Generation of novel adeno-associated virus (AAV) libraries with random mutation on AAV capsid through Error-prone PCR

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Directed evolution of AAV through several rounds of in vitro / in vivo selection is a powerful method to isolate variants with improved properties from large libraries of capsid mutants. AAV libraries used for directed evolution are based on wild-type AAV which has specific tropisms depending on AAV serotype. For directed evolution to be used successfully, it is important to maximize the diversity of AAV libraries and control mutation rate on AAV capsid during the production of the viral libraries. Here, we demonstrate that several AAV serotype based libraries are generated with Error-prone PCR and have high diversity of the libraries. Also, the mutation rate was controlled by manganese concentration. With these AAV libraries, we are conducting in vitro AAV libraries selection on Human Pulmonary Artery Smooth Muscle Cells (HPASMC) to improve transduction efficiency compared to wild type AAV.