

Lipid Nanoparticle Formulation Strategies for Peptide-Based Cancer Vaccines

Summary

This thesis advances the field of cancer immunotherapy by developing innovative cancer vaccine platforms using lipid nanoparticles (LNPs) and potent adjuvants to enhance immunogenicity and therapeutic efficacy. It begins with a comprehensive overview of vaccine technologies developed in response to the COVID-19 pandemic, highlighting both traditional and advanced platforms, with a particular focus on the role of LNPs in mRNA delivery and immune adjuvant incorporation. The research then introduces a novel series of ionizable biscarbamate lipids (IBLs) for use in LNP formulations, identifying S-Ac7-DOG as a promising candidate due to its superior mRNA expression. A method for formulating peptide antigens and a TLR7/8 agonist into LNPs is presented, demonstrating the system's ability to induce a robust CD8⁺ T cell response and confer protective immunity against tumors. The thesis further explores the use of various TLR agonists in LNP formulations, finding that these formulations, particularly LNP(poly(I:C)), are more effective in stimulating immune responses than soluble forms. Additionally, a novel technology for the universal encapsulation of peptides into nanoparticles is developed, significantly enhancing antigen-specific CD8⁺ T cell responses when co-delivering peptide antigens with TLR agonists. Finally, the work is contextualized within the broader international effort to advance personalized neoantigen vaccines, which promise greater tumor specificity and reduced off-target effects, highlighting their potential to elicit strong T-cell responses against cancer.