Enabling Influenza Virus-like Particles (VLPs) as a Universal Vaccine

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To provide broader protection and eliminate the need for the annual update of influenza vaccines due to mutations in the hemagglutinin (HA) and neuraminidase (NA) glycoproteins, biomolecular engineering of influenza virus-like particles (VLPs) to display more conserved proteins such as the matrix protein M2 has been explored. However, the incorporation of full-length M2 into influenza VLP has been left unrealized due to its cytopathic effects in cell culture systems. In this work, it shows that M2 induces significant cytopathic effects in Spodoptera frugiperda (Sf9) insect cells when expressed using baculovirus as the gene carrier. These effects include altered Sf9 cell morphology and reduced baculovirus replication, resulting in impaired influenza viral protein expression and thus VLP production. Based on the function of M2, it was hypothesized that blocking its ion channel activity could potentially relieve these cytopathic effects, and thus restore protein expression to improve VLP production. The use of the M2 inhibitor amantadine indeed results in improvements in Sf9 cellular expression not only of M2 (~3 fold) but also of the influenza HA (~7 fold) and matrix protein M1 (~3 fold) when co-expressed to produce influenza VLPs. This increased cellular expression of all three influenza viral proteins further leads to ~2 fold greater VLP yield. More importantly, the quality of resulting VLPs is significantly improved, as demonstrated by the ~2-fold, ~50-fold, and ~2-fold increase in antigen density to approximately 55 HA, 50 M1 and 160 M2 per influenza VLP, respectively. Taken together, this study represents a novel approach to enable the efficient incorporation of full-length M2 while enhancing both the yield and quality of influenza VLPs produced by Sf9 cells.

Awards Won:
Second Award of $1,500