High-Throughput Synthesis and Evaluation of Antiviral Copolymers for Enveloped Respiratory Viruses

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COVID-19 made apparent the devastating impact viral pandemics have on global health and order. Development of broad-spectrum antivirals to provide early protection upon the inevitable emergence of new viral pandemics is critical. In this work antiviral polymers are discovered using a combination of high-throughput polymer synthesis and antiviral screening, enabling diverse polymer compositions to be explored.[1] Amphipathic polymers, with ionizable tertiary amine groups are the most potent antivirals, effective against influenza virus and SARS-CoV-2, with minimal cytotoxicity. It is hypothesized that these polymers interact with the viral membrane as they showed no activity against a non-enveloped virus (Rhinovirus).[2] This presentation will showcase how the switchable chemistry of the polymers during endosomal acidification was evaluated using lipid monolayers, indicating a complex synergy between hydrophobicity and ionization drives polymer-membrane interactions. Structural characterization of polymer-lipid membrane interactions via scattering and QCM-D was used to probe the mechanism of action. Preliminary preclinical evaluation of the lead candidates in model endothelial experiments with primary patient cell lines, and in vivo models, will showcase the promise of this novel class of antiviral materials.

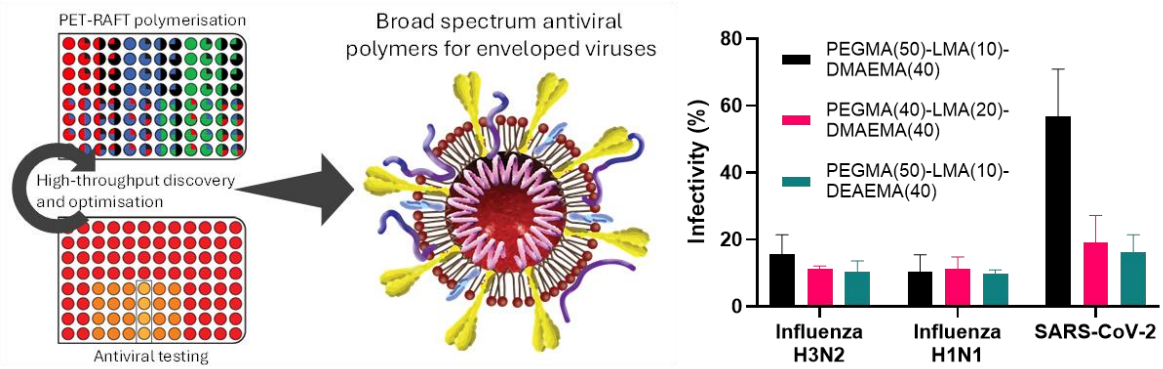

Figure 1: High-throughput synthesis and evaluation of antiviral polymers led to the identification of lead candidates with broad spectrum efficacy against enveloped respiratory viruses. Immunoplaque assay for viral infectivity was conducted on MDCK and Vero E6 cells.

References:

[1] Mengist, H. M.; Denman, P.; Frost, C.; Sng, J. D. J.; Logan, S.; Yarlagadda, T.; Spann, K. M.; Barner, L.; Fairfull-Smith, K. E.; Short, K. R.; Boase, N. R. B. *Biomacromolecules* **2024**, *25* , 7377-7391.
[2] Vigant, F.; Santos, N. C.; Lee, B. *Nature Reviews Microbiology* **2015**, *13*, 426-437.