MIMICKING THE HOST: GENE ADDITION VIA ADENO-ASSOCIATED VIRUS (AAV) TO REDUCE REJECTION IN ORGAN TRANSPLANTS

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Background. Organ transplantation is a crucial medical advancement, offering life-saving treatment for patients with end-stage organ failure. Despite significant progress, graft rejection remains a major cause of transplant failure. The immune system often attacks the transplanted organ as a foreign body, complicating long-term success. Although immunosuppressive therapies help reduce rejection risk, they have serious side effects, such as increased susceptibility to infections, malignancies, and organ toxicity.Recent research focuses on genetic engineering to address graft rejection. One promising approach is using Adeno-Associated Virus (AAV) vectors to deliver immune-modulatory genes to transplanted organs. AAV-based gene delivery can potentially promote immune tolerance by regulating T-cell activation. Genes like CTLA-4Ig or PD-L1 can be introduced to help the transplanted organ integrate into the recipient's immune system, reducing rejection likelihood.
Materials/Methods. A systematic review was conducted using PubMed, Scopus, and Web of Science (2000–2024). Peer-reviewed studies on AAV-mediated gene addition for reducing transplant rejection in English were included, while non-peer-reviewed and irrelevant articles were excluded. Findings were synthesized into key themes such as organ transplant rejection, immunosuppressive therapy, host immune profile, and AAV-mediated gene therapy.
Results. AAV-mediated gene addition, especially the delivery of CTLA-4Ig, has shown promise in reducing organ transplant rejection by inhibiting T-cell activation. AAV vectors, particularly AAV8 and AAV9, target liver cells and express CTLA-4Ig in hepatocytes, modulating immune responses. However, challenges persist, including variable transduction efficiency, immune responses against AAV vectors, and short gene expression duration. Pre-existing immunity against AAV vectors can limit gene delivery, and potential side effects such as immune reactions and genotoxicity remain concerns. Self-complementary AAV vectors reduce integration risks.
Conclusion. Advancements in vector design and gene therapy techniques may revolutionize organ transplantation. AAV-mediated gene addition could offer an alternative to traditional immunosuppressive therapies, improving long-term transplant success and reducing side effects. The goal is personalized gene therapy that mimics the host's immune profile, promoting long-term graft acceptance without lifelong immunosuppressive drugs. Continued research and clinical trials will be essential to fully realize AAV-based therapies in transplantation.
Keywords. Adeno-Associated Virus (AAV); Gene Addition; Organ Transplantation; CTLA-4Ig; Immune Tolerance.