2729. mRNA Vaccines Encoding Conserved Influenza Antigens Induce Robust and Durable Immunity in Rhesus Macaques
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Background: In response to immune pressure, influenza viruses evolve, producing drifted variants capable of evading immune recognition. One strategy for inducing a broad-spectrum immune response that can recognize multiple antigenically diverse strains of influenza is to target conserved proteins or protein domains. To that end, we assessed the immunogenicity of mRNA vaccines encoding the stem domain of hemagglutinin (HA) or nucleoprotein (NP) in nonhuman primates (NHPs).

Methods: Rhesus macaques were immunized three times intramuscularly, at 28 day intervals, with lipid nanoparticle-encapsulated mRNA encoding either HA stem (Yassine et al, 2015) or NP. Serum and PBMCs were collected up to 14 or 24 weeks, respectively, after the last vaccination. The magnitude and durability of humoral and cell-mediated immunity were evaluated. ELISA, competition ELISA, an in vitro anti-body-dependent cell-mediated cytotoxicity (ADCC) reporter biosay, and microneutralization assays were used to characterize feature immunity responses. Intracellular cytokine staining (IFN-gamma and IL-2) was used to assess antigen-specific T-cell responses.

Results: HA stem-immunized NHPs developed a robust anti-stem binding titer after a single vaccination and after two doses, sera antibodies recognized seven antigenically distinct Group 1 HA proteins. This broad antibody response persisted for at least 14 weeks post-dose 3 (PD3). Serum antibodies showed ADCC activity and competed with a well-characterized broadly neutralizing antibody, CR9114, for binding to HA stem. However, the polyclonal antibody had only limited activity against a panel of H1N1 viruses in a microneutralization assay. HA-specific CD4+ T-cell responses were detectable PD3. A robust antibody binding response was also detected in NP-vaccinated NHPs, titers remained high for at least 14 weeks PD3. Additionally, these animals developed robust NP-specific T-cell responses that persisted for at least 24 weeks PD3. On average, 0.5% of CD4+ and 4% of CD8+ T cells produced IFN-gamma in response to NP peptide stimulation at the peak of the response, 2 weeks after the last vaccine dose was administered.

Conclusion: Lipid nanoparticle-encapsulated mRNA vaccines encoding conserved influenza antigens induce a robust and durable immune response in NHPs.

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2730. Estimating Deaths Attributable to Influenza Mortality Using Traditional and Novel Forecasting Methods
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Background: Seasonally-adjusted linear models (‘Serfling’ models) serve as an open-source, R-package ‘Prophet’ for estimating the number of deaths attributable to influenza (M1) and to both seasonal (M2) and pandemic seasons (M3). The difference in performance of traditional time-series and viral activity-based models to a novel source allocation to public health programs (e.g., vaccination campaigns). We compared performance of traditional time-series and viral activity-based models to a novel source allocation to public health programs (e.g., vaccination campaigns). We compared performance of traditional time-series and viral activity-based models to a novel source allocation to public health programs (e.g., vaccination campaigns). We compared performance of traditional time-series and viral activity-based models to a novel source allocation to public health programs (e.g., vaccination campaigns).

Methods: Serfling model (M1), the Prophet model (M3) uses generalized additive models, implemented through the R-package ‘Prophet’. The difference is superior model performance, the attributable mortality estimated by these novel models may be preferred over traditional regression models. This study was funded by Sanofi Pasteur.

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2731. Does Last Season’s Influenza Vaccination Affect Current Season’s Vaccine Effectiveness in Young Children?
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Background: We evaluated influenza VE over two consecutive years vs. the current season against influenza illness during two H3N2-predominant seasons in children receiving care at emergency/urgent care (ED/UC) facilities in metropolitan Colorado.

Methods: We conducted a test-negative case-control analysis of 1478 children aged 6 months to 8 years enrolled at Children’s Hospital Colorado ED/UC with influenza-like illness during the 2016–2017 and 2017–2018 influenza seasons. The primary outcome was PCR-confirmed influenza and vaccination status was confirmed using electronic medical record and parental interviews. Vaccination status was defined as completely vaccinated (all doses of influenza vaccine according to child’s age); partially or not vaccinated children were defined as unvaccinated. Multivariable logistic regression models adjusted for high-risk medical condition, age, race and insurance status were used to calculate odds ratios (OR) and 95% confidence intervals. Vaccine effectiveness was calculated as (1 – OR) × 100.

Results: Of the 1224 (82.8%) children enrolled in the study with known vaccination status for both seasons, 361 (29%) tested positive for influenza. Overall, VE against influenza was 49% (95% CI, 33–61%) after adjusting for other covariates in the model. VE did not differ significantly between those vaccinated in both seasons and those vaccinated in only the current season (VE 69%, 95% CI 49–89%) (Table 1).

Conclusion: Our estimates of influenza VE for two predominantly H3N2-influenza seasons in Colorado are comparable to the CDC. VE for children 6 months to 8 years. VE against ED or UC-attended influenza illness in children did not vary significantly by prior season’s vaccination status.

Table 1—Vaccine Effectiveness over 2016-17 and 2017-18 influenza seasons, n=1224

| Predictor (vaccination status) | CRude (95% CI) | Adjusted* (95% CI) | Adjusted effective (%) | Adjusted p-value |
|--------------------------------|----------------|--------------------|------------------------|-----------------|
| Current season vs neither     | 0.45 (0.12, 0.65) | 0.29 (0.09, 0.50) | 71 (44.16)             | 0.17            |
| Both seasons vs neither        | 0.36 (0.14, 0.52) | 0.51 (0.32, 0.69) | 49 (35.89)             | <0.001          |
| Both seasons vs current season only | -0.16 (0.68, 0.28) | 0.31 (0.15, 0.49) | 69 (41.15)             | 0.15            |
| Both seasons vs prior season only | 0.03 (0.47, 0.74) | 0.56 (0.36, 0.79) | 44 (30.64)             | <0.001          |

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2732. Estimate of the Effectiveness of Influenza Vaccine among Children for the 2017–2018 Season
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Background: The 2017–2018 influenza season was one of the deadliest in decades, with 180 pediatric deaths, 80% among children who did not receive the vaccine. Circulating influenza strains change periodically, making it important to determine vaccine efficacy on an annual basis specifically in susceptible populations. The primary aim of our study was to estimate the effectiveness of the influenza vaccine for the 2017–2018 season. Secondary aims were to determine effect of weaning immunity and of previous season vaccination.

Methods: Children 6 months to 17 years tested for influenza during the 2017–2018 season at Children’s Hospital of New Orleans were included. Clinical charts were reviewed, and immunization status confirmed via the Louisiana Immunization Registry. Using a multivariable logistic regression model vaccine effectiveness (VE) was estimated by comparing vaccination status of influenza-positive vs. influenza-negative cases with the formula VE = (1 – OR) × 100%.

Results: 4,825 children were included; 22% of them tested positive for influenza, mostly influenza A (61.9%); 21% had received an influenza vaccine prior to illness: 69% among the influenza-positive and 23% among influenza-negative (P < 0.0001). Overall, VE for the 2017–2018 season was 43% (95% CI 30, 53); 44% for influenza A and 38% for influenza B. While receiving current year (2017–2018) vaccine had the most effect, receiving the previous year (2016–2017) vaccine had additional benefit. We found no waning immunity of the vaccine for the 2017–2018 season.

Conclusion: Influenza VE was modest for children in the local area of New Orleans and similar to the CDC’s findings for the nation as a whole. Previous year vaccination had a small, but significant benefit and there was no evidence of waning immunity in our cohort. Ongoing national and local surveillance is important to understand the benefit of influenza vaccination.

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