PL-5
Structural and functional analysis of enzyme targets for drug design
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Glutaminyl cyclase (QC) facilitates the formation of N-terminal pyroGlu. The pGlu is required in many bioactive peptides and its aberrant formation may cause diseases. We solved the crystal structures of human single zinc ion QC, having an α/β scaffold akin to that of two-zinc exopeptidases. Structural and kinetic analyses of several active-site-mutant enzymes suggest a catalysis mechanism. Glutathionylspermidine synthetase (GspS) synthesizes trypanothione. Unlike others using GSH, protozoa utilize trypanothione to regulate thiol redox balance and defense against oxidative stress. Synthesis of trypanothione requires ATP-dependent conjugation of GSH to spermidine by GspS. Five structures of E. coli GspS in complex with substrate, product or inhibitor reveal a mechanism involving two GSH binding sites, the biochemical features of parasite TryS and their broad specificity of polyamines. H. pylori 1,3-fucosyltransferase catalyzes the transfer of fucose to LacNac to produce the Lewis X sugar. Lewis antigens are expressed in the O-antigen of the H. pylori LPS and structurally similar to the host tumor-associated carbohydrate antigen. We solved three crystal structures, including the protein, the protein-GDP-fucose complex, and the protein-GDP complex. The dimeric enzyme has two Rossmann domains, typical of the GT-B family. Site-directed mutants were analyzed to elucidate the mechanism. Our results provide structural basis for the rational design of inhibitors against diseases related with those enzymes.

PL-6
Structure of the aquaporin-0 mediated membrane junction
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We present the structure of aquaporin 0, a water channel only found in the eye lens, and has two distinct functions: it forms a water selective pore in membranes, and acts as an adhesive protein in double membranes, forming cell to cell membrane junctions. We used electron crystallography to determine the structure of junctional aquaporin 0 to 1.9 Å resolution. When aquaporin-0 junction form, the water channels close and contain only three water molecules. Lipids mediate lateral crystal contacts in our two dimensional crystals. We present the structure of a eukaryotic membrane surrounding the protein.

PL-7
Kinetics, energetics and structural dynamics of cooperative cofilin-actin filament interactions.
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The actin regulatory protein cofilin binds actin filaments cooperatively and severs them, playing a critical role in the disassembly and reorganization of the actin cytoskeleton. Analysis using a nearest neighbor cooperative lattice binding model indicates that cooperativity is greater for flexible, non-muscle actin than rigid muscle actin filaments. The predicted cofilin cluster sizes and filament binding densities are small at cofilin concentrations where efficient filament severing is observed, indicating that a few bound cofilin molecules are sufficient to destabilize the filament lattice and promote fragmentation. Ions weaken isolated, non-contiguous cofilin binding without affecting cooperative filament interactions. Binding is coupled to the dissociation of ~1.7 thermodynamically bound counterions, which contribute ~40% of the total cofilin binding free energy (in the presence of 50 mM KCl). The non-contiguous and cooperative binding free energies are driven entirely by large, positive entropy changes, consistent with the cofilin-mediated increase in actin filament microsecond structural dynamics and torsional flexibility measured using time-resolved phosphorescence anisotropy. Cooperative binding arises from ~10 fold more rapid association and ~2-fold slower dissociation. The results suggest that cofilin-mediated dissociation of actin-associated ions weakens intersubunit interactions in the actin filament lattice that enhance cofilin binding site accessibility, favor cooperative binding and promote filament severing.

PL-8
Visual Learning and Memory in Drosophila from Genes to Behavior
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Tracing the memory localization of Drosophila in the visual learning paradigm is a challenging work all the while. Recently, our work shows that fan-shaped body in the fly's brain is likely to be responsible for the visual pattern memory. Rutabaga (rut) encodes a type I Ca2+/CaM-dependent adenylyl cyclase (AC1), which is a component of cAMP pathway. Compared with the control, rutabaga mutants show serious short-term memory defects in the test period immediately after the training. Since there is no significant difference in the basic sensitive ability - heat avoidance competence, perception ability and pattern discrimination ability. So the low memory must have been the result of AC1 functional deficiency. Using the enhancer GAL4/UAS expression system short term memory traces can be localized by restoring AC1 selectively in certain cells in the rut mutant. Each Gal4 line drove the wild type rut+ to be expressed at different brain area. Only some of them could rescue the memory defect back to the wild type level. These Gal4 lines were analyzed by inflorescent staining method and found that they all have a common transgenic expression in the fan-shape body. Put all the above results together with the ones gotten from central complex mutants in which they all show memory defect in the visual learning paradigm. We found that fan-shaped body is an important structure where the visual memory happens.