

2764. Generation of a Balanced, Tetravalent Dengue Vaccine Based on Contemporary Strains Using a Computational, Synthetic Biology-Based Platform
Ying Wang, PhD¹; Charles B. Stauff, PhD¹; Kanakatte Raviprakash, PhD²; J. Robert Coleman, PhD³; Steffen Mueller, PhD¹; ¹Codagenix, Inc., Farmingdale, New York; ²Naval Medical Research Center, Silver Spring, Maryland

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Background: The WHO estimates that there may be 50 million cases of dengue virus (DENV) infection worldwide every year. There is no safe vaccine against DENV licensed in the United States. The development of a balanced and effective anti-DENV vaccine is vital to preventing morbidity and mortality. Codagenix used its proprietary SAVE (Synthetic Attenuated Virus Engineering) platform to generate and test a live attenuated, tetravalent vaccine against DENV.

Methods: Codagenix used SAVE to substitute under-represented human codons and codon-pairs into the E protein sequences of contemporary strains of DENV1-4, producing either a fully human-cell-deoptimized prM-E (E-Min), or a partially deoptimized prM-E (E-W/Min) to allow for balancing of the vaccine's immunogenicity. Full genomes containing deoptimized E-Min and E-W/Min in the DENV2 backbone were transfected into cells to recover live-attenuated, human-cell-deoptimized vaccine strains. Mice were vaccinated with 10⁶ FFU of each DENV vaccine (alone or together), boosted on day 21 and assessed for neutralizing antibodies by PRNT50 and survival after lethal challenge with mouse-adapted wild-type (WT) DENV. Cynomolgus macaques were immunized with a mixture of 10⁶ FFU of each DENV vaccine strain. Two doses were administered on study day 1 and 57 and serum neutralizing antibodies were determined on day 57 and 85 by a microneutralization assay.

Results: SAVE deoptimized DENV viruses grew to wild-type (between 10⁷ and 10⁸ FFU/ml) levels at permissive temperatures (<37C). All vaccine strains generated neutralizing antibody levels comparable to WT. A tetravalent formulation containing all four E-Min strains protected mice from lethal challenge with DENV3. A tetravalent formulation of Codagenix DENV-E-W/Min vaccine elicited a robust and balanced neutralizing antibody response in non-human primates (NHPs) against all four DENV serotypes after a single dose. A second vaccine dose did not boost antibody titers significantly.

Conclusion: The ability to rationally balance the attenuation of multiple vaccine strains, thereby avoiding antibody-dependent enhancement, is a unique advantage of the Codagenix SAVE platform. Codagenix DENV vaccine viruses generated balanced, sterilizing immunity in NHPs after one dose.

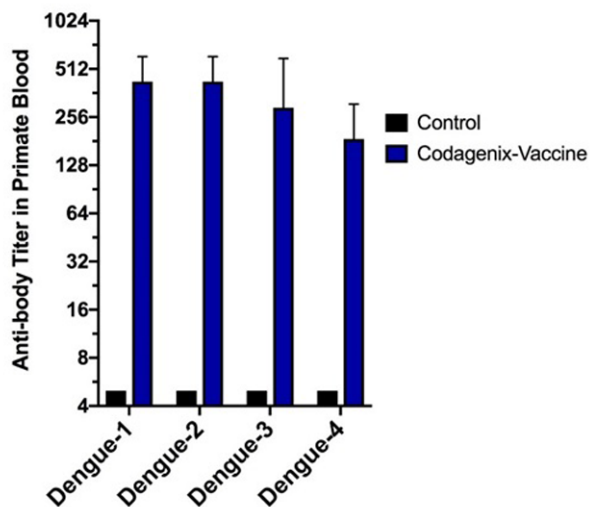


Fig. 1: Codagenix DENV vaccine elicits balanced immunogenicity in NHPs.

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2765. Pediatric Mumps during the 2015–2017 Mumps Resurgence in the United States

Marile Marlow, PhD, MPH; John Zhang, PhD; Nakia S. Clemmons, MPH; Mona Marin, MD; Manisha Patel, MD, MS; Manisha Patel, MD, MS; Centers for Disease Control and Prevention, Atlanta, Georgia

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Background: Numerous mumps outbreaks occurred in the United States over the last decade, with outbreaks affecting young adults on college campuses being among the largest and most widely publicized. However, at least half of mumps cases and outbreaks occurred in other age-groups and settings. We describe reported mumps cases among children and adolescents during 2015 through 2017.

Methods: The Centers for Disease Control and Prevention (CDC) analyzed reports of confirmed and probable mumps cases in persons aged ≤18 years (defined here as pediatric mumps) transmitted electronically through the Nationally Notifiable Diseases Surveillance System (NNSS) by the 52 reporting jurisdictions.

Results: Between January 1, 2015 and December 31, 2017, 49 jurisdictions reported 4,886 pediatric mumps cases (35% of all US reported cases, 13,807); 8 jurisdictions reported >100 cases each, representing 82% of all pediatric cases. Overall, 29 (1%) cases were in infants <1 yr, 406 (8%) were in children aged 1–4 years, 1,408 (29%) in children aged 5–10 years, 1,365 (28%) in adolescents aged 11–14 years, and 1,678 (34%) in adolescents aged 15–18 years. Most (3,548, 73%) cases did not travel outside the state during their exposure period; only 37 (1%) traveled outside the country. Cases in patients aged 1–4 years were more frequently non-outbreak associated (38%) than those in patients <1 years and 5–18 years (24% and 9%, respectively). Among 3,309 (68%) patients with known number of MMR doses received, 81% of those 5–18 years had ≥2 MMR doses, while 67% of those 1–4 years had ≥1 dose. Median time since last MMR dose for patients with 2 doses was 8 years (IQR: 4, 11 years). Four patients had meningitis and 1 had encephalitis; all were ≥10 years old and previously received 2 MMR doses. Of male mumps patients older than 10 years of age (2,113), 46 (2%) reported having orchitis; of these, 33 (72%) had 2 MMR doses. Sixty-four patients were hospitalized and there were no deaths.

Conclusion: About one-third of cases reported during the recent US mumps resurgence were in children and adolescents. The low rate of mumps complications compared with previous studies suggests mumps complications may not be adequately captured in national surveillance or identified by providers. Providers should remain vigilant that mumps can still occur among fully vaccinated pediatric patients, even those recently vaccinated.

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2766. Identification and Description of Mumps Cases in a Non-Outbreak Setting and Evaluation of the Effectiveness of Mumps Containing Vaccines Over Time

Ousseny Zerbo, PhD¹; Julia Glanternik, MD¹; Sharareh Modaresi, MD, MPH¹; Kristin Goddard, MPH²; Pat Ross, BA¹; Ned Lewis, MPH³; Nicola Klein, MD, PhD³; ¹Kaiser Permanente Vaccine Study Center, Oakland, California; ²Kaiser Permanente, Oakland, California; ³Kaiser Permanente Northern California, Oakland, California

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Background: Despite high coverage for 2 doses of MMR/MMRV vaccine, the United States and other countries have seen increases in outbreaks of mumps, mainly on college campuses and other close communities, which has been attributed to waning immunity to mumps. The objective of this study was to identify mumps cases within Kaiser Permanente Northern California, a large healthcare organization, and to assess waning of vaccine immunity against mumps in a non-outbreak setting.

Methods: Potential cases were identified by international classification of disease (ICD) 9 code 072, ICD 10 code B26 or by laboratory orders for mumps. We conducted medical chart reviews to confirm diagnoses, timing relative to vaccination and clinical characteristics. We selected cases and controls among KPNC born after 1988 who were members for ≥9 months before diagnosis or anchor date and who received their second dose at ages 4 to 6 years, matching cases with controls on geographical area. To assess for risk of mumps in relation to time since a second MMR/MMRV dose, we compared cases and controls using multivariable logistic regression adjusted for age, sex and calendar time of mumps diagnosis.

Results: Among 397 potential cases identified, chart review confirmed 178 (44.8%) as mumps. About half (87/178) were confirmed by both positive laboratory test and clinical diagnosis, with the remainder by clinical diagnosis alone. Median age at diagnosis for the 187 cases was 30 years (range 1 year–91 years). Most cases had parotitis (93%) and there were 7 cases of orchitis. The 34 cases with complete vaccination information were matched to 539,301 controls. The mean time since the second vaccine dose was shorter for cases compared with controls (6.5 years vs. 9.0 years, $P = 0.008$). After adjustment, there was no significantly increased risk of mumps associated with time since second MMR/MMRV dose (adjusted odds ratio = 1.08, 95% CI 0.57–2.05).

Conclusion: In the setting of a large healthcare organization, our results do not provide evidence of waning immunity following 2 doses of MMR/MMRV; however, identifying and confirming mumps cases were challenging and analyses were limited by small number of cases. Large future studies will be needed to confirm whether risk of mumps increases over time in non-outbreak settings.

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2767. Variation in Incidence of Pediatric Herpes Zoster by First- and Second-Dose Varicella Vaccine Formulations

Sheila Weinmann, PhD¹; Stephanie Irving, MHS¹; Padma Koppolu, MPH¹; Allison Naleway, PhD¹; Edward Belongia, MD²; Simon Hambidge, MD, PhD³; Michael L. Jackson, PhD, MPH⁴; Nicola Klein, MD, PhD⁵; Bruno Lewin, MD⁶; Elizabeth Liles, MD¹; Mona Marin, MD⁷; Ning Smith, PhD¹; Eric Weintraub, MPH⁷; Colleen Chun, MD¹; ¹Kaiser Permanente Center for Health Research, Portland, Oregon; ²Marshfield Clinic Research Institute, Marshfield, Wisconsin; ³Denver Health, Denver, Colorado; ⁴Kaiser Permanente Washington Health Research Institute, Seattle, Washington; ⁵Kaiser Permanente Northern California, Oakland, California; ⁶Kaiser Permanente Department of Research and Evaluation, Pasadena, California; ⁷Centers for Disease Control and Prevention, Atlanta, Georgia