Coronavirus: What is it? Where did it come from? Where is it going?

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I respectfully acknowledge that I live and work on the unceded territory of the xʷməθkwəy̓əm, Skwxwú7mesh, Stó:lō and Səl̓ílwətaʔ/Selilwitulh Nations.
Disclosures

Have received grant/contracts paid to my institution from:

• Roche
• Hologic
• Siemens

As these grants/contracts are unrelated mitigation is not required
Coronaviruses: What are they? Family of RNA viruses that infect many species

**Alphacoronavirus**
- Canine coronavirus
- Feline coronavirus
- Bat coronavirus HKU2
- Bat coronavirus HKU8
- Porcine respiratory coronavirus
- Porcine epidemic diarrhoea virus
- Transmissible gastroenteritis virus
- Human coronavirus 229E
- Human coronavirus NL63

**Betacoronavirus**
- Human coronavirus OC43
- Human coronavirus HKU1
- Murine coronavirus
- Bat coronavirus HKU4
- Bat coronavirus HKU5
- Bat coronavirus HKU9
- Severe acute respiratory syndrome CoV (SARS-CoV)
- Middle East respiratory syndrome CoV (MERS-CoV)
- **Severe acute respiratory syndrome CoV-2 (SARS-CoV-2)**
- Porcine haemagglutinating encephalomyelitis virus
- Hedgehog coronavirus
- Bovine coronavirus
- Canine respiratory coronavirus
- Equine coronavirus

**Deltacoronavirus**
- Bulbul coronavirus HKU11
- Thrush coronavirus HKU12
- Munia coronavirus HKU13
- Porcine coronavirus HKU15

**Gammacoronavirus**
- Infectious bronchitis virus
- Beluga whale coronavirus SW1
Factors that increase zoonoses include:

Zoonoses 101

• **Zoonotic sourced infections** → depend on the prevalence of the agent in their normal reservoir(s) → spillover rate to other species

• **Reservoir to human contact rate is important** → SARS vs MERS vs SARS-CoV-2 (humanized)

• **Transmission probability** → $R_o < 1$ stuttering introductions vs $R_o > 1$ sustained transmission (variants play a role)

Wu et al. Lancet 2020
Zoonoses 101 cont’d

• **Host immunity** → novel agent introduced into a non immune population → cross protection from prior exposure to other human coronavirus types (HKU1, OC43, NL63, & 229E)?

• **Dose** → more virus → greater transmission risk (HIV) → potential for more severe illness (Varicella) → masks
  
  • Children have less developed immune systems → shed more respiratory viruses, and are typically less symptomatic than adults → variant specific

• **Pathogenicity/virulence** → once humanized → person-to-person transmission → variants impact transmissibility!

Wu et al. Lancet 2020
“One Health” = Interface between humans, animals and the environment

Pre-emergence
- Anticipation
- Viral surveillance

Pathogen spillover
- Primary prevention
  - Reduction of deforestation, agriculture, wildlife trade

Emergence
- Early detection
- Syndromic surveillance

Localized transmission
- Containment
- Contact tracing
- Isolation

Epidemic
- Control & mitigation
- Widespread testing
- Quarantine
- Scale-up in healthcare, school and business closure

Pandemic
- All prior measures brought to a larger scale

Pathogen evolution in wild animals

Direct spillover
- Vectors
- Domestic animals

Human amplification

Global spread

Bernstein et al. The costs and benefits of primary prevention of zoonotic pandemics, Science Advances 2022
SARS-CoV-2: Where did it come from?

**Direct Zoonosis**
- A: Intermediate Animal Host
- B: Cave Visitor, Spelunker or other inadvertent Bat contact

**Laboratory-Related Origin**
- C: Laboratory Personnel Infection
- D: Lab Research, Lab Accident

Lytras et al. The animal origin of SARS-CoV-2. Science, 2021
Genomics – Whole Genome Sequencing

1. Enabled SARS-CoV-2 discovery
2. Sequence → creation of specific PCR tests
3. Vaccine design & therapeutic targets
4. Track spread
   - differentiate introductions of new strains from e.g., travel vs community transmission
   - determine outbreak sources: schools, LTCF, mink farms
   - monitor for variants
5. Reinfections, vaccine failures & escape mutants
SARS-CoV-2 Variants Based on WGS (n>130,000)

SARS-CoV2 samples genome sequenced by BCCDC
7-day rolling frequency since 1st January 2021. Top 20 lineages only shown, remainder classified as 'Other'

Lineage
- (Alpha) B.1.1.7
- (Delta) AY.103
- (Delta) AY.122
- (Delta) AY.126
- (Delta) AY.25.1
- (Delta) AY.27
- (Delta) AY.4
- (Delta) AY.44
- (Delta) AY.74
- (Delta) AY.93
- (Delta) B.1.617.2
- (Gamma) P.1.14
- (Omicron) BA.1
- AL.1
- B.1.1.519
- B.1.2
- B.1.36.36
- B.1.429
- B.1.438.1
- B.1.617.1
- Other

Samples sequenced per day (7 day rolling average)

VOC confirmation
Sequencing all positives received
Sequencing 100% week 1 each month
Sequencing all positives received
Sequencing a representative subset of positives received

James Zlosnik

Pangolin version: 3.1.17, PangoLEARN: 2022-01-05, Total sequences: 115,604
Travel vs Community Omicron BA.2 Spread

Variants can be introduced from travel or occur locally
Genomics Enables Assessment of how Mutations Impact Infectivity/Transmission/Immunity

Evasion of nAb
(T19R, S45F?, T95I? G142D, E156G/Δ157-158)

Increased ACE2 affinity
(L452R, T478K)

Increased Furin affinity/cleavage
(P681R, Q675H)

Decreased TMPRSS2 affinity
(P812S)

Decreased spike protein stability
(Q675H, A846S, P1162L)

Increased spike protein stability
(A647S, A845V)

Increased fusion?
(P812S, A846S D950N, P1162L)
Mutations arising in SARS-CoV-2 spike on sustained human-to-human transmission and human-to-animal passage
Chen and Senft, Covid-19 and emerging viral disease: the journey from Animals to humans 2020
• Pathways to immunity occur either from infection which can have severe consequences or vaccination!
• Immune response targets both structural & non-structural proteins
• Both antibody (Ab) & cell mediated immunity (CMI) are imp. for viral control
• Ab is easier to measure

Alanagreh el. Pathogens 2020
Where is it going?

We need to use genomics/molecular biology to create vaccines that protect against emerging variants & related viruses!

• Optimize current vaccines – regimens/boosters, mix & match
• Develop
  • “Variant specific” vaccines – combine different strains, multivalent
  • Next generation broadly protective SARS-CoV-2 vaccines which are able to protect against existing/future variants
• “Universal” coronavirus vaccines – protect against betacoronaviruses/pan-coronaviruses

Adapted Stanley Plotkin 2022
Su et al. Developing pan-β-coronavirus vaccines against emerging SARS-CoV-2 variants of concern 2022.
Wheatley et al. Immune imprinting and Sars-CoV-2 vaccine design. Trends in Immunology 2021
SARS-CoV-2 Conclusions

• What is it?
  • It’s a Betacoronavirus that is here to stay!
  • We are viewing this pandemic with genomic, molecular biology, & epidemiological tools that were unheard of in the past

• Where did it come from?
  • It started as a zoonosis & decided that it likes humans & other animals
  • Its survival depends on its ability to breed variants – more will emerge
  • It has relatives that pose a risk for future pandemics!

• Where is it going?
  • Current spike-based vaccines protect against severe disease but not omicron acquisition – vaccine durability & what happens with waning immunity remains a big unknown
  • We need better current and ongoing epidemiological population level correlates between vaccination status, infection status, & immunity
  • Climate change & globalization will impact the interface between humans, animals, & the environment – we need inter-sectoral ”One Health” approaches that build global pandemic resiliency
SARS-CoV-2 is the Pandemic’s Pandemic.

“A lie gets halfway around the world before the truth has a chance to get its pants on”

Winston Churchill