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Directed evolution of new viruses for therapeutic gene delivery

David V Schaffer
University of California, USA

Gene therapy - the transfer of therapeutic DNA into the cells of a patient to treat and potentially cure human disease, has been succeeding in addressing unmet medical needs in increasing number of human clinical trials over the past 5 years. These studies, which have utilized engineered viral carriers in which viral genes have been removed and replaced with therapeutic DNA to treat disease, have established that gene delivery vehicles based on viruses are efficient, safe, and capable of therapeutic gene transfer to numerous target cells and tissues. In particular, nanoscale vehicles or vectors based on the adeno-associated virus (AAV) are highly promising; however, numerous challenges limit their broader utility such as immune responses, physical barriers within complex tissue structures, low delivery efficiency to many cell types, and an inability to target delivery to specific cells. These challenges are not surprising, as nature did not evolve viruses for use as human therapeutics. Rational design has made progress in creating viral variants to address several shortcomings; however, in most situations there is insufficient mechanistic knowledge of underlying virus structure-function relationships to empower rational design with the capacity to engineer a virus. We have been developing directed evolution approaches to address a number of problems with AAV. Directed evolution - which emulates the natural evolution process, involves the iterative genetic diversification of a viral genome and functional selection for desired properties. Using this process, we have fundamentally shifted and improved a number of viral delivery properties with implications for clinical gene therapy.

Biography

David V Schaffer received his Bachelor of Science from Stanford University and PhD from MIT, and was then a postdoc at the Salk Institute before moving to UC Berkeley in 1999. He applies engineering principles to enhance stem cell and gene therapy therapeutics, work that includes molecular engineering of new viral vectors as well as technologies to investigate and control stem cells. He has received an NSF CAREER Award, Office of Naval Research Young Investigator Award, Biomedical Engineering Society Rita Shaffer Young Investigator Award, American Chemical Society Young Investigator Award, and College of Fellows of the American Institute of Medical and Biological Engineering.

schaffer@berkeley.edu