Preclinical evaluation of a novel coronavirus vaccine (CORVax) using electroporation of plasmid DNA encoding a stabilized prefusion SARS-CoV-2 spike protein alone or with transfection of plasmid IL-12

Shawn M Jensen, Christopher G Twitty, Christopher Paustian, Madeleine Laws, Glenna McDonald, Keith Wegmann, Tarsem Moudgil, Michael Afentoulis, Mia Han, Kellie Malloy Foerter, David A Cantor, Jack Y Lee, Bianca Nguyen, John Rodriguez, Kim Jaffe, Brian Plengs, Carlo bifulco, Daniel J O'Connor, Walter Urba, Rom S Leidner, Traci L Hilton, Hong-Ming Hu, Bernard A Fox

Earle A Chiles Research Institute, Providence Portland Medical Center, Portland, Oregon

Abstract: Preclinical data shows that EP of CORVax alone or combined with IL-12 was safe. EP of CORVax was able to elicit anti-Spike IgG antibodies (EC50 = 1/1683, 1/1683, 1/1683, 1/1683, 1/1683, 1/1683) approximately 40 days after the booster vaccination. In 2 of 2 experiments, CORVax combined with IL-12 significantly (p<0.001) increased the sVNT titer at 2 months, but this benefit was lost by 3 months.

Methods: A plasmid stabilized CoV2 spike (S) expression vector was constructed, a master cell bank generated and clinical grade plasmid manufactured. C57BL/6 and BALB/c were vaccinated via intramuscular (IM) and/or intradermal (ID) injections of Plasmids Encoding the CoV2 Spike Protein (Jpt Technologies). Spike230, Spike264, Spike732, and Spike1052 are 9mers containing 15 amino acid peptides spanning SARS-CoV-2 Spike protein (Jpt Technologies). Spike plasmid + IL-12 plasmid vaccinated mice (n=9) had significantly higher (p<0.001) pseudoneutralization inhibition compared to Spike plasmid (n=9) and Control (n=8) vaccinated mice. At 60 days post-vaccination, ELISA was used to determine the presence of anti-Spike RBD IgG antibody decay is shown for Spike plasmid + IL-12 plasmid vaccinated mice (n=9) and Spike plasmid vaccinated mice (n=9). RBD IgG antibody decay is shown for Spike plasmid + IL-12 plasmid vaccinated mice (n=9) and Spike plasmid vaccinated mice (n=9).

Conclusions: Early preclinical data shows that EP of CORVax can induce IgG responses to CoV2 Spike and the receptor binding domain (RBD) as well as apparent viral neutralizing activity. The addition of IL-12, at least transiently, increased sVNT titer. The plan is to investigate alternative vaccine boosting strategies while extending these studies into aged animals and initiate a clinical trial in the near future.

Grants support from Nancy Lematta, The Harder Family, Robert and Elsie Franz, Lynn and Jack Loacker, and the USC Institute for Global Public Health and The Arrowhead Trust

Figure 7. Serum was collected from mice 115 days following vaccination and assayed for the ability to inhibit ACE2R binding to Spike in pseudotyped virus-based virus infectivity assay. A significant Spearman correlation coefficient of 0.4 (p<0.05) was observed between RBD IgG and pseudoneutralization inhibition of binding at 150 and 300 dilutions of serum compared to control serum (n=9). The **p<0.0001, * p<0.005, and * p<0.05 were observed for dilution (1:200) compared to control serum. The spike plasmid, spike plasmid + IL-12 plasmid, and control vaccinated groups were represented by red, green, and blue lines, respectively.