COVID-19 :

new virus, pandemic and what is expected from vaccination

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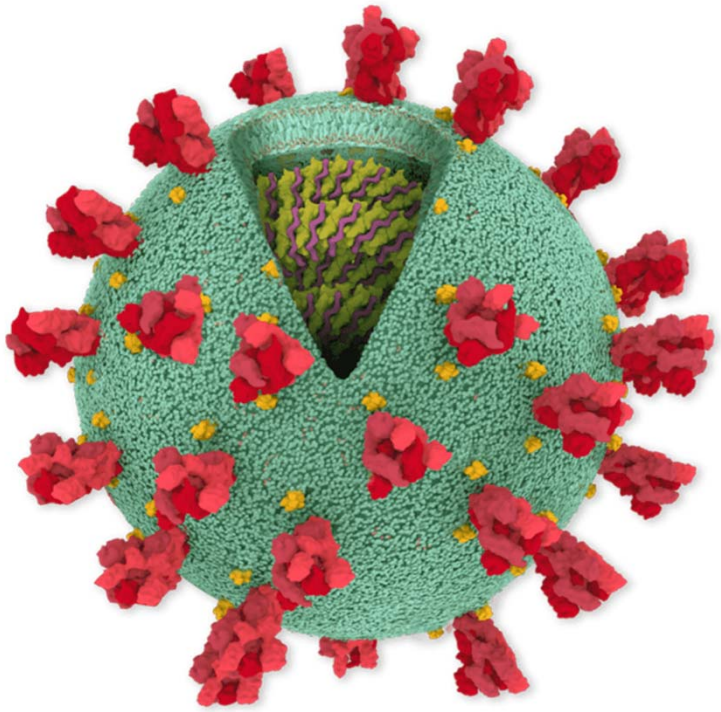
COVID-19 Pandemia in simple numbers

- Nearly **90 million** cases
- **2 million** deaths
- **222** countries involved
- America and Europe most involved Regions
- **Third wave** of infections now rampant in several countries
- **Many** SARS-CoV-2 variants around, some with mutations which further increase virus transmissibility (UK and South Africa 501 V)

(official data from WHO, December 10, 2021)

SARS-CoV-2 mediatic iconography



SARS-CoV-2 main features

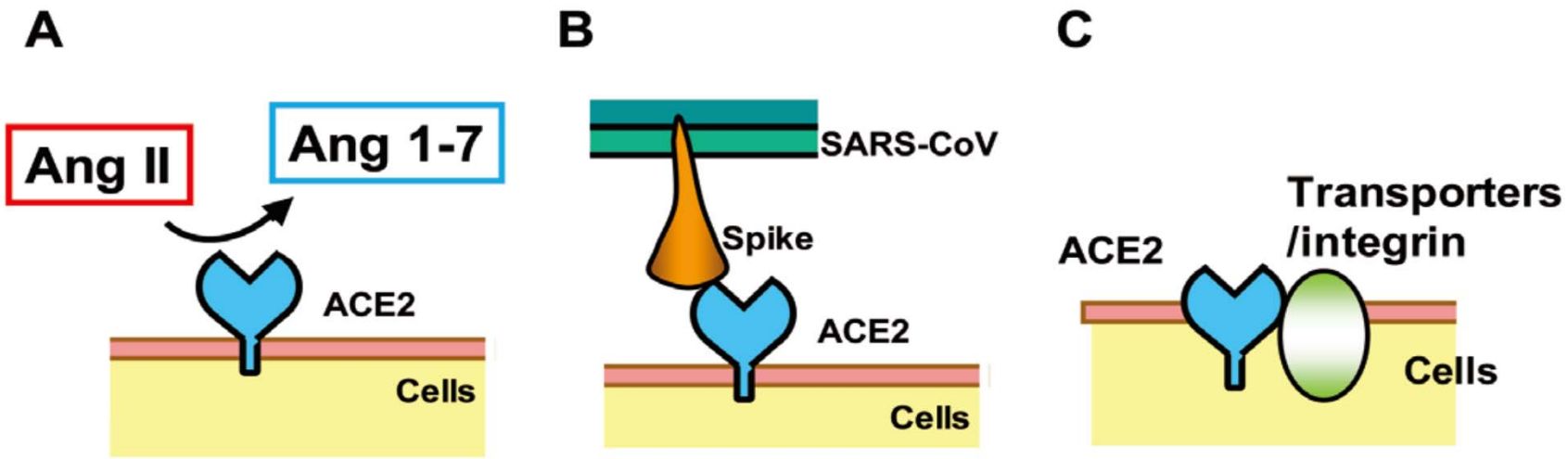
- Positive RNA genome, 30,000 nucleotides
- Spike protein
- Other structural proteins :M, N and E (membrane , nucleocapsid and envelope) proteins.
- 16 Non-structural proteins, including some which serve to inhibit host cell defenses
- Some other accessory proteins

COVID-10 Main Features

- Multi-organ illness, not only interstitial pneumonia
- The virus causes early inflammation, then cytokine storm (possible switch off innate immunity
- Risk factors, ageing and pre-existing systemic co-morbidities
- Case-fatality rate, relatively low (around 1-2%)

Absence of any specific, anti-viral therapy, only supportive (anti-inflammatory and anti-coagulants)

ACE Receptor, ACE 2 functions and SARS-2-CoV



From Cassone et al. Path-Global Health, 2020 ,18 165-167

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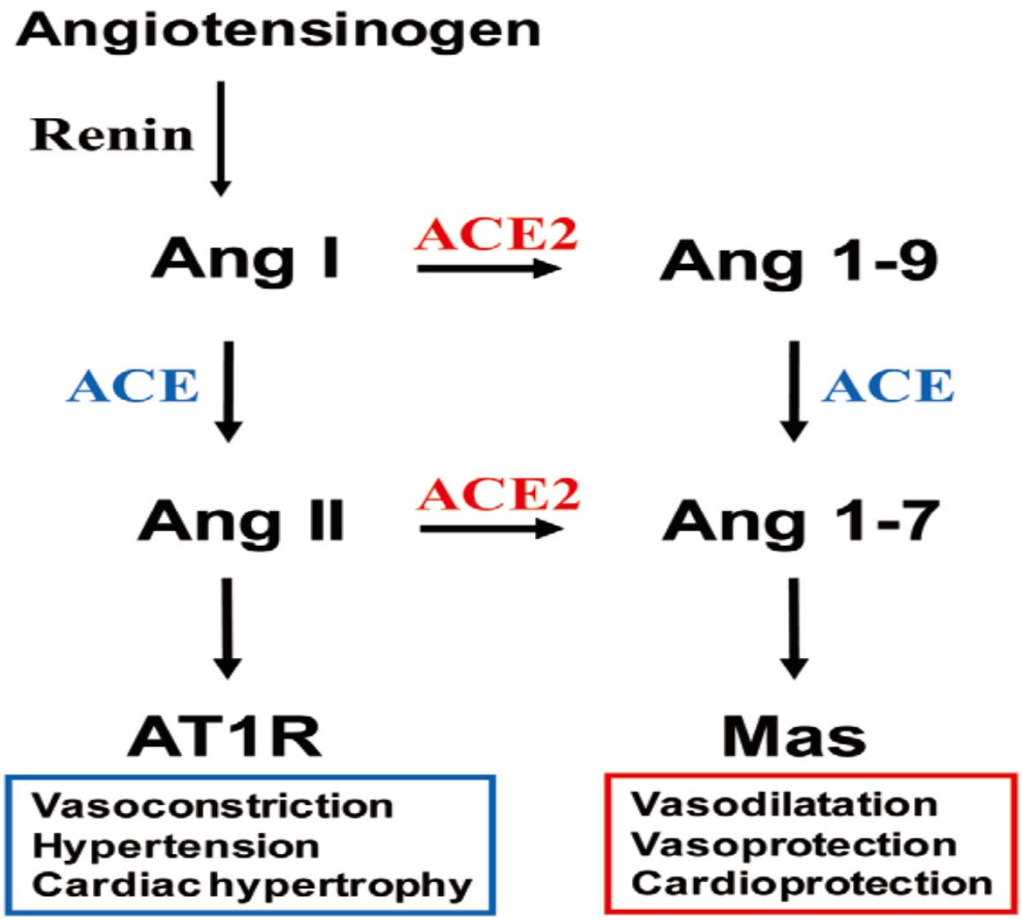
Slide 6

ac1 antonio cassone, 3/27/2020

The critical physiological role of ACE2



Some epidemiology

- Generation time : the average time an infected person transmits the virus to another person
- Serial time : the average time a sick person infects another person who develops symptoms of disease.
- In all models and with experimental evidence the generation time has been much shorter than the serial time

ROLE OF ASYMPTOMATIC INFECTION

Implications of asymptomatic transmission

- You can’t rely on isolation of symptomatic subjects only
- Need of large, if not mass, testing whenever possible
- High efficiency of forward and backward contact tracing for an effective quarantine measures

Dfferences between two simultaneously hit Italian regions during the first epidemic wave.

Feature	Lombardy	Veneto
N° cases	8452	3748
N° deaths	1611	382
N° tests	57682	214.238

(each feature/million residents; data from Cassone& Crisanti, Path.Glob. Health, 2021, in press)

Mass testing expectations

- Rapid antigenic tests
- Salivary tests
- Self-testing
- Mass screening

Progress in COVID-19 Therapy ?

- Repurposed Drugs (chloroquine, lhydroxychloroquine, lopinavir…)
- Remdesivir : last evidence against
- Convalescent plasma and mAbs : still not definitive
- Anti-inflammatory and anticoagulants : evidence in favour

The True Progress: Anti-SARS-CoV-2 vaccines generated and approved in ONE year!

- 1. Small RNA virus, sequence known and start working at vaccine production the same month
- 2. RNA and vectorial platform already largely experienced in pre-clinical work
- 3.Huge amount of money and human resources allocated (WARP SPEED Project and European Funds
- 4.Competition but also collaboration

COVID-19 vaccines available or next to

• Vaccine	Pfizer.Bion-Tech	Moderna	Astra-Zeneca
• Immunogen	Spike RNA	Spike RNA	Vectored
• Efficacy	>90%	>90%	65-90%?
• Logistic	hard	easier	standard

Herd immunity, R_0, and its inverse relationship with herd immunity following vaccination

• Disease	Measles	Influenza	COVID-19	UK Variant?
• R_0	18-20	2	3	6?-9?
• vaccine coverage	>95%	65-70%	70-80%	>90%?

Two-doses or a single dose when vaccine availability is low?

- With the available vaccines, there is no immunological rationale for a single dose approach and delay of second dose

- Next generation vaccines possible

- **Ethical issues**

Role of SARS-CoV-2 genome mutations : transmission enhanced, not pathogenicity

- D614G- Variant Origin unclear, first reported in Italian isolates*
- N501Y- UK variant
- N501V- South African Variant
- What's next? Mutations and what about vaccine protection?

* see Benvenuto et al. J.Infect. 2020 Jul;81(1):e24-e27

A critical question about mutations

- Will the high selective pressure exerted on virus by antibodies generated by the vaccines and the high numbers of vaccinated subjects cause virus adaptation and escape from vaccine antibodies?

- Rappuoli research team paper in BioRxiv,2020.12.28.424451; doi: https://doi.org/10.1101/2020.12.28.424451

Thanks very much for your attention!