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Editorial

Biomaterials for Gene Delivery: Translational Perspectives

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Gene therapy represents a paradigm shift in modern pharmaceutical sciences, enabling therapeutic intervention at the level of gene expression and molecular regulation. Advances in nucleic acid therapeutics, including plasmid DNA, siRNA, mRNA, and genome editing tools, have expanded the therapeutic landscape for cancer, genetic disorders, regenerative medicine, and immunotherapy [1,2]. However, the clinical translation of gene-based therapeutics remains fundamentally dependent on the development of safe, efficient, and controllable delivery systems. In this context, biomaterial-based platforms have emerged as essential enabling technologies, offering tunable, biocompatible, and scalable solutions for gene delivery [3].

Among emerging biomaterial systems, polymeric hydrogels have gained particular attention due to their structural similarity to the extracellular matrix and their ability to encapsulate and protect nucleic acids while enabling controlled and localized release [4]. In recent years, our research and others have demonstrated the potential of poly(vinyl alcohol) (PVA)-based hydrogels as versatile gene delivery platforms [2,4,5]. PVA is a synthetic, biocompatible, and mechanically tunable polymer capable of forming physically or chemically crosslinked networks that provide structural stability and controlled permeability. When engineered as DNA-loaded hydrogel matrices, PVA systems enable sustained release of genetic material, protect nucleic acids from enzymatic degradation, and facilitate cellular uptake over extended periods [6].

PVA-based DNA hydrogels represent a promising class of gene delivery scaffolds with applications in regenerative medicine, localized gene therapy, and tissue engineering. These biomaterials allow precise modulation of release kinetics by adjusting polymer concentration, crosslinking density, and network architecture [2,4]. Importantly, the hydrogel environment enhances nucleic acid stability while providing a protective and hydrated matrix that mimics physiological conditions. Such systems offer advantages in localized therapeutic applications, where sustained gene expression is required to promote tissue repair, angiogenesis, or cellular reprogramming [2].

Beyond injectable and implantable systems, transdermal gene delivery platforms represent a particularly attractive translational strategy. The skin provides an accessible and minimally invasive route for therapeutic delivery, avoiding systemic toxicity and improving patient compliance [7]. However, the stratum corneum presents a major barrier to nucleic acid transport. Biomaterial-based transdermal platforms, including hydrogel patches, microneedle-integrated systems, and bioadhesive polymer matrices, have demonstrated significant promise in overcoming these barriers. PVA-based hydrogel patches offer excellent mechanical flexibility, skin adhesion, and hydration properties, enabling localized and sustained delivery of nucleic acids across the skin barrier [8].

Transdermal gene delivery systems based on biomaterial scaffolds offer important advantages for the treatment of cardiovascular diseases, chronic wounds, inflammatory conditions, and localized genetic disorders [10]. These systems allow spatially controlled therapeutic delivery, minimizing systemic exposure

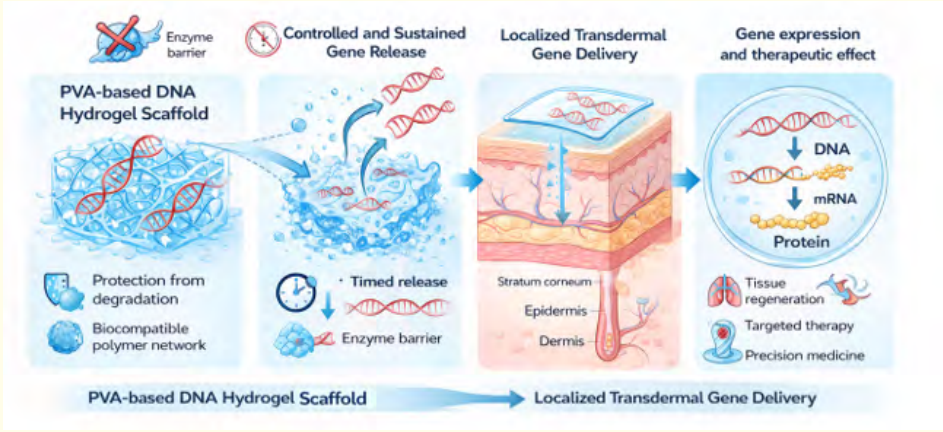

Figure 1: PVA-based DNA hydrogels enable protection, controlled release, and localized transdermal delivery of nucleic acids, supporting efficient gene expression and translational therapeutic applications [9].

while maximizing local therapeutic efficacy. Moreover, hydrogel-based transdermal systems can be engineered to respond to environmental stimuli, such as pH, temperature, or enzymatic activity, enabling intelligent and adaptive therapeutic release.

Controlled release represents a fundamental advantage of biomaterial-mediated gene delivery systems. Unlike conventional bolus administration, biomaterial-based platforms enable sustained and programmable release profiles, improving therapeutic efficiency while reducing dosing frequency [2]. This capability is particularly important for gene therapies requiring prolonged expression or repeated administration. By modulating material composition, network structure, and degradation kinetics, biomaterials can be engineered to achieve precise temporal control over nucleic acid release. Such controlled delivery enhances therapeutic outcomes while minimizing adverse effects [2,4].

From a translational perspective, biomaterial-based gene delivery systems offer significant advantages for clinical and industrial implementation. Synthetic polymers such as PVA are cost-effective, scalable, and compatible with established pharmaceutical manufacturing processes [4]. Their chemical stability and reproducibility facilitate regulatory approval and industrial production [5]. Moreover, biomaterial-based delivery systems eliminate many safety concerns associated with viral vectors, including immunogenicity and insertional mutagenesis. These features position biomaterial-based gene delivery platforms as strong candidates for next-generation gene therapeutics [11].

Future directions in biomaterial-based gene delivery are likely to focus on intelligent, multifunctional systems capable of integrating sensing, targeting, and controlled therapeutic release. Advances in polymer chemistry, nanotechnology, and biofabrication are expected to enable next-generation gene delivery platforms with enhanced safety, efficiency, and clinical applicability. Hydrogel-based systems, including PVA-DNA biomaterials and transdermal delivery platforms, hold significant promise for advancing localized and personalized gene therapy.

In conclusion, biomaterial-based gene delivery systems represent a transformative technology in pharmaceutical sciences. Platforms such as PVA-based DNA hydrogels and transdermal biomaterial scaffolds offer safe, controllable, and translationally viable alternatives to conventional gene delivery approaches. Continued innovation in biomaterials design and translational development will play a central role in shaping the future of gene therapy and precision medicine. As these technologies move from laboratory research to clinical and industrial application, biomaterial-based gene delivery systems are poised to become a cornerstone of next-generation therapeutic strategies.

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