NOVEL CORONAVIRUS

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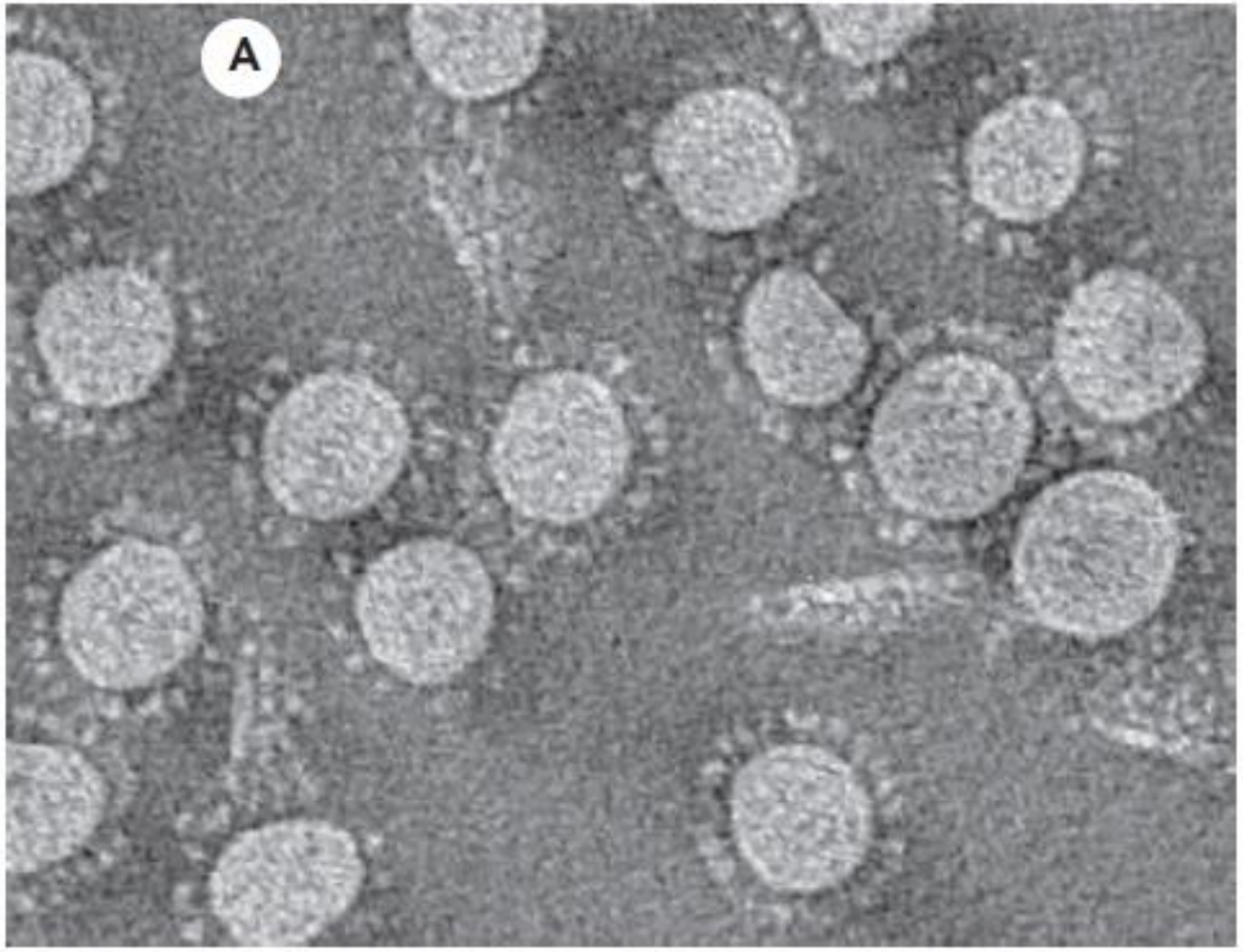
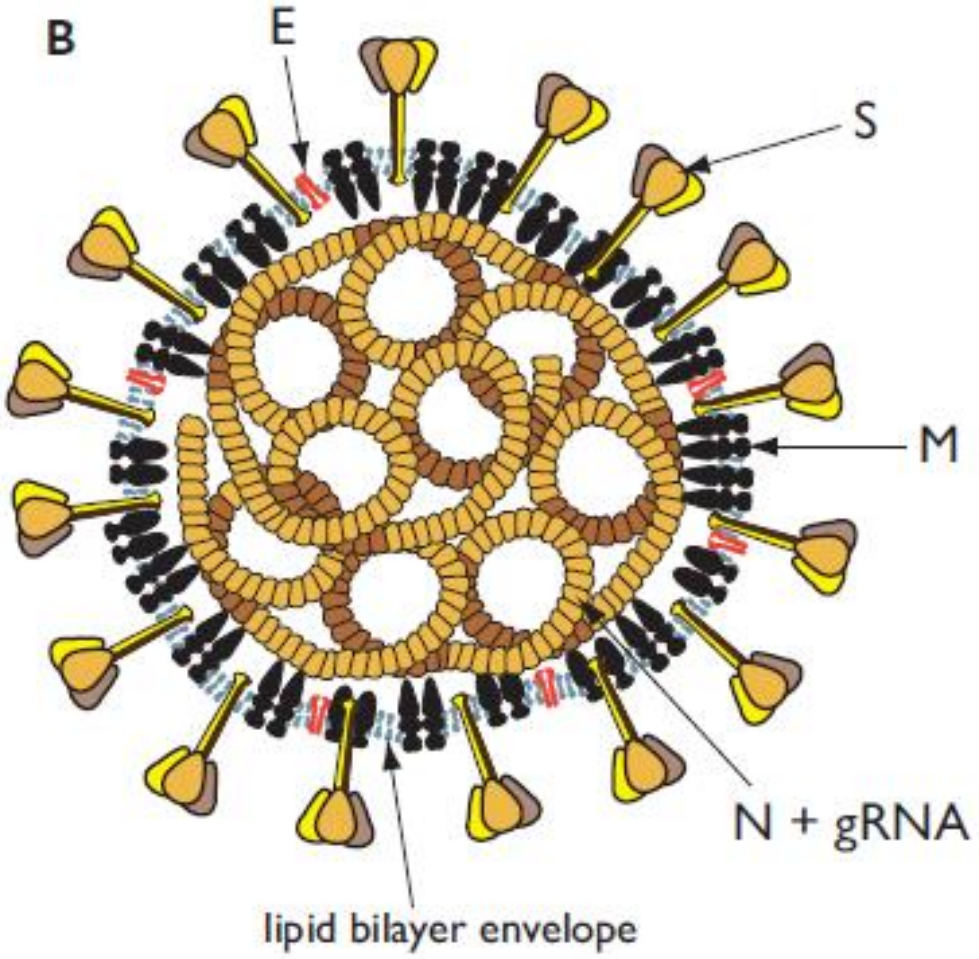
- Structure
- Pathogenesis and Clinical Syndromes
- Origin
- Why bats are blind to virus infection?
- Vaccination
- Treatment

STRUCTURE:



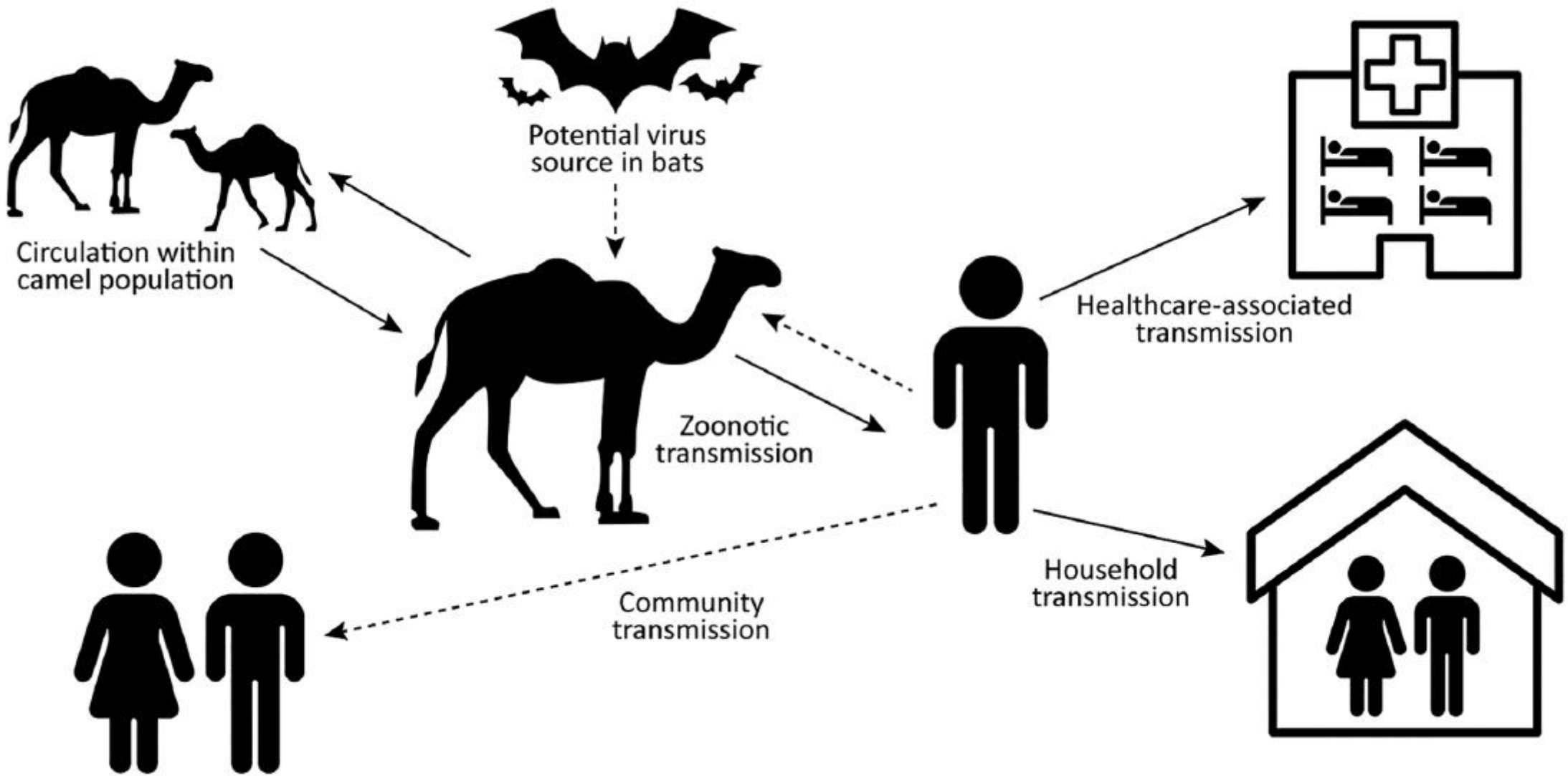


- **Family : Coronaviridae**
- **Order : Nidovirales**
- **Genera : alpha, beta, delta and gamma coronavirus**
- **emerging CoVs:**

1-Severe acute respiratory syndrome coronavirus (SARS-CoV)

2-Middle East respiratory syndrome coronavirus (MERS-CoV)

3- Novel coronavirus belonging to beta coronavirus.

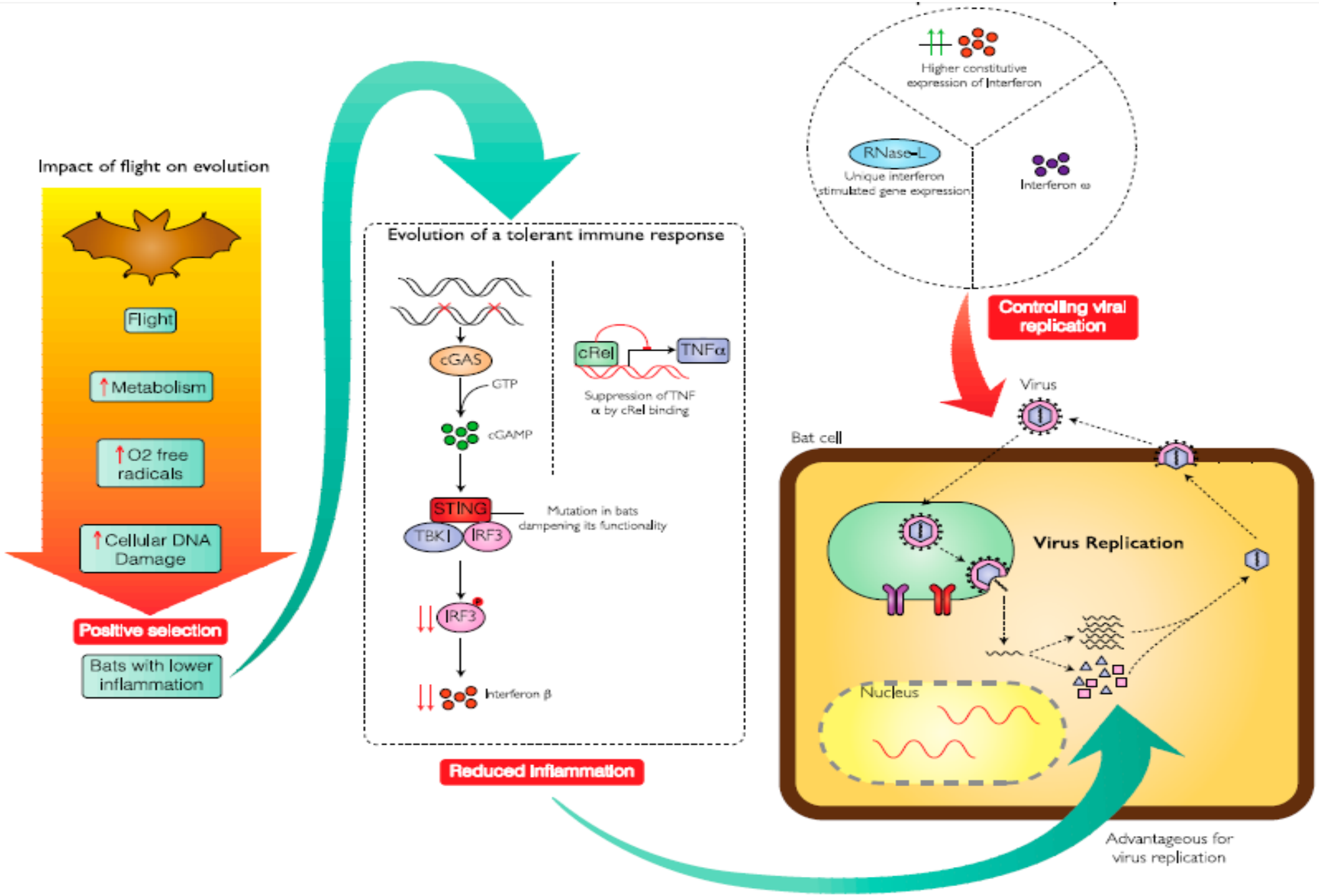

Potential virus source in bats
Circulation within camel population
Zoonotic transmission
Healthcare-associated transmission
Household transmission
Community transmission

- **The two highly pathogenic viruses, SARS- CoV and MERS- CoV, cause severe respiratory syndrome in humans, and the other four human coronaviruses (HCoV- NL63, HCoV-229E, HCoV- OC43 and HKU1) induce only mild upper respiratory diseases in immunocompetent hosts, although some of them can cause severe infections in infants, young children and elderly individuals**
- **Coronavirus can infect mammals, birds and reptile, including human, swine, cattle, horses, camels, cats, dogs, rodents, birds, bats, rabbits, ferrets, mink, snake, and various wildlife species**

SYNDROMES:

- **A range of disease has been observed: fever, dry cough, shortness of breath, and leukopenia pneumonia including difficulty breathing, and bilateral lung infiltration in the most severe cases.**
- **Patients have included mild cases needing supportive care.**
- **Host conditions including age, biological sex, and overall health including hypertension, diabetes, heart and/or kidney function issues that may have made them more susceptible.**

- The source of the 2019-nCoV is still unknown.
- In addition to seafood, it is reported on social media that snakes, birds and other small mammals including marmots and bats were sold at the Huanan South China Seafood Market.
- The WHO reported that environmental samples taken from the marketplace have come back positive for the novel coronavirus, but no specific animal association has been identified
- An initial report suggested that snakes might be the possible source based.
- More interestingly, an origin-unknown homologous recombination was identified within the spike glycoprotein of the 2019-nCoV5, which may explain its decreased pathogenesis, snake-to-human cross species transmission, and limited person-person spread


Impact of flight on evolution
Flight
↑Metabolism
↑O2 free radicals
↑Cellular DNA Damage
Positive selection
Bats with lower inflammation
Evolution of a tolerant immune response
cGAS
GTP
cGAMP
STING
TBK1
IRF3
IRF3
Interferon β
Mutation in bats dampening its functionality
cRel
TNFα
Suppression of TNF α by cRel binding
Reduced Inflammation
Higher constitutive expression of Interferon
RNase-L
Unique interferon stimulated gene expression
Interferon ω
Controlling viral replication
Virus
Bat cell
Virus Replication
Nucleus
Advantageous for virus replication

- Live attenuated virus with gene deletion
- Two whole virus vaccines
- DNA vaccine which encodes the full length or part of the S protein gene
- Most of them have been tested in mouse models and showed the ability to elicit neutralizing antibodies.

- Several bottlenecks

1-a lack of proper animal models for evaluating vaccine efficacy.

2-there are limitations from the s protein itself, such as mutations in the neutralization antibody epitopes in s protein that can cause virus escape non-neutralization antibody epitopes in vaccines that may elicit antibody-mediated disease enhancement (ade)

3- dna vaccines may recombine with other viruses.

4- pre-existing immunity may eliminate the vaccine by removing the general human virus vectors .

5-there is the problem of return on investment which may be slow and, hence, inhibit investments and slow down the clinical study.

- At the present, no specific antiviral therapy has been approved for treatment of infection by human CoVs.
- As development of vaccines and compounds for prevention and treatment of infection have been brought to priority status by WHO and governments , numerous drug studies have been done or are moving forward.
- Some of them focus on the CoV fusion/entry process either by inhibition of S1 mediated virus attachment or by blocking of S mediated virus-cell membrane fusion, and some of them interfere with viral replication .