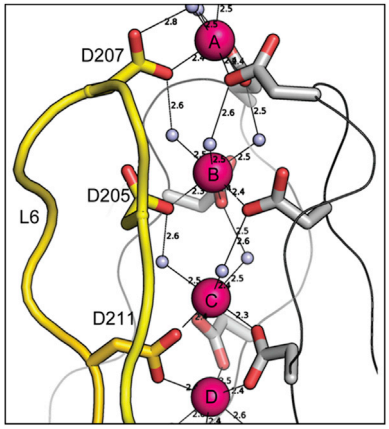
PAGE 665

The influenza virus glycoprotein hemagglutinin (HA) facilitates fusion of viral membranes with host endosomal membranes via a pH-dependent conformational change. Garcia et al. investigates how an acidic environment may promote HA activation by identifying key structural regions in HA that are altered by low pH.

Splicing and Dicing: VEGF-C Binding to Neuropilin-2

PAGE 677

Vascular endothelial growth factor-C (VEGF-C) is a potent lymphangiogenic cytokine that signals via the cell surface receptor Neuropilin-2 (Nrp2). Parker et al. demonstrate that VEGF-C binding to Nrp2 is regulated by C-terminal proteolytic maturation and identify a secreted splice form that functions as a selective inhibitor.



Brainy C1q-like Proteins

PAGE 688

C1q-like-1, -2, and -3 proteins bind to brain-specific angiogenesis inhibitor 3, an adhesion-type G-protein coupled receptor that may regulate dendritic morphology by organizing actin filaments. Ressl et al. report high-resolution crystal structures of the C1QL protein family. The structures reveal unique features among the C1q/TNF-superfamily that is likely associated with their specific brain functions.

Ankyrin and the 3M Syndrome

PAGE 700

The genetic disease 3M syndrome is a rare short-stature disorder with additional features such as facial and skeletal abnormalities. Nie et al. identify a "code" by which one 3M syndrome protein, CCDC8, interacts with a novel binding partner, ANKRA2, thereby unveiling an unexpected molecular mechanism important for the pathogenesis of this genetic disease.

Bacterial ABC Transporter Inhibition by an Antibody

PAGE 713

Ahuja et al. report on the inhibition of a bacterial ABC transporter for Mn(II) with an antibody fragment targeting its periplasmic substrate binding protein (SBP). Structural and functional studies reveal that the antibody prevents the interaction of SBP with the membrane transporter, blocking substrate import.

Guided by Ub and SUMO: PCNA in the DNA Damage Response

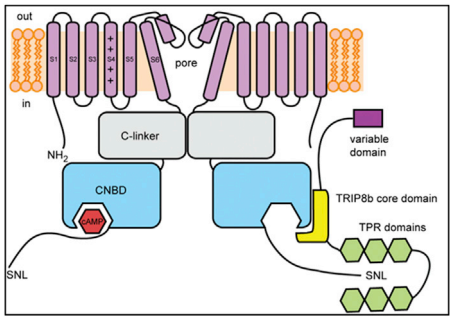
PAGE 724

Tsutakawa et al. combine computational modeling and small-angle X-ray scattering to show SUMOylated and ubiqitinated PCNA have strikingly different conformations in solution due to opposite electrostatics of the modifiers. The distinct conformations underlie distinct roles for PCNA-Ub and PCNA-SUMO in DNA damage responses.

Regulating HCN Ion Channels

PAGE 734

Binding of TRIP8b reduces the cyclic nucleotide dependence of hyperpolarization-activated cyclic nucleotide-gated channels. DeBerg et al. identify the interaction topology and suggest that TRIP8b regulates these channels by disrupting both cAMP binding and the coupling of cAMP binding to channel opening.



Metadynamics Reveals LFA-1 I-Domain Substates

PAGE 745

Kukic et al. identified three substates of the apo LFA-1 I-domain using replica-averaged metadynamics simulations with NMR restraints. The presence of the inactive, low, and intermediate affinity substates in apo LFA-1 I-domain represents an intrinsic property that can regulate the complex allosteric mechanism of the protein.

Forcing the Issue: Lipids and the Lactose Permeases

PAGE 754

Serdiuk et al. structurally localize the interactions that stabilize single lactose permeases (LacY) in phospholipid membranes. In the absence of phosphatidylethanolamine, LacY adopts perturbed conformations, thus suggesting an alternating topology. Drastic changes are located at helices VI and VII and the intervening loop.

From Interactome to Structural Insight

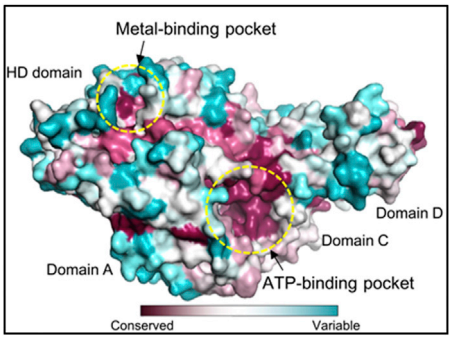
PAGE 762

Navare et al. apply in vivo chemical cross-linking mass spectrometry to reveal the first large-scale protein interaction network in *Pseudomonas aeruginosa* with over 600 cross-linked peptide pairs. Cross-linked sites provide constraints for useful complex structure prediction—even for membrane protein interactions.

Olf and FLRT: HeLa Cell Adhesion, but Neuron Repulsion

PAGE 774

Jackson et al. describe a crystal structure of mLPHN3 lectin and olfactomedin-like (Olf) domains, revealing the Olf β-propeller-fold and calcium-binding-site. Assays using HeLa cells and cortical neurons reveal a bifunctional role for Olf and its ligand, FLRT, leading to HeLa cell adhesion and neuron repulsion.



The Csm1 Subunit of the Csm Complex

PAGE 782

Csm1 is the largest subunit of the Csm interference complex. Jung et al. reveal that Csm1 is a multidomain protein that possesses ssDNA-directed nuclease activity on the HD domain. Csm1 might function as the catalytic subunit in DNA interference in a subset of the Csm holocomplex in the Type III-A CRISPR-Cas system.

IMPACT for Structural Proteomics

PAGE 791

Marklund et al. present IMPACT, which rapidly and accurately calculates collision cross-sections from structural models. This allows them to interrogate the size and shape variability of the proteome. Their approach will enable the application of ion-mobility mass spectrometry across structural biology and structural proteomics.

