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Epigenetics in Precision Medicine for Kidney Disease

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Epigenetic modifications include DNA/RNA methylation, histone modification, and non-coding RNAs. Among these, DNA methylation has been the most extensively and comprehensively studied. Modulating the epigenome has long been regarded as a promising therapeutic strategy for various diseases. While several approved therapies target cancer, their potential application in kidney diseases remains underexplored.

In kidney diseases, epigenetic modifications play critical roles in regulating gene expression and cellular function. Methylome-wide association studies (MWAS) have been conducted on renal tissue, peripheral blood, and urine, linking these findings to kidney disease phenotypes such as estimated glomerular filtration rate (eGFR), eGFR decline rates, and albuminuria. Additionally, MWAS data have been integrated with genome-wide association studies (GWAS), single-cell RNA sequencing, and single-cell ATAC sequencing, significantly advancing our understanding of the causal relationships between epigenetic changes and kidney diseases. These insights contribute to the development of novel biomarkers and precision medicine approaches.

However, epigenetic therapies face significant challenges, including lack of specificity, safety and tolerability concerns, and off-target effects. Current strategies aim to develop effector proteins that bind to sequence-specific DNA-binding domains (DBDs) to direct epigenetic modifications to precise genomic loci. This approach allows for the fine-tuning of gene expression rather than binary activation or silencing. Such "epigenomic programming" enhances therapeutic efficacy, reduces dosage requirements, minimizes side effects, and prolongs the duration of therapeutic effects.

Further specificity is achieved through advanced delivery systems, such as cell- or tissue-specific vectors. Many developers are now leveraging cell-specific lipid nanoparticles, which offer greater flexibility compared to adeno-associated viral vectors. These innovative therapeutic modalities, which harness epigenetics and epigenomics, have significant potential to revolutionize kidney disease treatment in the near future.