Localized gene delivery using adeno-associated viral vectors

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The capacity to mediate localized gene expression via substrate-mediated gene delivery would greatly enable numerous applications in gene therapy: i) by reducing systemic spread of vectors at the target delivery site and ii) by reducing immune responses against the vector, potentially preventing side effects in off-target regions. Immobilizing gene delivery vectors onto substrates, which serve for cell adhesion, can function to place the vectors directly inside the cellular microenvironment for subsequent cellular internalization. Importantly, this system has the potential to reduce the vector quantities required for high level of gene expression, such that the use of lower doses can potentially reduce cellular toxicity. We have developed a strategy to mediate immobilization of adeno-assoicated viral vectors (AAV) directly onto a substrate to which cells subsequently adhere, thus maintaining high local concentration of AAV vectors with the cell microenvironment as well as increasing the extent of physical contact with the attached cells. The development of systems with the capacity to mediate localized gene expression as well as high efficiency gene delivery will have strong potential for numerous disease therapies.