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Anti-SARS-CoV-2 platform based on maleimide-functionalized liposomes

The rapid spread of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has led to an unprecedented public health crisis worldwide. The intensive work on vaccine development, prompted by the COVID-19 pandemic, has led to milestone achievements in mRNA and liposome-based technologies and raised the general interest in lipid nanocarriers. However, due to the limitation of vaccine-induced immunity as well as the emergence of new virus mutations, the challenge remains to develop specific, targeted drugs that inhibit the progression of the infection. In response to that call, we developed a platform against the SARS-CoV-2 virus using maleimide-functionalized liposomes, inhibiting the viral binding with the ACE2 receptor, thus blocking the infection progression. A polyethylene glycol molecule containing a maleimide functional group was used to immobilize a short peptide sequence with high affinity towards the viral spike protein. To ensure high homogeneity and long-term stability of peptide-liposome preparations, extensive optimizations were made towards e.g. lipid composition of the nanocarrier and manufacturing approaches. We found that changes in cholesterol content and using various phosphatidylglycerol species not only affect long-term stability but also alter the functionality of peptide-liposome formulations in vitro. We used two techniques to calibrate liposomes: a high-pressure homogenization and extrusion. Although better parameters were achieved with the latter, after optimization of liposome composition both techniques allowed to generate homogeneous, stable preparations. The inhibitory effect of the peptide-liposomal preparation was confirmed in vitro on ACE2-expressing cells using a syncytia-forming assay and a luciferase-labeled pseudovirus. In addition to the anti-SARS-CoV-2 peptide, the same maleimide-functionalized liposomes were used to immobilize the anti-influenza peptide. Based on elaborated techniques and protocols, equally stable formulations were obtained, demonstrating our maleimide-based liposomal platform's great potential against COVID-19, influenza, and other infections caused by RNA viruses.

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References

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