COVID-19 Conversations

Angela Rasmussen
VIDO-InterVac, University of Saskatchewan
Center for Global Health Science and Security, Georgetown University

COVID19Conversations.org
#COVID19Conversations
Viruses, Variants, and Vaccines: Making Sense of Mutation

Angela L. Rasmussen, Ph.D.
Georgetown Center for Global Health Science and Security
(soon: VIDO-InterVac, University of Saskatchewan)
Territorial Acknowledgement and Equity Statement

I am presenting today from the unceded ancestral homelands of the Duwamish people. I acknowledge and honor the First people of these territories and their Tribal governments, their histories and ancestry, and their roles today in caring for these lands.

I also would like to acknowledge that there is a history of systemic inequity in academic science that spans centuries. My prior institution, Columbia University, and my current institution, Georgetown University, were founded using profits from the trans-Atlantic slave trade and the sale of enslaved people. In addition, they excluded women and people of color from the academic community for more than 200 years, leaving a long and painful legacy of racial and gender-based inequality that continues to this day. I encourage all to consider how they can contribute to making public health research a more equitable enterprise.
Mutation and virus evolution

Gago et al, Science, 2009
There are many variants
Evolution in action

Selected SARS-CoV-2 lineages
Dec 5th 2019 to Feb 21st 2021

- E484K mutation
  Associated with antibody resistance
- N501Y mutation
  Associated with increased transmissibility
- Variant of concern/under investigation
- Mutation recently found in some sequences

- Contains the root of the pandemic
- Mutation D614G becomes fixed, raising viral transmissibility

Spike protein gene

Original: SGGUGUUGUUC
Code for glutamic acid (E)

E484K: SGGUGUAUGUUC
Code for lysine (K)
SARS-CoV-2 genome organization

Variants in the strictest sense contain mutations anywhere in the genome, regardless of their function (or lack thereof)

Kim *et al*, *Cell*, 2020
The (for now best studied) variants of concern

**B.1.1.7 (501Y.V1)**
- T1001I (nsp3/PL2pro)
- A1708D (nsp3/PL2pro)
- I2230T (nsp3/PL2pro)
- 3675-3677del (nsp6)
- **P4715L (nsp12/RdRp)**
- 69/70del
- 144del
- N501Y*
- A570D
- D614G
- P681H
- 144del
- N501Y*
- D614G
- T716I
- S982A
- D1118H
- Q27Stop
- R52I
- Y73C
- D3E
- R203K
- G204R
- S235F

**B.1.351 (501Y.V2)**
- T265I (nsp2)
- H417N (nsp2)
- K1655N (nsp3/PL2pro)
- K3353R (nsp5/3CLpro)
- **P4715L (nsp12/RdRp)**
- D80A
- 241del
- K417N*
- E484K*
- N501Y*
- D614G
- A701V
- Q57H
- P71L
- P80A
- T205I

**P.1 (501Y.V3)**
- H417T (nsp2)
- S1188S (nsp3/PL2pro)
- K1795Q (nsp3/PL2pro)
- 3675-3677del (nsp6)
- **P4715L (nsp12/RdRp)**
- L18F
- T20N
- P26S
- D80R
- D138Y
- R190S
- K417N*
- E484K*
- N501Y*
- D614G
- H655Y
- T1027I
- V1176F
- S253P
- E92K
- G18F
- S202C
- R203K
- G204R
- P80R
- S202C
- R203K
- G204R

Present in 2/3 variants
Present in 3/3 variants
Possible mechanisms of increased transmissibility

- Increased fitness
- Receptor binding affinity
- Increased virion stability
- Immune evasion

Increased viral shedding
Longer interval of contagiousness
Increased infectivity
Increased environmental stability
Impact of immune evasion on transmission

Protection against infection
Protection against disease

Altmann et al, Science, 2021

Sabino et al, Lancet, 2021
Antibody neutralization via RBD isn’t everything

Some big remaining questions:

- How much does prior immunity (vaccines, convalescent) provide sterilizing protection?

- What impact does this have on viral shedding?

- What is the overall impact on transmission at population level?
## Summary of variants

<table>
<thead>
<tr>
<th></th>
<th>B.1.1.7</th>
<th>B.1.351</th>
<th>P.1</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alternate name</strong></td>
<td>501Y.V1</td>
<td>501Y.V2</td>
<td>501Y.V3</td>
</tr>
<tr>
<td><strong>Country identified</strong></td>
<td>United Kingdom</td>
<td>South Africa</td>
<td>Brazil</td>
</tr>
<tr>
<td><strong>Mutations</strong></td>
<td>23</td>
<td>21</td>
<td>17</td>
</tr>
<tr>
<td><strong>Spike mutations</strong></td>
<td>8</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td><strong>Key RBD, spike mutations beyond N501Y in all</strong></td>
<td>E69/70 deletion, P681H 144Y deletion, A570D</td>
<td>E484K, K417N, orf1b deletion</td>
<td>E484K, K417T, orf1b deletion</td>
</tr>
<tr>
<td><strong>Other mutations, including N-terminal</strong></td>
<td>T716I, S982A, D1118H</td>
<td>L18F, D80A, D215G, Δ242-244, R264I, A701V</td>
<td>L18F, T20N, P26S, D138Y, R190S, H655Y, T10271</td>
</tr>
<tr>
<td><strong>Transmissibility Δ</strong></td>
<td>&gt;50% increased</td>
<td>No</td>
<td>Not established</td>
</tr>
<tr>
<td><strong>Lethality Δ</strong></td>
<td>Not resolved</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td><strong>Immune evasion</strong></td>
<td>Unclear</td>
<td>Yes</td>
<td>Yes, less than B.1.351</td>
</tr>
<tr>
<td><strong>Vaccine efficacy (preserved vs severe infections in all so far)</strong></td>
<td>Modest reduction ~10% point decline in 2 trials (Novavax, AZ)</td>
<td>Yes, reduced in 2 (J&amp;J, Novavax) ~20-30% point decline. No efficacy v mild infections w/AZ</td>
<td>Preserved in J&amp;J trial</td>
</tr>
<tr>
<td><strong>Countries reported</strong></td>
<td>94</td>
<td>48</td>
<td>25</td>
</tr>
<tr>
<td><strong>US States reported</strong></td>
<td>46</td>
<td>17</td>
<td>5</td>
</tr>
</tbody>
</table>

Eric Topol
Disclosures

• Paid consultant for W2O, Edelman, Guidepoint, and IMG Expert Services
• Paid advisor for Siemens Healthineers
• Member of MJH Life Sciences COVID-19 Coalition
• Own stock in Illumina, Pacific Biosciences, ThermoFisher Scientific, & NanoString Technologies
• Research funded by DARPA, DTRA, NIAID, and FastGrants