The Chinese University of Hong Kong
Department of Biomedical Engineering

Engineered design of mucus penetration nanoparticles for inhalable vaccines

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Abstract

Mucosal drug delivery has gained significant attention due to its advantages over traditional injection, e.g., convenience and avoidance of blood-borne diseases. During mucosal administration, a key factor that must be considered is the mucus barrier. Various surface modification strategies, including PEG and zwitterionic polymer, have been explored for mucus-penetrating carriers. However, the microenvironment of mucus varies under different physiological or pathological conditions, and the influence of surface properties of nanoparticles on their mucus penetration in various microenvironments remains unclear. In our study, we have prepared a comprehensive library of amine-, carboxyl-, and PEG-modified nanoparticles with controlled surface ligand densities. We demonstrated that surface properties are critical factors in determining their mucus penetration, which is affected by the mucus pH microenvironments, the type of surface modification, and the ligand density of NPs. PEG- and amine-modified particles exhibited pH-independent immobilization under iso-density conditions, while carboxyl-modified particles exhibited enhanced movement only in weakly alkaline mucus. Biophysical analysis indicated that the penetration behavior was mediated by the NP-mucin interaction, including electrostatic interaction and hydrogen bond. Based on these mechanistic insights, we have engineered mucosal vaccine delivery nanoparticles. In a prophylactic vaccination model, these particles have been shown to enhance both humoral and cellular immune responses, leading to the production of antigen-specific mucosal and systemic immune responses. Our study reveals the underlying mechanisms of mucus penetration and provides valuable insights for the rational design of prophylactic and therapeutic mucosal vaccines.

Biography

Dr. Bingbing Sun received his B.S. and M.S. in Chemical Engineering from Dalian University of Technology (DUT), and a Ph.D. in Chemical Engineering from the University of Washington. He completed his postdoctoral training at the University of California, Los Angeles (UCLA). He started his academic career in the Department of Chemical Engineering at DUT in 2016. Currently, he is a tenured full professor and serves as the Executive Dean of Dayu College at DUT. His research interests include vaccine adjuvants, biomaterials, nano-bio interface, and immunoengineering. He serves as editorial board member for Scientific Reports and is also on the earlier career researchers editorial board for BMEMat

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