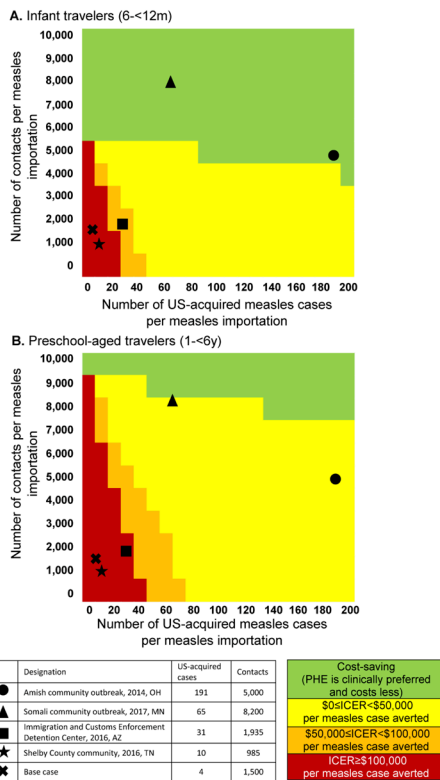


**Figure 1.** Two-way sensitivity analyses examining the value of MMR vaccination at the PHE across a range of possible risk of exposure to measles during travel and the percentage of MMR-eligible travelers vaccinated. Abbreviations: MMR: measles-mumps-rubella; PHE: pretravel health encounter; ICER: incremental cost-effectiveness ratio.



**Figure 2.** Two-way sensitivity analyses of the value of MMR vaccination at the PHE varying the number of contacts traced per measles importation and the number of US-acquired measles cases per measles importation at a risk of measles exposure associated with travel to Europe (434 exposures/10M travelers). Abbreviations: PHE: pretravel health encounter; ICER: incremental cost-effectiveness ratio.

**Disclosures.** All authors: No reported disclosures.

**2770. Intrapulmonary Vaccination with an M Protein-Deficient Respiratory Syncytial Virus (RSV) Vaccine Protects Infant Baboons Against an RSV Challenge**  
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**Background:** RSV infection is a major cause of lung disease in infants, yet there is no licensed vaccine. We are developing a live RSV vaccine with a deletion of the M protein (“Mnull RSV”). The RSV M protein is responsible for assembling newly synthesized RSV proteins into intact virus. Mnull RSV infects cells, replicates all proteins except M, and incites antibody and T-cell responses but, in the absence of the M protein, cannot replicate and infect other cells. We wished to show that vaccination with Mnull RSV directly into the lung in early infancy induces persistent neutralizing antibody (NA) responses that protect infant baboons against an RSV challenge.

**Methods:** Two-week-old infants were vaccinated with a single dose of Mnull RSV ( $8 \times 10^7$  vaccine units) or a sham preparation instilled into an endotracheal tube. Infants were observed continuously for signs of rapid breathing using infrared cameras. Four to six months later, serum RSV NA titers were determined, and infants were challenged intratracheally with the human RSV A2 strain. Respiratory rates were calculated daily. On days 0, 5, 7, and 12 after infection, arterial blood was drawn for blood gas analysis, lung function was assessed using a pneumotachometer, and bronchoalveolar lavage was performed for virus titrations.

**Results:** At 4–6 months following vaccination, RSV NA was present at a mean titer of 192 in sera of Mnull RSV recipients, but was undetectable in sera of sham vaccinated animals. Animals were then challenged with RSV, and sham vaccinated animals developed increased respiratory rates, increased alveolar-arterial (A-a) oxygen gradients, and BAL viral titers on day 5 were 3,500 pfu/mL. In contrast, Mnull RSV vaccinated animals had lower respiratory ratios throughout the length of the study ( $P = 0.038$ ), lesser A-a gradients (improved oxygenation) vs. controls, and no virus was recovered from BAL fluids ( $P < 0.0001$ ).

**Conclusion:** Intrapulmonary vaccination of infants with Mnull RSV at 2 weeks of age results in strong RSV NA responses that persist beyond the length of an average RSV season. Mnull RSV recipients were protected against tachypnea, reduced oxygenation and viral replication for at least 4–6 months following vaccination. We will next study intrapulmonary vaccination administering Mnull RSV via a nebulizer.

**Disclosures.** All authors: No reported disclosures.

**2771. Seroprotection against Measles, Rubella, Tetanus, and Diphtheria Among Children in Haiti—2017**

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**Background:** Measles, rubella, and maternal and neonatal tetanus have been verified to be eliminated in Haiti, but a diphtheria outbreak has been ongoing since 2014. To evaluate progress toward maintaining vaccine preventable disease (VPD) elimination and control, we conducted the first survey to estimate immunity to these VPDs among children in Haiti.

**Methods:** We conducted a nationally representative, two-stage cluster survey in 2017, stratifying Haiti into 2 regions: (1) West Region, the highly urban West department that includes one-third of Haiti’s population; (2) Non-West Region (all other departments). We sampled 4,286 households to recruit at least 910 children aged 5–7 years. We obtained vaccination history and dried blood spots from one eligible child per household. Antibody concentrations to VPDs were measured on a multiplex bead assay. We compared seroprotection and vaccination coverage estimates.

**Results:** Among 1146 enrolled children, tetanus (83%, 95% CI: 80%–86%) and diphtheria (83%, 95% CI: 81%–85%) seroprotection were higher than coverage with  $\geq 3$  doses of tetanus and diphtheria containing vaccine (DTP3) (68%, 95% CI: 61%–74%). No participants had antibody concentrations consistent with long-term immunity to tetanus or diphtheria. Measles (87%, 95% CI: 85%–89%) and rubella (84%, 95% CI: 81%–87%) seroprotection were higher than or similar to coverage with at least one dose of measles-rubella (MR) vaccine (84%, 95% CI: 80%–87%) (Figure 1). MR second-dose coverage was 20% (95% CI: 16%–24%). Seroprotection in the West Region was lower than in the non-West region for all VPDs.

**Conclusion:** Discordance between DTP3 coverage and seroprotection might be due to underestimating vaccination coverage by recall. Lack of long-term protection against tetanus or diphtheria is consistent with declining antibody concentrations by school-age after the primary DTP series, indicating the need for a booster dose. Seroprotection against measles and rubella viruses was lower than levels needed to prevent transmission, particularly in the West region; re-introduction of either virus could lead to an epidemic. Haiti should reach  $\geq 95\%$  DTP3 and two-dose MR coverage and add tetanus and diphtheria vaccine booster doses per global recommendations.

Figure 1. Vaccination Coverage and Seroprotection Among 5-7 Years Old – Haiti, 2017.

Figure 1a. Tetanus and Diphtheria Vaccination Coverage and Seroprotection Among 5-7 Years Old – Haiti, 2017.

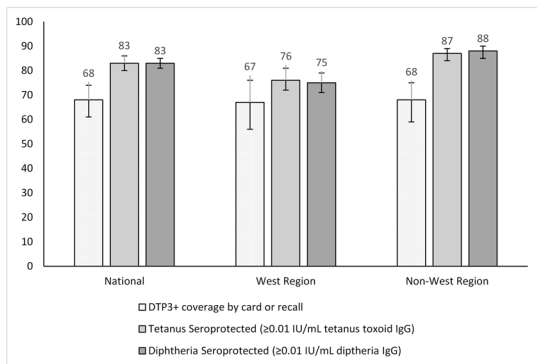
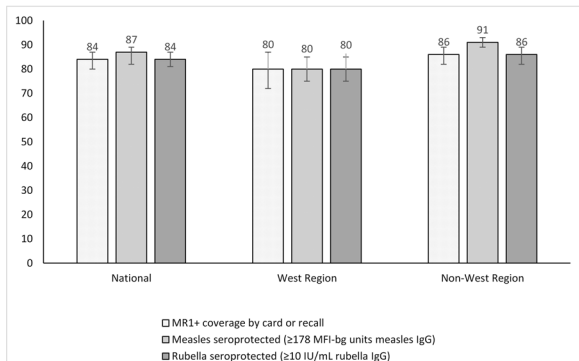


Figure 1b. Measles and Rubella Vaccination Coverage and Seroprotection Among 5-7 Years Old – Haiti, 2017.



**Disclosures.** All authors: No reported disclosures.

## 2772. HCMV gB Ectodomain Subunit and gB mRNA Vaccines Reduce AD-3 Immunodominance and Elicit More Durable Antibody Responses Than gB/MF59 Immunization

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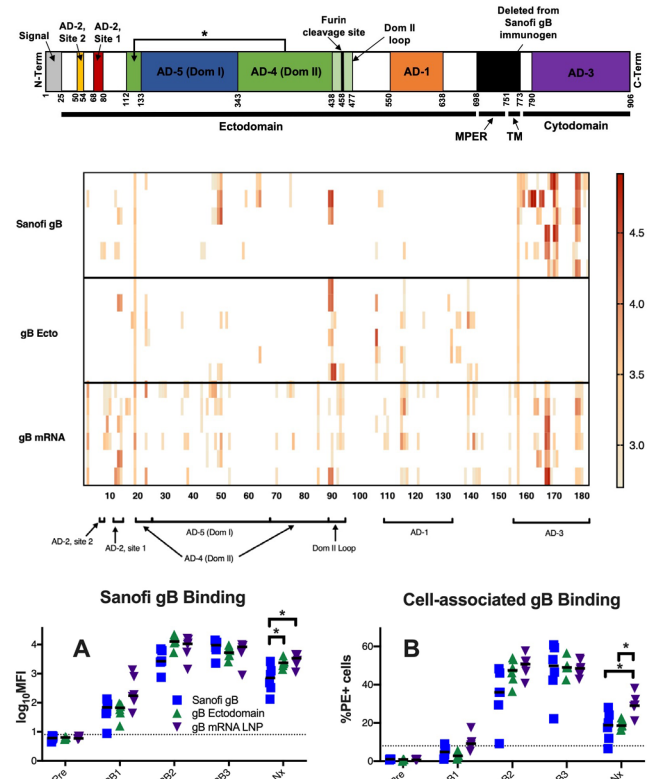
**Background:** A vaccine to prevent maternal acquisition of human cytomegalovirus (HCMV) during pregnancy is one potential strategy to reduce the incidence of congenital disease. The MF59-adjuncted glycoprotein B (gB/MF59) protein subunit vaccine is the most efficacious tested to-date, though achieved only 50% efficacy in phase 2 trial. We previously identified that gB/MF59 vaccination elicited poor heterologous virus neutralization and an immunodominant response against non-neutralizing/cytosolic antigenic domain 3 (AD-3) (Figure 1). Thus, we sought novel gB vaccination strategies to improve functional antibody responses and reduce AD-3 immunodominance.

**Methods:** Groups of juvenile New Zealand White rabbits ( $n = 6$ ) were administered 3 sequential doses of gB protein with an MF59-like squalene adjuvant IM, gB ectodomain protein (lacking AD-3) + squalene adjuvant IM, or lipid nanoparticle (LNP)-packaged nucleoside-modified mRNA encoding gB ID.

**Results:** The AD-3 immunodominant IgG response seen in human vaccinees was closely mimicked in rabbits, with 78% of binding antibodies directed against this region in the gB protein group compared with 1% and 46% in the ectodomain and mRNA-LNP-vaccinated groups respectively (Figure 2). All vaccines were highly immunogenic with similar kinetics and comparable peak gB-binding/functional antibody responses. However, both ectodomain and mRNA-LNP-immunized rabbits exhibited enhanced durability of IgG binding to gB protein ( $P = 0.04$  and  $0.02$ , respectively), and

the mRNA-LNP group had more durable binding of cell membrane-associated gB ( $P < 0.001$ ) (Figure 3). Additionally, ectodomain and mRNA-LNP-vaccinated rabbits had increased durability of antibodies targeting neutralizing epitopes AD-4 and AD-5 ( $P < 0.01$ ). Finally, low-magnitude gB-specific T-cell activity was observed in the gB protein and mRNA-LNP groups, though not in ectodomain-vaccinated rabbits.

**Conclusion:** Altogether these data suggest that gB ectodomain subunit and gB mRNA-LNP vaccine formulations reduced targeting of non-neutralizing epitope AD-3 and elicited more durable IgG responses than gB protein vaccination. These next-generation HCMV vaccine candidates aiming to improve upon the partial efficacy of gB/MF59 vaccination should be further evaluated in preclinical models.



**Disclosures.** All authors: No reported disclosures.

## 2773. Safety and Immunogenicity Study of Eastern Equine Encephalitis Vaccine

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**Background:** Eastern equine encephalitis virus (EEEV) is an alphavirus with a high mortality rate and serious neurological sequelae in infected persons making this virus an important human pathogen.

**Methods:** Following written informed consent, eligible subjects received two priming doses of EEEV vaccine, inactivated, TSI-GSD 104, 0.5 mL subcutaneously on days 0 and 28 days followed by a mandatory booster, 0.1 mL intradermal, at 6 months. Serum samples were collected pre-vaccination, days 21–35 following dose 2, as well as before and 21–35 days after dose 3. Sera with a Plaque Reduction Neutralization Test<sub>80</sub> titer (PRNT<sub>80</sub>)  $\geq 1:40$  were considered responders with adequate titers for the purpose of biocontainment suite entry.

**Results:** Sixty-seven (67) subjects were enrolled in this study to receive the primary vaccination series. All 67 subjects received at least 1 primary vaccination; 66 completed the 2 primary doses; 58 completed the 2 primary doses and the 6-month dose. Of these, 38 (56.7%) reported one or more adverse events. Fatigue was reported in 13 (19.4%), headache in 9 (13.4%), upper respiratory tract infection in 6 (9.0%), nausea in 5 (7.5%), pyrexia in 5 (7.5%), oropharyngeal pain in 4 (6.0%), myalgia in 4 (6.0%), injection site pain in 7 (10.4%), injection site hematoma in 4 (6.0%) and injection site erythema in 3 (4.5%) subjects. Adverse events were mostly mild or moderate and transient. PRNT<sub>80</sub> titers  $\geq 1:40$  was observed in 39/65 (60%) subjects who received both primary doses of EEEV vaccine compared with 48/57 (84%) subjects who completed the 2-dose primary series and the 6-month dose and also had blood drawn for titer. Females had a higher response rate (61.5%) at the pre 6-month boost titer than did males (34.3%) ( $p = 0.0231$ ). Similarly, the pre 6-month boost geometric mean titer (GMT) for females