2764. Generation of a Balanced, Tetravalent Dengue Vaccine Based on Contemporary Strains Using a Computational, Synthetic Biology-Based Platform

Ying Wang, PhD; Charles B. Stauff, PhD; Kanakatte Raviaprakash, PhD; J. Robert Coleman, PhD; Steffen Mueller, PhD; Codagenix, Inc., Farmingdale, New York; Naval Medical Research Center, Silver Spring, Maryland

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Background: The WHO estimates that there may be 30 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 SAFE (Synthetic Attenuated Virus Engineering) platform to generate and test a live attenuated, tetravalent vaccine against DENV.

Methods: Codagenix used SAFE to substitute under-represented human codons and codon-pairs into the E protein sequences of contemporary strains of DENV-1 to 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 10^6 FFU of each DENV vaccine (alone or together), boosted on day 21 and assessed for neutralizing antibodies by PRNT50 and seroconversions after lethal challenge with mouse-adapted wild-type (WT) DENV. Cynomolgus macaques were immunized with a mixture of 10^6 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: SAFE deoptimized DENV virus grew to wild-type (between 10^4 and 10^6 FFU/ml) levels at permissive temperatures (<37°C). 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 prM-E/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 SAFE 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

Marilyn 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 (NNDSS) by the 52 reporting jurisdictions.

Results: Between January 1, 2015 and December 31, 2017, 49 jurisdictions reported 46,169 mumps cases (35% of all US reported cases, 13,807) of these 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 yrs, 1,408 (29%) in children aged 5–10 yrs, 1,365 (28%) in adolescents aged 11–14 yrs, and 1,678 (34%) in adults aged 15–18 yrs. 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 yrs were more frequently non-outbreak associated (38%) than those in patients <1 yrs and 5–18 yrs (24% and 9%, respectively). Among 3,509 (68%) patients with known number of MMR doses received, 81% of those 5–18 yrs had ≥2 MMR doses, while 67% of those 1–4 yrs had ≥1 dose. Median time since last MMR dose for patients with 2 doses was 8 yrs (IQR: 4, 11 yrs). Four patients had meningoencephalitis; all were ≥10 yrs old and previously received ≥2 MMR doses. Of male mumps patients older than 10 yrs of age (2,113), 46% (2,020) reported havingorchitis; 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 re-emergence occurred in children and adolescents ≥5 yrs old. Reports 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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