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Advancing influenza virus treatment: in vitro and ex vivo studies of PI3K inhibitor-loaded lipid nanoparticles

Inhalt

Influenza A viruses (IAVs) continue to pose a major global health threat. Annual vaccination provides only limited protection against emerging subtypes, and rising resistance to approved antivirals highlights the need for alternative therapeutic strategies. Host-directed therapies, such as targeting phosphatidylinositol 3-kinases (PI3Ks) exploited by IAVs during replication, offer promising alternatives. At the same time, advances in nanotechnology have established lipid nanoparticles (LNPs) as effective carriers that enhance drug stability, bioavailability, and targeted delivery. This study explores the combination of the PI3K inhibitor pictilisib with LNPs as a potential antiviral strategy. To improve circulation and distribution, LNPs commonly include "stealth"polymers. Here, established polyethylene glycol (PEG) Lipids were compared to poly(2 oxazoline) (POx) Lipids. PEG is widely used but associated with immunogenicity, whereas POx offers similar shielding with lower risk of hypersensitivity. Using both systems, pictilisib was efficiently encapsulated and retained antiviral and anti inflammatory activity comparable to the free drug in vitro. Notably, ex vivo experiments showed that POx-LNPs loaded with pictilisib were more effective than free pictilisib, indicating improved stability and local availability. These findings suggest that PI3K targeted LNP formulations may provide a promising approach for further development of future IAV intervention strategies.

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