partitioning is driven by the spatial recruitment of proteins to the cell pole in the bacterial model system *Caulobacter crescentus*. The polar organizing protein PopZ assembles as a polymeric network at one and then the opposite cell pole where it respectively anchors the original and the newly replicated DNA. Previous super-resolution imaging experiments in our lab have determined the cytosolic locations of the partitioning system proteins, ParAB, during directional DNA segregation (Ptacin *et al*., 2010), but the role of the PopZ network in the biochemical reaction cycle of these proteins has not yet been explored. To determine precise positioning of the partitioning system proteins in relation to the PopZ polymeric network, we utilized quantitative two-color 3D super-resolution microscopy in live *Caulobacter* cells. We measured the shapes and volumes of the PopZ networks with tens of nanometer resolution and, by counting the localized PopZ proteins within each network, we determined that PopZ localizes with a globally conserved volume density. These results indicate that PopZ may serve as a homogeneous scaffold that spatially compartmentalizes the biochemical interactions of the partitioning system proteins. This model is supported by two-color super-resolution images that clearly reveal where and how the Par system proteins overlap with the PopZ networks. These data thus provide key mechanistic insights into the spatial regulation of ParAB protein activity during DNA segregation and partitioning.

325-Pos Board B80
Interaction of Human Islet Amyloid Polypeptide with Model Membranes in the Presence of a Novel Oligomer Modulator "anle138B"
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Amyloid formation in the pancreas by islet amyloid polypeptide (IAPP) is closely associated with type-2 diabetes. Compelling evidence indicates that membranes play a crucial role in contributing to IAPP amyloid formation and that IAPP amyloid formation leads to cell membrane disruption [1]. Since both IAPP amyloid formation and membrane damage are considered perilous to the insulin producing beta-cells, their inhibition may be an effective strategy for the prevention and/ or treatment of the disease. Here, we present the results of lipid monolayer insertion, vesicle leakage and ThT aggregation assays of IAPP in the presence of anti-amyloid compounds. Among several tested inhibitors, ''anle138b'', a novel modulator of oligomer formation [2] was particularly effective in inhibiting IAPP fibril formation and membrane disruption. Interestingly, the protective activity of anle138b was most significant even at low sub-stoichiometric proportions (1 to 10 molar ratio of anle138b to IAPP). We investigate the effect of anle138b on synthetic fragments of IAPP and model membranes to further dissect the molecular mechanism of the inhibition. Our findings so far suggest that anle138b is a potent amyloid blocker, that reduces membrane damage by effectively hindering IAPP aggregation and that has the potential to be a disease-modifying agent for type-2 diabetes.
[1] Engel M et al., PNAS. (2008) - 105 :6033.
[2] Wagner J et al., Acta Neuropathologica (2013) - 125: 795.
Keywords: IAPP, membrane models, anle138b, amyloid inhibitor.

Virus Structure and Assembly

326-Pos Board B81
Assembly of Transmembrane Domains of Human Papillomavirus Type 16 E5 Protein- a Molecular Dynamics Simulation Study
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Human papillomaviruses (HPV) infect mucosal and cutaneous epithelial cells leading to precancerous lesions. The HPV genome encodes three oncoproteins: E5, E6 and E7. E6 and E7 are the main transforming proteins of HPV, which are studied very well but the role of E5 is poorly understood. E5 of HPV-16, one of the ''high risk'' types of HPV strains, is an 83 amino acid hydrophobic membrane protein, with three hydrophobic transmembrane domains (TMDs) and short regions at the N and C termini that extend beyond the lipid bilayer. It oligomerizes into dimers which form channels most likely as hexameric bundles.
The three transmembrane domains of E5 are identified using secondary structure prediction programs. These TMDs are assembled into a monomer by a 'concerted' docking approach in which the conformational space of the three helices is screened by simultaneously altering distance, tilt and rotational angle between them. In a consequent step loops linking the three helices are added using the program Loopy. Finally three monomers are assembled into a hexameric bundle. The bundle with TMD2 lining the pore remains intact when inserted into a hydrated lipid bilayer. It forms an almost fully water filled pore during 100 ns MD simulations. The pore of the bundle is mostly mantled by hydrophilic residues and the pore diameter is consisted with the experimental findings.

327-Pos Board B82
Protein Interactions Regulate Virus Assembly and Replication
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Hepatitis B virus (HBV) capsids are metabolic compartments for reverse transcription. Capsids are constructed from 120 self-assembling core protein (Cp) dimers. Assembly of capsids is regulated by the protein-protein interactions at core protein interface. We hypothesize that the Cp interactions are tuned for virus replication not for capsid stability.
To test this hypothesis we designed Cp mutants with different contact energies. The starting point for our design was the structure of HBV capsid bound to heteroaryldihydropyrimidines (HAPs), small antiviral molecules that accelerate capsid assembly and strengthen Cp association by binding to a hydrophobic pocket at the Cp interface. We created mutants that filled the HAP pocket with different sized hydrophobic amino acids (V124A, V124L, V124F and V124W). The biophysical assembly properties of these mutants correlated well with the substitution. There was a linear relationship between the change in buried surface area and capsid association energy with an estimated −9 cal/(mol Å2).
However, in cell culture, these mutants have pleiotropic effects on DNA replication. Only the wild type Cp supported maximal DNA production. Mutants with stronger or weaker association energy were destructive to virus replication. Together, these data support our hypothesis that capsid association is tuned for virus replication. The proper stability of the capsid ensures its biological role in virus life cycle.

328-Pos Board B83
A Disulfide in HBV Core Protein Dimer Allosterically Modifies Capsid Assembly and Stability
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During the Hepatitis B virus (HBV) life cycle, assembly and disassembly of the capsid need to be highly regulated. The HBV capsid is formed by 120 copies of the homodimeric core protein. Capsid assembly is allosterically regulated, implying that dimer transitions from assembly-inactive to assembly-active states. Indeed, the intra-dimer interface (which is distant from the site if inter-dimer contact) in free dimer is substantially different than in dimer from capsid (Packianathan et al (2010)). The intra-dimer interface contains a pair of completely conserved cysteines at position 61 that can form a disulfide bond.
Within capsid, C61-C61 oxidized 7 times faster than in free dimer indicating dimer within capsid adopts a conformation that strongly promotes disulfide formation. However, compared to reduced dimer, oxidized protein assembled slowly and into lower yields of capsid. In addition, urea disassembly studies showed that capsids formed by oxidized dimer are less stable to urea treatment than reduced capsids.
These results indicate that oxidized protein adopts a conformation unfavorable for capsid assembly. Sucrose gradient centrifugation and electron microscopy confirmed these findings and revealed that oxidized dimer forms a higher proportion of small, 90-dimer particles than reduced protein.
Our results show that structural changes at the dimer interface can dramatically alter the assembly behavior and stability of the capsid. This distal effect is consistent with allosteric regulation of assembly. Our data also suggest an unsuspected biological role for the C61-C61 disulfide bond. We propose that newly expressed, reduced protein subunits assemble with high fidelity into capsids packaging the RNA genome. As the life cycle progresses oxidation of the capsid occurs resulting in metastable capsid particles that have a lower energy barrier to disassembly, facilitating the release of the genome.

329-Pos Board B84
Exceptional Heterogeneous Elasticity and One-Way Valve Mechanism of the PHi29 Head-Tail Connector
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The bacteriophage Φ29 DNA packaging motor, comprising ATPase, pRNA and head-tail connector, transports viral DNA inside the prohead against a