What is Omicron & how do we identify it?
And why is everyone so worried?

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What is a “variant of concern”, anyway?
Transmission $\rightarrow$ Sequences $\rightarrow$ Phylogeny

Image: Nextstrain 2020-2021
Variant of Concern:
A cluster of sequences with mutations we’re concerned about

Transmission process

Sampled case

Mutation

Transmission

Sequences from Samples

A

B

Reconstruction

Is it impacting?

Transmission

Immune evasion

Clinical outcome

Image: Nextstrain & E Hodcroft 2020-2021
Identify & Track Variants by Mutations

Alpha

Beta

Gamma

Delta

501Y 681H

80A 484K 501Y

484K 501Y 655Y

452R 478K 681R

Not a complete representation of all spike mutations
We’ve had other Variants of concern, why does everyone seem so worried this time?
Omicron has a worrying set of mutations - Particularly in concerning positions
4 unique spike mutations in alpha variant

26 unique spike mutations in Omicron (B.1.1.529) variant

6 unique spike mutations in beta variant

8 unique spike mutations in gamma variant

7 unique spike mutations in delta variant

Venkatakrishnan et al, OSFPreprints 2021.
Where is Omicron in the world?

And how do we find it?
Omicron is being detected in increasing number of countries
Omicron Sequences Around the World

nextstrain.org/groups/neherlab/ncov/21K.Omicron
How can we find Omicron?

- Omicron has a tiny part of Spike missing \((S:69/70\text{del})\) which makes a particular sign on some PCR tests (“SGTF” or “S gene drop-out”)

Sequencing should still be used to confirm while Omicron is rare!

<table>
<thead>
<tr>
<th>Gene</th>
<th>Non-Omicron</th>
<th>Omicron</th>
</tr>
</thead>
<tbody>
<tr>
<td>ORF1</td>
<td>+ for SARS-CoV-2</td>
<td>+ for SARS-CoV-2 and May be Omicron!</td>
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<tr>
<td>S</td>
<td>+ for SARS-CoV-2</td>
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<tr>
<td>N</td>
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Caveats & details of SGTF are left out on this simplified slide!
Where did Omicron come from?
Omicron sits on a ‘Long Branch’
- Doesn’t have many ‘relatives’

► This makes it harder to tell how it has evolved
Omicron sits on a ‘Long Branch’
- Doesn’t have many ‘relatives’

- This makes it harder to tell how it has evolved

- Some theories:
  - Immunocompromised individual 😷
  - Undetected circulation 😷
  - Animal reservoir 🐱

- Could also be a combination!
- Personally: 1 and/or 2 most likely

Image: nextstrain.org/ncov/gisaid/global
What about the ‘new’ Omicron we’ve heard about? (BA.1 & BA.2)
BA.2 is more like Omicron than anything else - but it’s different

- The first Omicron sequences were BA.1
- Only recently did we identify BA.2, which is similar
- We don’t yet know if they will have the same *phenotype* (impact on how the virus behaves)
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<tr>
<td>Omicron BA.1</td>
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<tr>
<td>Omicron BA.2</td>
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Result:
- +
- + & maybe Omicron

Image: nextstrain.org/groups/neherlab/ncov/21K.Omicron/2021-12-02
Key Points

- Omicron has more mutations in Spike than we’ve seen in other variants
  - Could impact transmissibility, clinical outcome, immune evasion
- Omicron is now found worldwide & spreading locally
- We don’t know much about Omicron’s history or where it came from
- Omicron is now divided into two lineages
  - Too early to know if they behave differently