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신장 집합관 세포에서 항이뇨호르몬 수용체 V2R를 매개로 한 siRNA 전달

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정현준, 임정숙, 최효정, 이미숙, 김종호, 김상엽, 김소연, 김은정, 권태환

Vasopressin V2R-targeting Peptide Carrier Mediates siRNA Delivery into Collecting Duct Cells

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Internalization of receptor proteins after interacting with specific ligands has been proposed to facilitate siRNA delivery into the target cells via receptor-mediated siRNA transduction. In this study, we demonstrated a novel method of vasopressin V2 receptor (V2R)-mediated siRNA delivery against AQPs (AQP2 or AQP4) in primary cultured inner medullary collecting duct (IMCD) cells of rat kidney. We synthesized the dDAVP conjugated with nine D-arginines (dDAVP-9r) as a peptide carrier for siRNA delivery. The structure of synthetic peptide carrier showed two regions (i.e., ligand domain to V2R (dDAVP) and siRNA carrying domain (nine D-arginine)) bisected with a spacer of four glycines. The results revealed that 1) synthesized dDAVP-9r peptides formed a stable polyplex with siRNA; 2) siRNA/dDAVP-9r polyplex could bind to the V2R of IMCD cells and induced AQP2 phosphorylation (Ser 256); 3) siRNA/dDAVP-9r polyplex was stable in response to the wide range of different osmolalities, pH levels, or to the RNases; 4) fluorescein-labeled siRNA was delivered into V2R-expressing MDCK cells by siRNA/dDAVP-9r polyplex; and 5) siRNA/dDAVP-9r polyplex effectively delivered siRNA into the IMCD cells, resulting in the significant decrease of protein abundance of AQP2 or AQP4. Therefore, for the first time to our knowledge, we demonstrated that V2R-mediated siRNA delivery could be exploited to deliver specific siRNA to regulate abnormal expression of target proteins in V2R-expressing kidney cells. The methods could be potentially used in vivo to regulate abnormal expression of proteins associated with disease conditions in the V2R-expressing kidney cells.

Key Words: 아쿠아포린, 집합관, siRNA 전달
Aquaporin, Collecting duct, siRNA delivery