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Designing multivalent immunogens for vaccine optimization

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Databases now contain thousands of sequences for emerging pathogens. High definition structures have been determined for many of their proteins and even whole viruses. The current challenge is to incorporate this information into the design of 21st century vaccines, which can provide better protection against rapidly evolving pathogens. Conventional vaccines begin by modifying a single strain or combining several wild type strains. The starting point is often a historical isolate, which may have been passaged multiple times in different labs. We have developed methods to extract the information in large multiple sequence alignments to design reference sequences for viral families, and immunogens to protect against many different viruses. First, a PCP-consensus sequence that is most similar in its physical chemical properties to all the sequences in an alignment is chosen. This sequence can then be modified by altering the regions of maximum variability, and known epitopes, to obtain a stable protein that can generate protective antibodies against many different related pathogens. The PCP consensus sequence for a group of proteins (e.g., for each Dengue serotype) provides a rational reference that can be used to select the naturally occurring strain that is closest to the mean for the family. This talk will show how the method can be used to produce a tetravalent antigen against all four Dengue strains and to define the common properties of enterovirus VPgs and allergenic proteins.

Biography

Catherine H. Schein received a PhD in Microbiology at the Swiss Federal Institute of Technology (ETH-Zurich), after completing a MSc from MIT in Biochemical Engineering and a BA from the University of Pennsylvania in biochemistry. She began her career at Biogen, where she developed processes for and directed recombinant production of human interferons and other cytokines. She returned to basic research at the ETH and UTMB. Her current projects are on methods for defining B-cell epitopes in allergens and viral proteins and identifying inhibitors of enteroviruses and bacterial toxins.

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