City University of Hong Kong
Department of Biomedical Sciences
presents a seminar

香港城市大學
City University of Hong Kong
專業 創新 胸懷全球
Professional · Creative
For The World

"Structure-guided iterative evolution of antigenically advanced AAV variants for therapeutic gene transfer"

by

Dr Long Ping Victor Tse
Gene Therapy Center
University of North Carolina

Date : 14 Oct 2016
Time: 4:00pm to 5:30pm
Venue: Meeting room 2-130, 1/F, Block 2, To Yuen Building, CityU

Abstract

The problem of pre-existing neutralizing antibodies (NAbs) against Adeno-associated viruses (AAV) poses a major and unresolved challenge for clinical gene therapy using recombinant AAV vectors. In order to enroll for ongoing clinical trials, patients must satisfy stringent exclusion criteria requiring very low to undetectable titers of anti-AAV NAbs. Here, we combine structural information from cryo-reconstruction of capsid-antibody complexes and antigenic footprint mapping with accelerated evolution to select antigenically advanced AAV variants. By iteratively engineering common antigenic motifs (CAMs) on the AAV capsid, we generate new capsid surface topologies that are not present on ancestral, extant, or mosaic AAV strains. One variant, AAV-CAM130, derived from AAV serotype 1, mediates robust gene transfer to cardiac tissue as well as the brain. More importantly, CAM130 efficiently evades anti-AAV1 neutralizing sera obtained from pre-immunized mice and rhesus macaques. Further, the CAM130 variant displays robust escape from broadly neutralizing antibodies in naïve primate and human serum samples at dilution factors as high as 1:5, thereby eliminating exclusion criteria mandated by several ongoing clinical trials. The technology platform described herein can be applied to any AAV strain - natural isolate, or engineered variant. Thus, our approach yields antigenically advanced AAV vectors that can evade NAbs across multiple species and expands the cohort of patients eligible for gene therapy.

Contact

Ms Irene Wong (3442-4707, Irene.Wong@cityu.edu.hk)

All are welcome