Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

2042-Pos
Global molecular features of G protein coupled receptors conformation revealed by machine learning
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The G protein-coupled receptors (GPCRs) are membrane proteins with clinical and physiological significance. GPCRs are the target for one-third of the FDA-approved drugs and play a major role in regulation of many biological pathways inside the cells. Understanding features associated with GPCR conformational dynamics is crucial in the development of new therapeutic targets. The grand challenge with the elucidation of the GPCR conformational changes is its intricate and subtle dynamics which varies based on the structure-function relationship. To this end, it is necessary to quantitatively describe the significant features in the GPCR dynamics and correlate the atomic level motions to the features. In this study, we identified the key global motifs that can be used to predict the GPCR conformation by taking advantage of Machine Learning (ML). We have worked on GPCRdb dataset to predict the activity level and identify the significant microswitches. We proposed 3 ML approaches (XGBoost, 3D-Convolutional Neural Networks, and Graph Neural Networks) to predict the conformation of GPCR proteins. We predicted the percentage activation of each of the GPCR conformation. Using ensemble learning and by ranking the feature importance, we characterized the features that globally are significant in the activation mechanism of all GPCRs.

2043-Pos
Computationally engineered ACE2 decoy binds with nanomolar affinity with the SARS-CoV-2 spike protein
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Even with the availability of vaccines, therapeutic options for COVID-19 still remain highly desirable, especially in hospitalized patients with moderate or severe disease. Soluble ACE2 (sACE2) is a promising therapeutic candidate that neutralizes SARS CoV-2 infection by acting as a decoy. By using computational mutagenesis, we designed a number of sACE2 derivatives carrying 3 to 4 mutations. The top predicted sACE2 decoy based upon the *in silico* mutagenesis scan was subjected to molecular dynamics and free energy calculations for further validation. After illuminating the mechanism of increased binding for our designed sACE2 derivative, the design was verified experimentally by flow cytometry and BLI binding experiments. The computationally designed sACE2 decoy (ACE2-FFWF) bound the RBD of SARS-CoV-2 tightly with low nanomolar affinity and 9-fold affinity enhancement over the wildtype. Furthermore, cell surface expression was slightly greater than wildtype ACE2, suggesting the design is well folded and stable. Having an arsenal of high-affinity sACE2 derivatives will help to buffer against the emergence of SARS CoV-2 variants. Here, we show that computational methods have become sufficiently accurate for the design of therapeutics for current and future viral pandemics.

2044-Pos
Using deep mutational scanning to identify the determinants of antibiotic resistance
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Current drug discovery platforms have proven incapable of supplying enough new antibiotic types to meet the challenge of rapidly developing clinical resistances. New techniques that specifically incorporate potential resistance adaptations during design are necessary. In cases of known specific resistance mechanisms, a biophysical approach may allow rational development of existing drugs that escape resistance. In this work, we use deep mutational scanning (DMS), a next-generation sequencing-based technique that reports on the site-specific fitness effects of mutations across an entire protein, to investigate the contribution of Virginiamycin acetyltransferase (VatD) to several streptogramin analogues. While generating this, we have developed a simplified workflow for generating programmable DMS libraries incorporating insertions and deletions, providing a novel measure of a sequence-function relationship. Based on our dataset we propose strategies to increase the longevity and efficacy of antibiotics.

2045-Pos
Polyvalent guide RNAs for CRISPR antivirals
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CRISPR biotechnologies, primarily used as a tool for precision gene editing, have an emerging potential for antiviral diagnostics, therapeutics, and prophylactics. However, despite significant differences in the goals and desired outcomes between gene editing and antiviral applications, the methods for designing the guide RNAs (gRNAs) that determine the polynucleotide sequence a CRISPR effector will degrade remain the same for both: gene editing requires extreme ''specificity'' by permitting CRISPR activity only at a single target and not any other similar sequences, while antiviral applications require tolerance to clinical polymorphisms and suppression of viral mutational escape, which is often accomplished by targeting multiple viral sequences at once. We hypothesized that, if we could match target sequences in a viral genome to other targets with some shared sequence homology in the same viral genome–pairs of which we find are prevalent genomes of RNA virus genomes–and exploit the differing tendencies of CRISPR effectors to tolerate imperfect complementary between the gRNA and their targets, the sequence of a single ''polyvalent'' guide RNAs (pgRNAs) could be biophysically engineered to maximize CRISPR activity at multiple viral targets while still avoiding the host. We find that our engineered polyvalent gRNAs with RNA-targeting CRISPR-Cas13 can robustly suppress viral RNA and spread in *Nicotiana benthamiana*, andantiviral activity *in vivo* with a single polyvalent RNA is comparable to two multiplexed ''monovalent'' gRNAs (with multiplexed pgRNAs antiviral activity performing even better). *in vitro*, we find that pgRNAs can be engineered to trigger Cas13's ''collateral activity'' at viral target pairs differing by 25%, and with DNA-targeting CRISPR-Cas9 can degrade viral DNA targets with divergence up to 40%. These results represent a powerful new approach to CRISPR antivirals and highlight the need for approaches that address the differential requirements of precision gene editing *vs.* CRISPR antivirals.

2046-Pos
Enhancing the biostability of nucleic acid nanostructures
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Nanometer-sized features and molecular recognition properties make DNA a useful material for nanoscale construction, but degradation in biological fluids poses a considerable roadblock to biomedical applications of DNA nanotechnology. Here, we report the remarkable biostability of a multistranded motif called paranemic crossover (PX) DNA. Compared to double stranded DNA, PX DNA has dramatically enhanced (sometimes >1000 fold) resistance to degradation by four different nucleases, bovine and human serum, and human urine. We trace the cause of PX's biostability to DNA crossovers, showing a continuum of protection that scales with the number of crossovers. These results suggest that enhanced biostability can be engineered into DNA nanostructures by adopting PX-based architectures or by strategic crossover placement. We also explore potential chemical modifications for enhancing the biostability of nucleic acid nanostructures (eg: 2'-5' linkages) and develop general strategies that can be used to create robust nucleic acid nanostructures for biophysical and biomedical applications.

2047-Pos
Controlled laser-induced fabrication of multichannel solid-state nanopore sensors for studying single-molecule protein dynamics
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Nanopores have emerged in recent years as a sensitive and informative sensor for probing biomolecules at a single-molecule level. Nanopore sensing is achieved by recording the ion flux through a small pore submerged in an aqueous electrolyte by applying a voltage bias across it. The essential parameters of an analyte are then deduced through resistive pulses in the ionic current as it is electrokinetically captured and driven through the pore. Solid-state nanopores have recently gained traction as high-resolution sensors for protein characterization because unlike their lipid-embedded