Variants and vaccines

Why do we have variants?
Impact on vaccines
What can be done about it?

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Outline

1. Why do we have variants and why do we have them now?
2. What should we call them?
3. What do variants mean for vaccines?
4. What can we do about it?
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1. Why do we have variants and why do we have them now?
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Understanding variants is all about evolution
Darwin’s evolutionary principles: peppered moths as an example

1. Individuals vary

2. Variation is heritable

3. Some variants are advantaged in terms of survival and reproduction “selection pressure”

4. Population evolves to reflect increasing numbers of these advantaged “successful” variants “survival of the fittest”
1. Short generation time

2. Millions of offspring

3. Can have error-prone mutations – especially RNA viruses

(Quantity rather than quality)

Especially concerning if lots of transmission
Individuals vary
Variation is inherited
Survival advantage with selection pressure
Successful variants predominate
RNA genome of SARS CoV-2 has 30,000 bases “building blocks”

Each “building block” can be one of 4 things:
- Adenine
- Cytosine
- Uracil
- Guanine

3 bases code for 1 amino acid – called a “codon”

Amino acids make up the proteins in SARS CoV-2
Genetic change can occur when:

Mutations ~ errors in genetic replication

Substitution of a single base ~ “point mutation”

Fragments of DNA inserted or deleted from genome
Do mutations matter?

Mutations happen all the time

SARS CoV-2 mutates slowly (about 2 changes in 30,000 bases per month)
- Flu = twice as fast
- HIV = 4x as fast

Many mutations make no difference to the amino acids produced
But some do
= “meaningless” vs “meaningful” mutations

Without any selection pressure – expect similar frequency of meaningless and meaningful mutations
Number of bases evolving with meaningful mutations shot up in November

Corresponded with the emergence in October 2020 of several variants with similar mutations in different countries.
What changed?
3 possible explanations

Growing immunity

Increased transmission

Chronic infection (especially with immune treatment)
Shown to happen in the laboratory

Light green = SARS CoV-2 viruses
3 possible explanations

Growing immunity

Increased transmission

"The more humans that get infected, the greater the chances of it adapting itself to humans," Anthony Fauci
What would give a virus an advantage?

Growing immunity

Increased transmission

1. Produce more particles
2. Better survival
3. Better at entering human cells

Evade immune system

more severe disease
Outline

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4. What can we do about it?
A variant by any other name

- Challenges with naming viruses
- Tension between scientifically correct
  - functional change
  - ancestry

vs
memorable & pronounceable
A variant by any other name

• Challenges with naming viruses

• Tension between scientifically correct
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memorable & pronounceable
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- Challenges with naming viruses
- Tension between scientifically correct
  - functional change
  - ancestry
  vs
memorable & pronounceable without stigma
A variant by any other name

• Challenges with naming viruses
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Proposal: Focus on the amino acid that has changed:

old amino acid – position in the protein – new amino acid

N
501 Y
(“NellY”)
→ increase binding to human cells

old amino acid – position in the protein – new amino acid

E 484 K
(“EeeK”)
→ evade immune system
What do variants mean for vaccines?
How do vaccines work?

Vaccines introduce a weak or inactive form of the disease to the body.

The body reacts by stimulating the immune system and creating antibodies.

The antibodies remember the disease and can defend against it if a person becomes exposed to it.

'Eek': New mutations in UK worry experts as virus surge continues
Evidence about vaccine efficacy with 501Y.v2 (B.1.351)

• Most important data comes from clinical trials – 3 reported to date from SA during 501Y.v2 period
  - Novavax – efficacy in SA 49% (55% vs. mild COVID-19; 60% if excl PLHIV) vs 89% in UK
    >90% of vaccine failures due to 501Y.v2
  - J&J – single dose vaccine – efficacy in SA 64% (3% of participants had HIV) vs 66% in other settings
    95% of vaccine failures due to 501Y.v2
  - Both Novavax and J&J 85% effective against severe disease even in SA.
  - Astra Zeneca:
    - 22% (95% CI: -50 to 60%) effectiveness against mild to moderate disease overall
    - 75% (95%CI: 9 to 96%) effectiveness before emergence of 501Y.v2
    - 95% of failures were 501Y.v2
In vitro studies of antibody responses vs 501Y.v2 (B.1.351) in vaccinees

Astra Zeneca / Oxford

Antibody responses in vaccinees

Old virus 501Y.v2 virus

Moderna

But other aspects of immune system – not just antibodies

Don’t know what laboratory measures can indicate protection “correlates of protection”

Pfizer
Re-infection risk with 501Y.v2 (B.1.351)

- Proven reinfections with 501Y.v2 but modelling studies suggest no greater re-infection risk vs other lineages
- 501Y.v2 resistant to convalescent sera
  (Wibmer et al. bioRxiv; 19 Jan 21; Cele et al. medRxiv; 26 Jan 21; Wang et al. bioRxiv 26 Jan 21)
What can be done?

- Molecular surveillance
  - Identify variants
  - ? Change vaccines

- Multivalent vaccines

- Predict likely mutations

↓ Transmission (remember: for viruses more is more)

Protect yourself and others this summer

- Sick? Stay home & arrange a test
- Keep physical distance
- Wear a mask
- Cover your cough
- Open doors & windows
- Avoid crowds, close-contact & confined spaces
- Wash/sanitise hands often
Thank you

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South African COVID-19 Variant Research Consortium

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Big shout out to the virologists who have stepped up time and again to deliver on SARS-CoV-2 testing, while also doing sequencing for molecular surveillance, implementing antigen tests and doing antibody testing for sero-surveillance. Thank you!

For those who look at Cape Town’s #SARSCoV2 test positive rate and frustrated about not doing more tests, we are doing roughly 4 times the test with a third of staff in isolation/quarantine while turnaround time is slightly up compared to 2 months ago. #thestraggleisreal