An Intersection between Genetics and COVID-19

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May 7, 2021
Outline

• Biology review
  • Humans and viruses
• SARS-CoV-2 virus, its cousins, and its animal hosts
• Genetic technology and novel vaccine development
• Epigenetics approach to identifying risk factors for severe COVID-19 disease
Human Biology Review

- Chromosomes comprise double-stranded DNA
Human Biology Review

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- Transcription is process of transcribing DNA to messenger RNA (mRNA)
Human Biology Review

• Chromosomes comprise double-stranded DNA
• Transcription is process of transcribing DNA to messenger RNA (mRNA)
• Translation is process of translating mRNA to proteins via assembling amino acids
mRNA starts with the 5’ end
Virology
Viruses

DNA viruses

RNA viruses

Single-stranded

Double-stranded

Positive-sense

Negative-sense

Naked

Enveloped

Coronavirus

4 Human coronaviruses

SARS-CoV-1

MERS

SARS-CoV-2

Variants
Zoonotic viruses

- Influenza
- West Nile virus
- Rabies
- Dengue fever
- Ebolavirus

- HIV
  - Jumped the species barrier at least two independent times
SARS
Animals linked to SARS-CoV-1

- Masked palm civet cats
- Racoon dogs
- Horseshoe bats

[Links]
https://www.pinterest.com/pin/225180050089265247/
Animals linked to SARS-CoV-2

• Pangolin
• Horseshoe bats
• Mink

https://www.thethirdpole.net/en/nature/pakistan-pangolin-scales/
https://www.pbs.org/wgbh/nova/article/mink-covid-virus-mutation/
Virus variants

• All viruses change and mutate.
  • Most mutations are not good for the virus.
  • Only small percent of mutations are beneficial to the virus.
  • Because the virus replicates itself billions/trillions/gazillions of times across the globe, those rare times the mutation is beneficial for the virus is enough for it to turn into a new strain or variant.

• More effective strains replace the old, less effective strains.
Tracking the Variants of COVID-19

Reported in the US
• P.1 = 5,153
• B.1.1.7 = 84,081
• B.1.351 = 1,147
• B.1.429+B.1.427 = 37,615
• B.1.525 = 642
• B.1.617+ = 325

Reported in Oklahoma
• P.1 = 2
• B.1.1.7 = 118
• B.1.351 = 4
• B.1.429+B.1.427 = 17
• B.1.525 = 1
• B.1.617+ = 2

https://www.gisaid.org/hcov19-variants/
Vaccine Development
Brief timeline of synthetic mRNA development

• 1990: researchers at University Wisconsin inject mice with mRNA to express selected genes
• 1989-2005: Dr. Kariko at University of Pennsylvania studying mRNA delivery systems
  • 1989-1995: Failed to obtain research grants  
  • 1996-2005: Modest success
• 2005: Dr. Kariko made breakthrough discovery: modified nucleosides that slipped past immune system
• 2009: Dr. Rossi uses synthetic mRNA to develop stem cells
  • No need to use embryos

Continued timeline of synthetic mRNA development

• 2010: Dr. Rossi co-founds Moderna
• 2013: BioNTech (German company) hires Dr. Kariko as senior VP over mRNA work
  • BioNTech focus on cancer therapy use of mRNA
• Jan 10, 2020: Chinese scientists post SARS-CoV-2 genetic sequence
• Feb 24, 2020: Moderna has first vials of experimental vaccine
  • Computer programming used to develop sequence
• July 28, 2020: Moderna initiated late-stage vaccine trial
Background on mRNA vaccines: Pfizer and Moderna

mRNA vaccines instruct the immune system to recognize a specific part of the virus

SARS-2-CoV -> mRNA that encodes the spike protein is synthesized and packaged inside a lipid coating

Cell -> Cells use the mRNA to make a spike protein that is recognized by the immune system
Epigenetics
Genetics and risk of severe COVID-19 morbidity

- Study of 407 people with confirmed COVID-19
  - Age ≤ 61 years
  - Mild disease: 194 patients; Severe disease 213 patients (hospitalized with respiratory support)
- Study population split into prediction and validation cohorts
  - Stratified by disease severity
- 44 CpG sites significantly associated with COVID-19 disease severity
  - Genes associated with immune system and interferon release
- Using validation cohort, epigenetic signature able to predict severe disease with 88.2% specificity and 77.8% sensitivity
- In general population: 13.3% of people have epigenetic signature
  - Approximate percent of population who get severe COVID-19
Summary

• Genetics and the building blocks of life
  • Viruses mutate and find new hosts for survival
• Synthetic mRNA technology not new, but still in its infancy
• Risk factors for severe COVID-19 disease likely associated with genetic factors
Questions?