Synopsis of Original Research Paper

Maintenance of skin homeostasis by intradermal siRNA delivery using novel nano particles

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To advance the therapeutic outcome of the skin disease, small interfering RNA (siRNA) is expected. However, the therapeutic use of siRNA requires a drug-delivery system because unmodified naked siRNA is immediately degraded by nucleases, it penetrates poorly through the plasma membrane, and it induces interferon responses after systemic injection. For safe and effective delivery of siRNA, we developed binary complex based on dendrigraft poly-L-lysine (DGL) and ternary complex which was constructed by addition of γ-polyglutamic acid (γ-PGA) to binary complex. The siRNA which could knock down the firefly luciferase gene was used as a model siRNA. The complexes were approximately 50-140 nm in particle size. The binary complex showed a cationic surface charge although an anionic surface charge was observed in the ternary complex. The binary complex and the ternary complex showed a significant silencing effect in the mouse melanoma B16-F10 cell expressing luciferase regularly (B16-F10/Luc cells). The binary complex showed significant cytotoxicity and blood agglutination although the ternary complex decreased these toxicities. Furthermore, the ternary complexes showed significantly silencing effects in the tumor-metastasized mice *in vivo*. Thus, we developed the siRNA vector having a potential to become a new nucleic medicine in skin disease therapy.