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Potent anti-viral vaccine adjuvant based on pH-degradable nanogels with covalently linked small molecule imidazoquinoline TLR7/8 agonist

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Abstract

Improving the immunogenicity of subunit vaccines, in particular skewing of the immune response towards Th1 type immunity, is crucial for the development of effective vaccines against intracellular infections and for the development of anti-cancer vaccines. Small molecule TLR7/8 agonist hold high potential for this purpose, but suffer from an undesirable pharmacokinetic profile, resulting in systemic inflammatory responses. An effective solution to this problem is covalent ligation to a larger carrier. Here, a degradable nanogel carrier containing a covalently linked imidazoquinoline (IMDQ) TLR7/8 agonist is explored as adjuvant for vaccination against the respiratory syncytial virus (RSV). *In vitro* and *in vivo* experiments in mice provide a solid rational base for preferring nanogels over soluble polymers as IMDQ carrier in terms of cellular uptake and lymph node accumulation.