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WHO Meeting on Correlates of Protection Against SARS-CoV-2
September 3, 2021
Duke is serving the Moderna program

Monogram is serving the Janssen, Novavax, AstraZeneca and Sanofi programs

Both assays are FDA approved

Objectives:
• Immune correlates
• Licensure for ages ≥18 yrs
• Immunobridging regulatory approvals (e.g., teens, children, modified dose, variant vaccines)
• Boosting (when and with what?)

The two assays, though similar technologies, generate ~3-fold difference in titers for convalescent sera and vaccine sera.

Calibration is needed to aid decision-making based on data from these two assays.
Similarities:

- Lentivirus (HIV) backbone
- SARS-CoV-2 full-length Spike (D614G variant)
- Firefly luciferase reporter gene readout (Luminescence)
- HEK-293T cells used for pseudovirus production (transfection)

Differences:

- PV production
  - Duke utilizes TMPRSS2
  - Monogram does not

- Target cells
  - Duke utilizes HEK-293T/ACE2 cells (stable transduction)
  - Monogram utilizes HEK-293T/ACE2/TMPRSS2 cells (transient co-transfection)

- Assay procedure
  - Duke is manual
  - Monogram is semi-automated
Calibration of Two Validated SARS-CoV-2 Pseudovirus Neutralization Assays for COVID-19 Vaccine Evaluation


- Three sample sets:
  - 248 convalescent sera (early pandemic, D614G dominant)
  - 90 samples from recipients of Moderna mRNA-1273 vaccine (30 baseline, 30 post 1st, 30 post 2nd)
  - WHO International Standard (20/136)

- Three calibration approaches:
  - Approach 1: Calibrate to the WHO-IS
  - Approach 2: Calibrate to the convalescent sera by using a bivariate normal distribution model
  - Approach 3: Calibrate to the convalescent sera by using a linear regression model

- Apply the calibration to test equivalency of nAb titers in vaccine sera between the two labs.
Distributions of ID50 titers measured by the Duke and Monogram labs of convalescent patient samples, vaccine recipient samples, and the WHO International Standard.
Scatterplots of calibrated neutralizing antibody titers using three calibration approaches applied to vaccine sera collected 4 weeks post first (turquoise) and second (orange) mRNA-1273 dose.

WHO-IS

**Approach 1**

CCC: 0.75 (95% CI: 0.60, 0.85)

**Approach 2**

CCC: 0.87 (95% CI: 0.85, 0.87)

**Approach 3**

CCC: 0.77 (95% CI: 0.71, 0.82)

WHO-IS

Convalescent sera, bivariate normal distribution model

Convalescent sera, linear regression model

CCC: concordance correlation coefficient
Comparisons of the performance of Approach 1 (WHO-IS) based on calibration using arithmetic mean, geometric mean, or median ID50 titers

**Arithmetic Mean**

- **Approach 1**
  - CCC: 0.75 (95% CI: 0.60, 0.85)

**Geometric Mean**

- **Approach 1**
  - CCC: 0.56 (95% CI: 0.39, 0.69)

**Median**

- **Approach 1**
  - CCC: 0.38 (95% CI: 0.24, 0.50)

**CCC**: concordance correlation coefficient
Application of WHO-IS Calibration to Correlates Analyses

Immune Correlates Analysis of the mRNA-1273 COVID-19 Vaccine Efficacy Trial
Peter B. Gilbert, David C. Montefiori, Adrian McDermott, et al.

Correlates of Protection Against Symptomatic and Asymptomatic SARS-CoV-2 Infection

mRNA-1273 vaccine

<table>
<thead>
<tr>
<th>Duke Assay:</th>
<th>Calibrated ID50</th>
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<tbody>
<tr>
<td>Estimated efficacy</td>
<td></td>
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<tr>
<td>70%</td>
<td>4</td>
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<tr>
<td>90%</td>
<td>83</td>
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ChAdOx1 nCoV-19 vaccine

<table>
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<th>Monogram Assay:</th>
<th>Calibrated ID50</th>
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<tbody>
<tr>
<td>Estimated efficacy</td>
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</tr>
<tr>
<td>70%</td>
<td>8</td>
</tr>
<tr>
<td>90%</td>
<td>140</td>
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