

Intratracheal therapy using oligodeoxynucleotides and/or genetically modified
lactic acid bacteria-derived biological molecules

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This plenary lecture is intended to highlight current projects using bioactive compounds such as small molecules, synthetic oligodeoxynucleotide (ODN), and single-chain variable fragment (scFv) to target their delivery to the lungs. For the treatment of inflammatory diseases and cancer of the lungs, there could be considerable benefit of increased efficacy, reduced dose, and fewer side effects to administering such bioactive component directly to the target sites. First, the talk focuses recent progress in the use of nano/microparticles as carriers of small active compound and ODN to target their direct delivery to the lungs. A representative project using small active compound is planned for repositioning the oral tyrosine kinase inhibitor nintedanib, a medicine used to treat interstitial lung diseases, for inhalational use. The particle formation technology enables us to create the easily solubilized medication suitable for inhalation, resulting in favorable attenuation of disease progression in pulmonary fibrosis model. Another particle formation method could develop local intratracheal immunotherapy with immunostimulatory ODN that contributes to shifting the immune milieu surrounding the tumor from suppressive to tumoricidal and maintaining long-term anti-tumor immunity. Based on our growing attention of the intratracheal delivery system, the current project expands the use of genetically modified lactic acid bacteria (gmLAB) that secretes bioactive protein/scFv. Nasally administering the gmLAB could migrate to the lungs and deliver/produce the bioactive molecules in the lungs, leading further transferred to the systemic circulation. Perhaps of greatest importance, local delivery of these bioactive agents would prove useful in the prevention/treatment of lung diseases. In addition, this approach may lead to the development of microbial therapeutics that will contribute to the prevention or suppression of many types of diseases.

Keyword: Oligodeoxynucleotide, gmLAB, intratracheal therapy, lung disease.

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