CORONAVIRUSES: Emerging pathogens

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Coronaviruses are a family within the Nidovirus order; named for the nested subgenomic mRNAs generated during infection.
Coronavirus Timeline

- **OC43 229E**
  - Common cold
  - OC43 can infect lower respiratory tract

- **Basic CoV Biology**

- **1960-70**
  - MHV model
  - Animal viruses, vaccines
  - Human cold CoVs

- **1980**
  - HKU1
  - Pneumonia
  - NL63; Bronchiolitis, croup

- **1990**
  - SARS-CoV
  - Bat CoVs

- **2000**
  - MERS-CoV

- **2010**
  - SARS-CoV-2

- **2020**
  - Pathogenic human coronaviruses
  - SARS-CoV, MERS-CoV, SARS-CoV-2
  - Severe acute respiratory disease coronavirus disease-2019 or COVID-19
SARS-CoV interspecies transmission

How many times did this happen?

Over in eight months, 8098 infections, 9.6% mortality
87% in China and Hong Kong

Images from various internet sites
MERS-CoV interspecies transmission

Neoromicia capensis
Bat

Mostly in Arabian peninsula

Camels are a reservoir for MERS-CoV
Still new cases 2020
2428 cases, 35% mortality

Camel

Human
limited human to human spread

Korea
SARS-CoV-2 interspecies transmission

Bat → ??? → Intermediate species Malayan pangolin → Human

34.7 M infections
1,030,880 deaths

US  7.3 infections
209,318 deaths

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Coronavirus genome structure

**Conserved replicase proteins 16 nsps**

**Accessory proteins**

**Alphacoronaviruses**
- Duvinacovirus
- Setracovirus

**Betacoronaviruses**
- Lineage a, Embecovirus
- Lineage b, Sarbecovirus
- Lineage c, Merbecovirus

**Coronavirus genome structure**

- **229E, NL63**: 229E, NL63
- **SARS-CoV**: SARS-CoV
- **SARS-CoV-2**: SARS-CoV-2
- **MERS-CoV**: MERS-CoV

**Accessory proteins**

- AAA3'
- 5'

**Prominent proteins**

- SPIKE
- E
- M
- N
- 3CLpro
Coronavirus conserved proteases and replicase

nspl: multiple host antagonist activities
nsp3: host antagonist activities
DUB macrodomain

ORF1a

nsp1: 3C-like protease
nsp8: primase
nsp10: activator

nsp13: helicase NTPase
nsp15: EndoU; dsRNA accumulation
nsp14: ExoN Proof reading mRNA capping
nsp16: mRNA capping

RNA dependent RNA polymerase RdRp
Replication of genome and transcription of mRNAs
remdesivir

ORF1b

nsp12
nsp13
nsp14
nsp15
nsp16
How do we know SARS-CoV-2 was not engineered by humans?

• Similar viruses are found in bats

• It does not resemble any known recombinant viruses

• It seems impossible that anyone would know how to design a virus with the properties of SARS-CoV-2
For the future

• Vaccine development
• Develop antivirals for future outbreaks or spillovers
  • Spike protein RBD may differ while replicase proteins are conserved
• Continue to identify and characterize Coronaviruses and other viruses from bats and other species
• Support basic virology research