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(PTP). Comparing with the animal enzymes, PTPS from *E. coli* (ePTPS, eQueD) possesses much stronger catalytic activity to cleave the side chain of the pterin substrate rather than the conversion from H_2NTP to PTP and catalyzes the conversion of H_2NTP to 6-carboxy-5,6,7,8-tetrahydropterin (CPH4).
In this study, we have determined the crystal structures of a wild type ePTPS and a Cys26Ala mutant ePTPS complexed with sepiapterin. In the crystal, ePTPS forms a hexamer stacked by two closely interacting trimers in the asymmetric unit although ePTPS exists as a trimer and a dodecamer in solution, which was confirmed by gel-filtration chromatography and chemical cross-linking experiment. Each monomer (121 residues) folds into a single domain of two α helixes, two short α helixes and four β sheets with one Zn^{2+} ion. The overall structure of ePTPS, Zn^{2+} ion binding site and active site residues were similar to other PTPS with r.m.s.d. of 0.5 to 1.8 Å. Comparing with the mammalian PTPS structures, large differences were found in loop regions around the active site due to low sequence similarities. The structure of wild type ePTPS was almost identical to the ePTPS complexed with sepiapterin. However, the α1 helix (residues Ile51 to Pro63) in the complex positioned more closely toward the sepiapterin by 2.1 Å than in the apo-form. Conformational change by substrate-binding was observed that the side chain Trp50 rotated 180° to the active site, participating in substrate binding.

268-Pos Board B68
Bottom-Up Multiscale Simulations of Silk Fiber Mechanics
Senbo Xiao, Murat Cetinkaya, Frauke Graeter.
Silk is an intriguing protein-based material that combines elasticity and strength to an extent not yet reached by any synthetic material today. Silk fibers are composed of highly-ordered beta-sheet crystals and an amorphous peptide matrix that both contribute to its outstanding mechanical properties. However, how the way of organization of these two components affects silk fiber mechanics has remained unclear. To quantify the mechanics of silk fibers and its components, we here in a bottom-up approach extract elastic and rupture parameters of silk composite units from all-atom molecular simulations and a novel force distribution analysis serve as input for finite element analysis [1,2]. By doing so, we can derive macroscopic fiber mechanics from the nano-structure, in quantitative agreement with experiments. One of our most striking predictions is that a serial arrangement of silk crystals in the fiber, as commonly observed in form of lamellae for other block copolymers, outperforms a random distribution, in sharp contrast to the current view of silk fiber organization [3]. We also show why the typical beta-strand length of eight residues in silk crystals is mechanically optimal [2]. Finally, a smaller cross-sectional area of silk crystals (~1nm^2) in fibers provides a better reinforcement of the amorphous phase than larger ones. [3] We expect our straightforward multiscale approach to serve as a guideline for the design of silk-like synthetic materials.
1. S Xiao, W Stacklies, M Cetinkaya, B Markert, and F Graeter. Biophys J, 96(10):3997–4005, May 2009.
2. S Xiao, W Stacklies, C Debes, and F Graeter. Soft Matter, 2010.
3. M Cetinkaya, S Xiao, B Markert, W Stacklies, and F Graeter. in review, 2010.

269-Pos Board B69
Topology of Gene Delivery Systems
David V. Svintradze.
Gene therapy is a promising future of the treatment of diseases, but it faces problem such is: DNA or RNA (gene vectors), after administration into a living body become deactivated due to immunological reaction or enzymatic attack. Solution is gene delivery systems or gene vector binding inactive materials. If the gene vector is embedded in inactive biomaterial then it is protected from immunological reaction, but, so far, it is not fully understand which bioinactive material is the most effective for designing self gene delivery systems (gene delivery systems with no side effects). The nature found solution to the problem in a simple manner: adenoviruses. But viruses have side effects, obviously because function of viruses is predetermined to be effective, careless of side effects, delivery machines. There are, commonly used three different types of gene delivery systems: cationic lipid based delivery, adenovirus based delivery and protein based delivery systems. We show that all the above mentioned delivery systems have similar topology which becomes visible only after proper application of geometric topology to macromolecules. The question to ask is whether the similar topology is occasional or it is the necessary topology for gene delivery systems. More precisely: is the host cell sensitive to the geometric structures of the delivery systems? The analyses of existing structural data about delivery systems allow us to answer the questions. The comparison of topology of gene delivery system to the possible topology of nuclear pore system shows that pore topology is similar to the topology of gene delivery system. The similarity between gene delivery systems is governed by topology of gene and is dictated by structure of DNA.

270-Pos Board B70
PSI:Biology-Materials Repository: Developing a Public Resource for Structural Biology Plasmids
Catherine Cormier, Jason Steel, Michael Fiacco, Jin Park, Jason Kramer, Joshua LaBaer.
The PSI:Biology-Materials Repository (PSI:Biology-MR; http://psimr.asu.edu) provides centralized archival and distribution of plasmid and expression vector samples and their associated annotations created as part of the Protein Structure Initiative (PSI) structural genomics/biology effort. Our facility has developed an informatics and sample processing pipeline to fully track, sequence analyze, and annotate each plasmid deposited in the PSI:Biology-MR. The plasmid annotations, which include the full length sequence, vector information, and associated publications, are stored in a freely available, searchable database called DNASU (http://dnasu.asu.edu). Each plasmid also links to external resources, including the PSI Structural Biology Knowledgebase (http://sbkb.org), which facilitates cross-referencing of a particular plasmid to additional protein annotations and experimental data. Currently, over 32,000 PSI expression plasmids and 75 empty vectors are available in DNASU. In addition to the PSI collection, DNASU distributes more than 118,000 plasmids, including over 35,000 human clones and nearly complete genomic collections from several organisms. In order to avoid the complexity of material transfer agreement (MTA) processing and the resulting delays this causes, the PSI:Biology-MR has developed and successfully implemented the Expedited Process MTA. This is a network of institutions that agree to the terms of transfer in advance of a material request, thus eliminating the delay researchers would typically encounter while their institution is processing the MTA. Overall, the PSI-MR's repository of expression-ready plasmids along with the expedited process for receiving these plasmids allows the research community to dissect the biological function of proteins whose structures have been identified by the PSI.

Protein Ligand Interactions: Allostery & Protein-Protein Interactions

271-Pos Board B71
Probing Allosteric Binding Site Mapping in the Free Fatty Acid 2 receptor
Irina G. Tikhonova, Nicola J. Smith, Richard J. Ward, Leigh A. Stoddart, Brian D. Hudson, Evi Kostenis, Trond Ulven, Joanne C. Morris, David R. Adams, Graeme Milligan.
Understanding of orthosteric and allosteric communications in the G protein coupled receptors (GPCRs) at molecular level may lead to new strategies in rational design of selective and efficacious drugs. A recently de-orphanized GPCR, the free fatty acid receptor 2 (FFA2) with a potential role in the regulation of appetite and energy homeostasis is modulated by a selective ago-allosteric ligand, a phenylacetamide (*S*)-4-chloro-α-(1-methylethyl)-*N*-2-thiazolylbenzeneacetamide (4-CMTB) and such, is a viable example to study these communications. In this work we have explored molecular basis of agonistic and allosteric properties of 4-CMTB and its analogues by employing computational modelling and pharmacological studies. Thus, we used available crystal structures of the ligand-activated GPCRs to model the binding site of 4-CMTB and examined computationally predicted residues of the transmembrane helices and loops by mutagenesis. Interestingly, although some single and double mutations of conserved and non-conserved residues affected the binding of a natural agonist, propionate, none of them changed the potency of 4-CMTB. The more substantial change, the swap of the second extracellular loop (EL2) between FFA2 and FFA3, abolished allosterism and not agonsim of 4-CMTB. Conformational analysis of EL2 in FFA2 revealed the possible mechanistic basis of allosteric communication. The results will be discussed in light of a general strategy to identify an allosteric binding site in GPCRs known to be more permissive with respect to the chemical structure bound to it compare to an orthosteric binding site. Importance of receptor conformational diversity and membrane environment in mapping of an allosteric binding site will be highlighted.