Background. The ongoing COVID-19 pandemic has thus far resulted in substantial worldwide mortality. As of November 2020, COVID-19 vaccines became available following Emergency Use Authorization (EUA) issued by the FDA. Recent longitudinal studies published as of March 2021 demonstrated that vaccine hesitancy remains high despite improvements compared to 2020. This study sought to explore the perceptions, beliefs, attitudes, and knowledge surrounding COVID-19 and identify determinants uniquely associated with vaccine hesitancy.

Methods. A cross-sectional electronic survey was created based on CDC & IDSA recommendations. The survey was distributed from March 2021 until June 2021 randomly to faculty members, healthcare workers, and students (≥18 years old) across 3 major academic centers (Case Western Reserve University, Spectrum Health, and the American University of Beirut Medical Center [AUBMC]). Data collected included socio-economic characteristics, demographics, knowledge, and attitudes pertaining to COVID-19 and vaccination. A multivariable regression model was utilized to evaluate for independent associations between variables and vaccination willingness/hesitancy as the primary outcome.

Results. In total, 7,197 participants completed the survey with an overall response rate of 94%. Females constituted 75.7% of the study population. Overall, 87.8% of the study cohort indicated willingness to get vaccinated. Factors associated independently with vaccination hesitancy included: younger age, lower attained education, lower knowledge score, physician recommendation against vaccination, not receiving the influenza vaccine annually, and other beliefs and attitudes as reported in table 1.

Table 1. Independent predictors of COVID-19 vaccine hesitancy among study respondents

Variable	aOR	95% CI	p-value
Age	0.67	0.56-0.80	< 0.001
Education	0.73	0.63-0.85	< 0.001
Smoking	1.37	1.06-1.76	0.016
Doctor advised against the vaccine	5.02	2.50-10.07	< 0.001
Previously received annual influenza vaccination	0.51	0.44-0.58	< 0.001
COVID-19 knowledge score	0.65	0.58-0.74	< 0.001
"COVID-19 vaccine is more dangerous than COVID-19 infection"	9.21	4.70-18.07	< 0.001
"COVID-19 infection does not worry me"	2.30	1.78-2.99	< 0.001
"The COVID-19 vaccine can change human DNA"	1.54	1.13-2.11	0.007
"The COVID-19 vaccine can sometimes lead to infertility"	1.45	1.00-2.09	0.05
"I believe that the COVID-19 vaccine development was rushed"	3.69	2.81-4.85	< 0.001
"I would get the COVID-19 vaccine if my health care provider recommended it"	0.03	0.02-0.04	< 0.001

Conclusion. Most survey respondents indicated willingness to receive COVID-19 vaccination. The perception or belief that vaccination is more harmful than COVID-19 disease represented an especially robust barrier against vaccination. Since recommendations made by healthcare providers were strongly associated with either vaccination hesitancy or willingness to get vaccinated, developing educational strategies at this level could enhance vaccine acceptance in an effort to curb the pandemic.

Disclosures. **Robert A. Bonomo, MD**, **entasis** (Research Grant or Support)**Merck** (Grant/Research Support)**NIH** (Grant/Research Support)**VA Merit Award** (Grant/Research Support)**VenatoRx** (Grant/Research Support)

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577. COVI-VAC™, a Live Attenuated COVID-19 Vaccine, Provides Single Dose Protection Against Heterologous Challenge with SARS-CoV-2 Beta (B.1.351) in the Syrian Golden Hamster Model

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Background. Although multiple COVID-19 vaccines are currently in use, emergence of novel SARS-CoV-2 variants with reduced neutralization raises concern of future vaccine escape. COVI-VAC™ is a live attenuated SARS-CoV-2 strain based on WA/1 being developed as an intranasal COVID-19 vaccine. COVI-VAC is attenuated through removal of the furin cleavage site and introduction of 283 silent, deoptimizing mutations that maintain viral amino acid sequence but slow viral replication in vivo by up to 5 logs. Notably, COVI-VAC presents all viral antigens in their native conformation and is not limited to spike. COVI-VAC demonstrated attenuation, immunogenicity and single dose protection in both the Syrian golden hamster and non-human primate models and currently in Phase 1 clinical trials. In this study, we evaluated efficacy of COVI-VAC against challenge with the Beta/B.1.351 variant in Syrian golden hamsters.

Methods. Syrian golden hamsters, 7-10 weeks of age were, vaccinated intranasally with 8.25×10^4 PFU COVI-VAC (n=28) or vehicle control (n=16). Twenty seven days post-vaccination, animals were challenged intranasally with 3×10^4 PFU of wildtype (WT) SARS-CoV-2 Beta. Animals were weighed daily. Further analysis is being conducted with serum and key tissues from pre and post challenge timepoints to include neutralizing antibody, biodistribution (subgenomic qPCR) and histopathology.

Results. COVI-VAC prevented weight loss following challenge with the heterologous variant of SARS-CoV-2, B.1.351/Beta (Figure). Results of additional analyses will be available before the IDWeek meeting.

Change in Weight following SARS-CoV-2 Beta Challenge
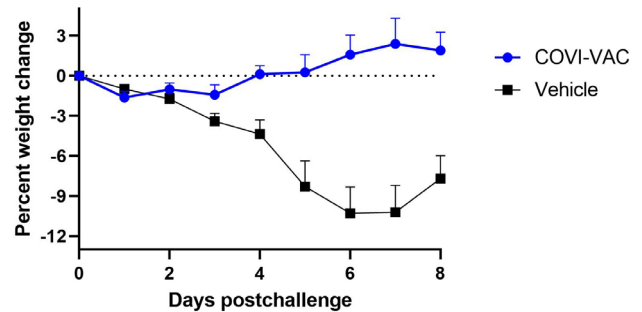
Conclusion. COVI-VAC is protective against heterologous challenge with SARS-CoV-2 Beta. By presenting all viral antigens, COVI-VAC may be less affected by viral evolution than spike-based vaccines.

Disclosures. **Anna Kushnir, PHD**, **Codagenix Inc** (Employee) **Steffen Mueller, PhD**, **Codagenix Inc** (Board Member, Employee, Shareholder) **Sybil Tasker, MD, MPH, FIDSA**, **Codagenix Inc** (Employee, Shareholder) **J. Robert Coleman, PhD**, **Codagenix Inc.** (Board Member, Employee, Shareholder)

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578. INO-4800 DNA Vaccine Induces Neutralizing Antibodies and T cell Activity Against Global SARS-CoV-2 Variants

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Background. Global surveillance has identified emerging SARS-CoV-2 variants of concern (VOC) associated with increased transmissibility, disease severity, and resistance to neutralization by current vaccines under emergency use authorization (EUA). Here we assessed cross-immune responses of INO-4800 vaccinated subjects against SARS-CoV-2 VOCs.

Methods. We used a SARS-CoV-2 IgG ELISA and a pseudo neutralization assay to assess humoral responses, and an IFNγ ELISpot to measure cellular responses against SARS-CoV-2 VOC in subjects immunized with the DNA vaccine, INO-4800.

Results. IgG binding titers were not impacted between wild-type (WT) and B.1.1.7 or B.1.351 variants. An average 1.9-fold reduction was observed for the P.1 variant in subjects tested at week 8 after receiving two doses of INO-4800 (Figure 1a). We performed a SARS-CoV-2 pseudovirus neutralization assay using sera collected from 13 subjects two weeks after administration of a third dose of either 0.5 mg, 1 mg, or 2 mg of INO-4800. Neutralization was detected against WT and the emerging variants in all samples tested. The mean ID_{50} titers for the WT, B.1.1.7, B.1.351 and P.1. were 643 (range: 70-729), 295 (range: 46-886), 105 (range: 25-309), and 664 (range: 25-2087), respectively. Compared to WT, there was a 2.1 and 6.9-fold reduction for B.1.1.7 and B.1.351, respectively, while there was no difference between WT and the P.1 variant (Figure 1b). Next, we compared cellular immune responses to WT and SARS-CoV-2 Spike variants elicited by INO-4800 vaccination. We observed similar cellular responses to WT (median = 82.2 IQR = 58.9-205.3), B.1.1.7 (79.4, IQR = 38.9- 179.7), B.1.351 (80, IQR = 40.0-208.6) and P.1 (78.3, IQR = 53.1-177.8) Spike peptides (Figure 2).

Figure 1: INO-4800 Humoral and neutralizing response against SARS-CoV-2 variants
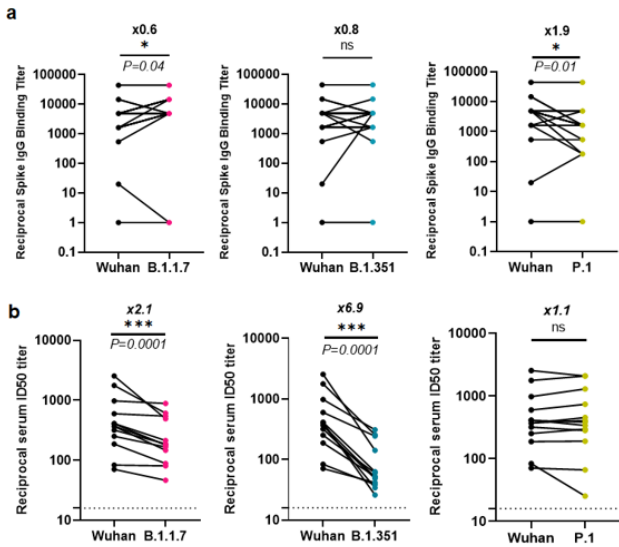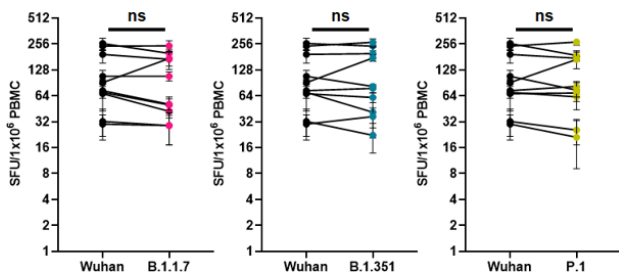

Figure 2: INO-4800 Cellular immune response against SARS-CoV-2 variants

Conclusion. INO-4800 vaccination induced neutralizing antibodies against all variants tested, with reduced levels detected against B.1.351. IFNγ T cell responses were fully maintained against all variants tested.

Disclosures. **Viviane M. Andrade, PhD**, **Inovio Pharmaceuticals Inc.** (Employee) **Aaron Christensen-Quick, PhD**, **Inovio Pharmaceuticals, Inc** (Employee) **Joseph Agnes, PhD**, **Inovio** (Employee, Shareholder) **Jared Tur, PhD**, **Inovio** (Employee) **Charles C. Reed, PhD**, **Inovio Pharmaceuticals** (Employee, Shareholder) **Richa Kalia, MS**, **Inovio Pharmaceuticals** (Employee, Other Financial or Material Support, I have stock options with Inovio Pharmaceuticals as an employee.) **Idania Marrero, MD, PhD**, **Inovio Pharmaceuticals** (Employee, Shareholder) **Dustin Elwood, PhD**, **Inovio Pharmaceuticals** (Employee) **Katherine Schultheis, MSc**, **Inovio Pharmaceuticals** (Employee) **Emma Reuschel, PhD**, **Inovio Pharmaceuticals** (Employee) **Trevor McMullan, MSc**, **Inovio** (Shareholder) **Patrick Pezzoli, BS**, **Inovio** (Employee) **Kimberly A. Kraynyak, PhD**, **Inovio Pharmaceuticals** (Employee, Other Financial or Material Support, Stock options) **Albert Sylvester, MS**, **Inovio** (Employee, Shareholder) **Mammen P. Mammen Jr., MD**, **Inovio Pharmaceuticals** (Employee) **J Joseph Kim, PhD**, **Inovio** (Employee) **David Weiner, PhD**, **Inovio** (Board Member, Grant/Research Support, Shareholder, I serve on the SAB in addition to the above activities) **Trevor R. F. Smith, PhD**, **Inovio** (Employee, Shareholder) **Stephanie Ramos, PhD**, **Inovio Pharmaceuticals** (Employee) **Laurent Humeau, PhD**, **Inovio Pharmaceuticals** (Employee) **Jean Boyer, PhD**, **Inovio** (Employee) **Kate Broderick, PhD**, **Inovio** (Employee)

579. Design and Immunogenicity of a Pan-SARS-CoV-2 Synthetic DNA Vaccine
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Session: P-25. COVID-19 Vaccines

Background. First-generation COVID-19 vaccines are matched to spike protein of the Wuhan-H1 (WT) strain. Convalescent and vaccinee samples show reduced neutralization of SARS-CoV-2 variants of concern (VOC). Next generation DNA vaccines could be matched to single variants or synthetically designed for broader coverage of multiple VOCs.

Methods. The synthetic consensus (SynCon®) sequence for INO-4802 SARS-CoV-2 spike with focused RBD changes and dual proline mutations was codon-optimized (Figure 1). Sequences for wild-type (pWT) and B.1.351 (pB.1.351) were similarly optimized. Immunogenicity was evaluated in BALB/c mice. Pre-clinical efficacy was assessed in the Syrian Hamster model.

Figure 1. Design Strategy for INO-4802
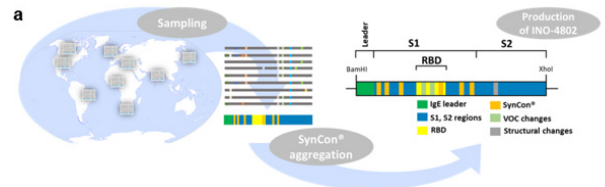
Results. INO-4802 induced potent neutralizing antibody responses against WT, B.1.1.7, P.1, and B.1.351 VOC in a murine model. pWT vaccinated animals showed a 3-fold reduction in mean neutralizing ID50 for the B.1.351 pseudotyped virus. INO-4802 immunized animals had significantly higher (p = 0.0408) neutralizing capacity (mean ID50 816.16). ID50 of pB.1.351 serum was reduced 7-fold for B.1.1.7 and significantly lower (p = 0.0068) than INO-4802 (317.44). INO-4802 neutralized WT (548.28) comparable to pWT. INO-4802 also neutralized P.1 (1026.6) (Figure 2). pWT, pB.1.351 or INO-4802 induced similar T-cell responses against all variants. INO-4802 skewed towards a TH1-response. All hamsters vaccinated with INO-4802 or pB.1.351 were protected from weight loss after B.1.351 live virus challenge. 4/6 pWT immunized hamsters were completely protected. pWT immunized hamsters neutralized WT (1090) but not B.1.351 (39.16). INO-4802 neutralized both WT (672.2) and B.1.351 (1121) (Figure 3). We observed higher increase of binding titers following heterologous boost with INO-4802 (3.6 – 4.4 log2-fold change) than homologous boost with pWT (2.0 – 2.4 log2 fold change) (Figure 4).

Figure 2. INO-4802 Induces Functional Humoral Immune Response Against SARS-CoV-2 Variants of Concern
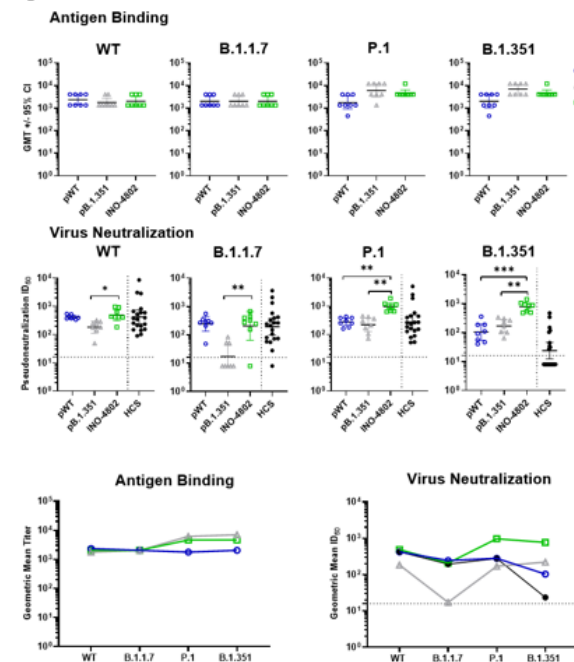

Figure 3. INO-4802 Protects Hamsters Against Challenge With B.1.351 Live Virus