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Title: Intratracheal administration of dry powdered low-molecular-weight chitosan/siRNA complexes suppressed gene expression in the airway, alveoli, and metastatic tumors in murine lung

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Body: Introduction; There is an increasing number of efforts to deliver small interfering RNA (siRNA) to lung. Although many different formulations with siRNA have been optimized in in vitro studies, only a few have been reported successful in vivo. Objectives; As a carrier of siRNA, we chose low-molecular-weight chitosan (LMWC) and succeeded in producing dry powder of LMWC/siRNA complexes. In the present study, we tried to determine whether intratracheal administration of dry powdered LMWC/siRNA complexes suppressed gene expression in murine lung. Methods; Dry powdered LMWC/siRNA targeting green fluorescent protein (GFP-siRNA) and Lewis lung carcinoma cells stably expressing GFP (LLC-GFP) were prepared. Dry powder of LMWC/GFP-siRNA complexes was intratracheally administered to GFP transgenic mice and the C57BL/6 mice injected with LLC-GFP cells through tail vein. The fluorescence in the lung tissue sections was analyzed with a BIOREVO fluorescence microscope (BZ-9000; KEYENCE, Japan). Results; Intratracheal administration of LMWC/GFP-siRNA complexes was found to suppress the fluorescence level of bronchial epithelium and alveoli in the lung of GFP transgenic mice. It was also effective at reducing the fluorescence level in metastatic lung tumors consisting of LLC-GFP cells. Conclusion; The results of the present study suggest that LMWC is an effective carrier for siRNA delivery to the lung, and powdered LMWC/siRNA complexes may become a promising tool to knock-down a specific gene expression in various lung diseases.