mutations. The bacterial SOS response system regulates DNA repair and other pathways responsible for the cellular response to DNA damage. Among genes upregulated during the SOS response is the umuD gene, encoding the manager protein UmuD that subsequently undergoes self-cleavage to remove its N-terminal 24 amino acids to form UmuD'. The umuD gene products are involved in managing the cellular response to DNA damage through their interactions with damage-bypass DNA polymerases DNA pol IV and pol V. Umud and Umud' also interact with the alpha DNA polymerase and beta processivity clamp subunits of the replicative DNA polymerase III. We probed the interactions between Umud or Umud' and the alpha polymerase subunit and determined that the umuD gene products interact with alpha at two sites: the N-terminal PHP domain, which is responsible for interactions with the epsilon proofreading subunit, and the C-terminal domain, which harbor interaction sites for the beta clamp, the tau subunit of the clamp loader, and single-stranded DNA (ssDNA). The C-terminal domain of alpha preferentially binds to full-length Umud. With FRET, we subsequently showed that Umud but not Umud' inhibits the interaction between alpha and beta, suggesting that early in the SOS response to DNA damage, Umud could displace alpha from the beta processivity clamp. Furthermore, optical tweezers experiments revealed that Umud specifically inhibits the interaction between alpha and ssDNA. Together, these observations suggest that Umud plays a key role in regulating the replication fork after DNA damage.

**Symposium: Biophysics of Personalized Medicine**

**1167-Symp Imaging and Treating Tumors by Targeting their Acidity with a Ph-Sensitive Insertion Peptide**

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Critical to this function, well-described BBB efflux pumps in the ATP-binding cassette (ABC) superfamily serve to limit drug penetration across the BBB. Conversely, the BBB also serves in the delivery of selected nutrients, such as amino acids, vitamins, and nucleosides, to the central nervous system. A large number of SLC transporters show enriched and high levels of expression in the human BBB. Importantly, transporters with primary roles in drug disposition in the liver and kidney are also highly enriched in the BBB. Collectively, a dynamic view of the BBB will be presented with broad implications to the delivery of drugs to the human brain.

**1169-Symp Noninvasive Personalized Genomics**

Charles Cantor.

Boston University, Boston, MA, USA.

Whenever there is cell death, apoptotic cell free DNA fragments appear in the circulation of the host. These fragments, typically 145-160 base pairs in size, represent a minute fraction of total DNA in the host circulation. If care is taken to avoid host cell breakage, the apoptotic DNA fragments can be analyzed to provide information about the genome of the cells that produced them. In pregnancy, analysis of apoptotic DNA fragments has allowed the development of very effective noninvasive aneuploidy testing. Indeed it is possible to reconstruct the entire fetal genomic DNA sequence from these fragments. In cancer it is possible to view copy number, sequence, and epigenetic differences between the tumor and the host by analyzing circulating free DNA. While this work is still at early stages it is reasonable to predict that an array of useful noninvasive cancer diagnostic tests should soon result from such studies. It is furthermore likely that a careful search for informative apoptotic DNA fragments will differ in methods and from DNA in the circulation of a normal host might lead to methods for the early detection of other clinical situations that are characterized by inappropriate cell death.

**1170-Symp Translating a Trillion Points of Data into Therapies, Diagnostics, and New Insights into Disease**

Atul J. Butte.

Stanford University, Stanford, CA, USA.

There is an urgent need to translate genome-era discoveries into clinical utility, but the difficulties in making bench-to-bedside translations have been well described. The nascent field of translational bioinformatics may help. Dr. Butte’s lab at Stanford builds and applies tools that convert more than a trillion points of molecular, clinical, and epidemiological data — measured by researchers and clinicians over the past decade — into diagnostics, therapeutics, and new insights into disease. Dr. Butte, a bioinformatician and pediatric endocrinologist, will highlight his lab’s work on using publicly-available molecular measurements to find new uses for drugs including drug repositioning for inflammatory bowel disease, discovering new treatable inflammatory mechanisms of disease in type 2 diabetes, and the evaluation of patients presenting with whole genomes sequenced.