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遺伝子導入用葉酸修飾ナノプレックスの開発

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[Aim] Systemic injectable and efficient gene delivery vector has become the most critical issue to realize successful clinical gene therapy. Simple complexes of liposome and nanoparticle with DNA are somewhat effective for *in vitro* gene transfection, but they fail regrettably to induce significant gene transfection following intravenous injection. Due to the effectiveness of OH-Chol-nanoparticle complex with pCMV-luc DNA (OH-Chol-nanoplex) for gene transfection *in vitro* and in xenograft tumors by intratumor injection (OH-Chol=cholesteryl-3β-carboxyamindoethylene-*N*-hydroxyethylamine), here we reported that OH-Chol-nanoplex coated by anionic liposome, namely lipid coated nanoplex (LCN) and then LCN was modified by folic acid, as gene delivery vector *in vitro* and *in vivo*. The folate-targeting effect and gene transfection ability of LCN were investigated in KB cells.

[Methods and results] Heparin decomplexation and gel filtration chromatography experiments confirmed that OH-Chol-nanoplex was successfully coated by anionic liposome simply by mixing them together. However, lipid coating resulted in low gene transfection ability compared with bare OH-Chol-nanoplex. As evaluated by flow cytometry and luciferase assay, folic acid modification of LCN significantly increased the cellular uptake and gene transfection in KB cells with high selectivity.

[Discussion] The lipid coating of nanoplex might decrease the cellular uptake of DNA and hamper DNA dissociation after internalization into KB cells. We are now trying to increase the gene transfection ability of LCN by optimizing the lipid composition and functional modification.