



# SOT Inhalation and Respiratory Speciality Section Webinar



## SARS-CoV2 infection: 'A silent threat for smokers/vapers'

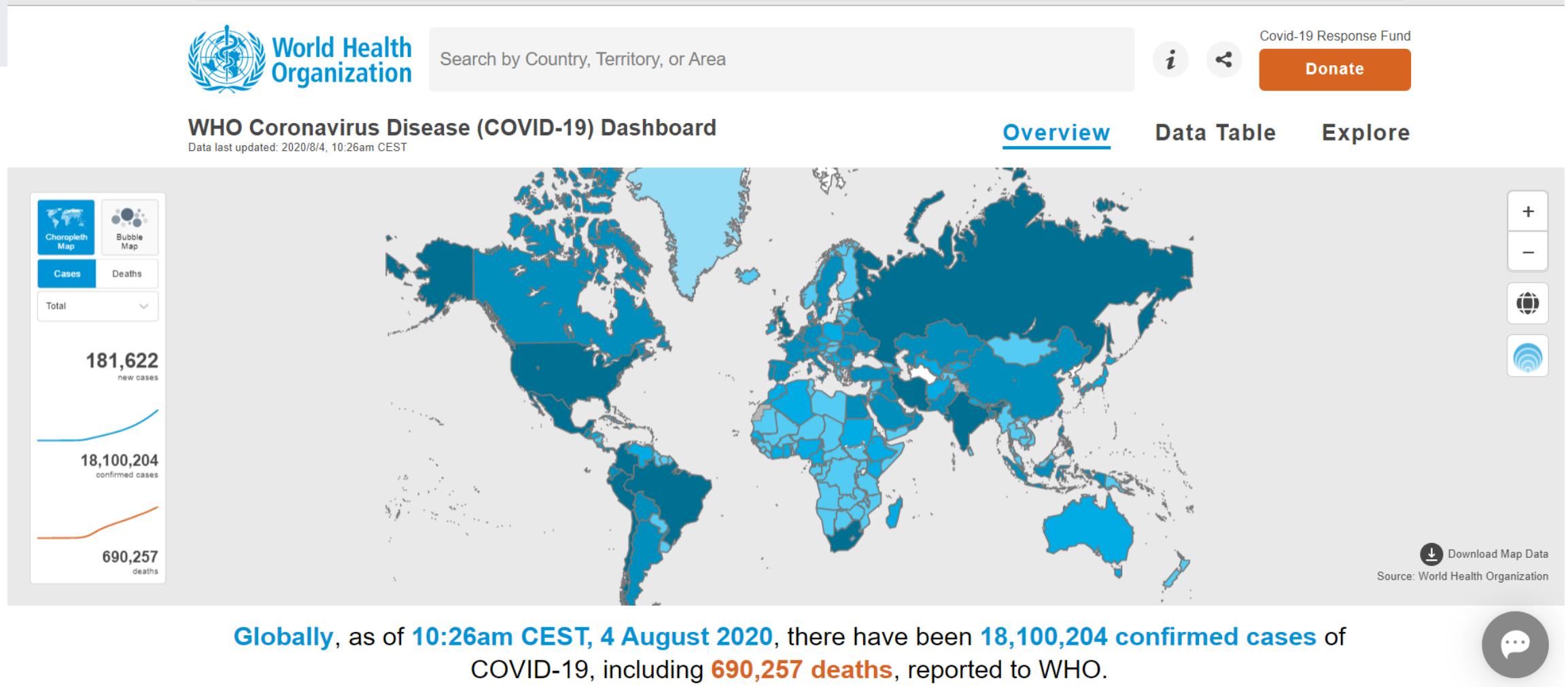
A hand is shown interacting with a futuristic, transparent interface that displays various types of COVID-19 viral particles (SARS-CoV2) in a 3D, molecular-like format. The particles are colorful, with some being blue and others red or yellow, and they appear to be floating or interacting with the interface.

Gagandeep Kaur

Postdoctoral Associate

University of Rochester Medical Center

# Coronavirus Disease-2019



**Source:** <https://covid19.who.int/>. Retrieved on August 4, 2020.

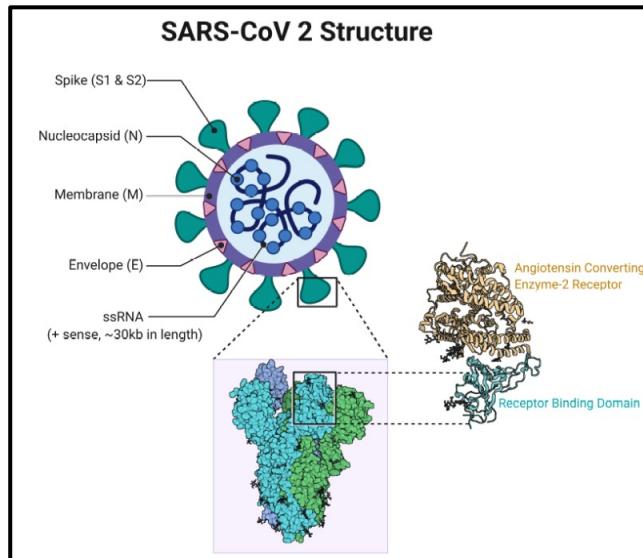
# SARS-CoV2: not an unknown virus !

Characteristics	Influenza	SARS	MERS	Covid-19
Causative Agent	Influenza A & B	SARS-CoV	MERS-CoV	SARS-CoV2
Symptoms	Fever, chills, runny nose, soar throat, head and body aches with fatigue.	Fever, headache, dry cough, shortness of breath without upper respiratory tract symptoms.	Fever, cough, shortness of breath.	Fever or chills, cough, shortness of breath, muscle or body ache, loss of sense of smell and taste, sore throat and congestion.
Reproduction number	1.3	3	0.3-0.8	2.2-2.7 *
Case Fatality Rate	0.05-0.1%	9.6-11%	34.4%	~3.4% -6.4%*
Incubation Period	1-4 days	2-10 days	6-14 days	2-14 days*

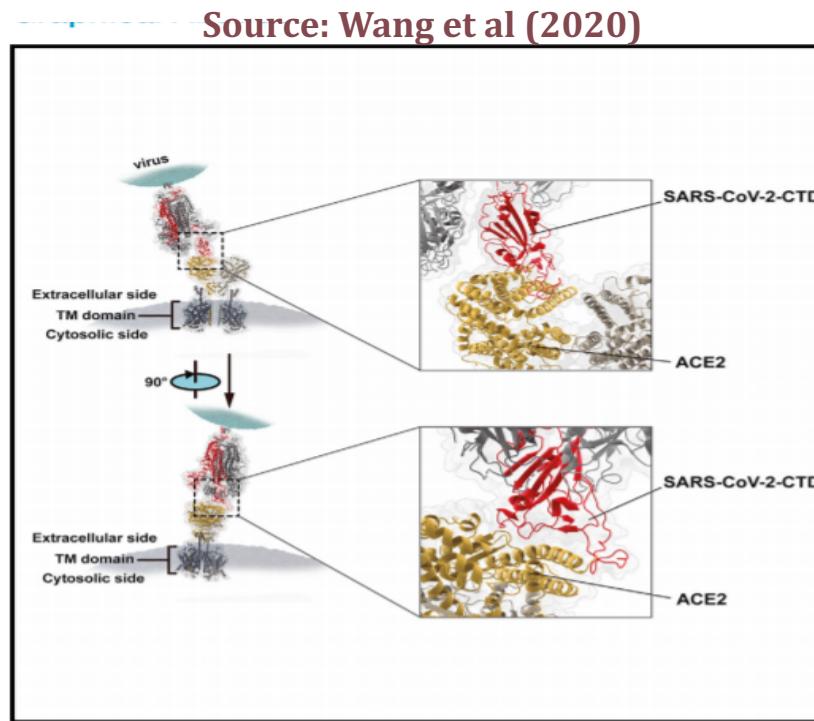
\* Covid-19 data as of July 2020.

# Structure and Antigenicity

Crown-like appearance attributed to glycosylated cell surface spike (S) protein with two functional domains-S1 and S2.

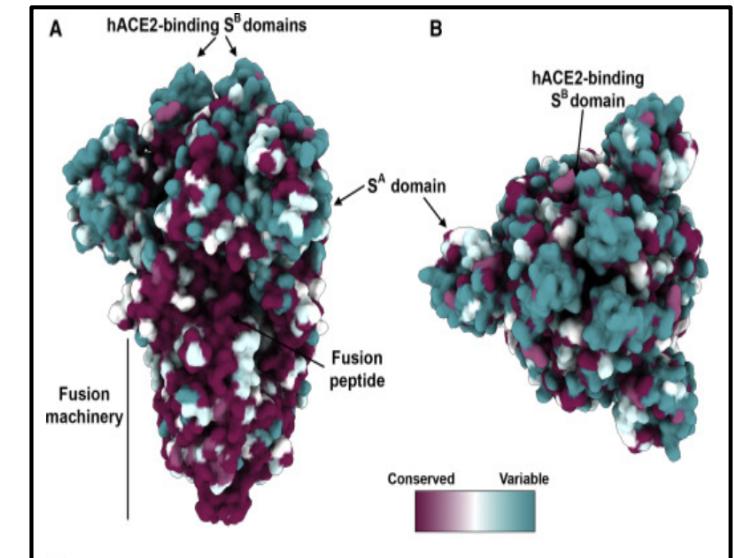


Source: Casella et al (2020)



Interacts with hACE2 via S protein C-Terminal Domain

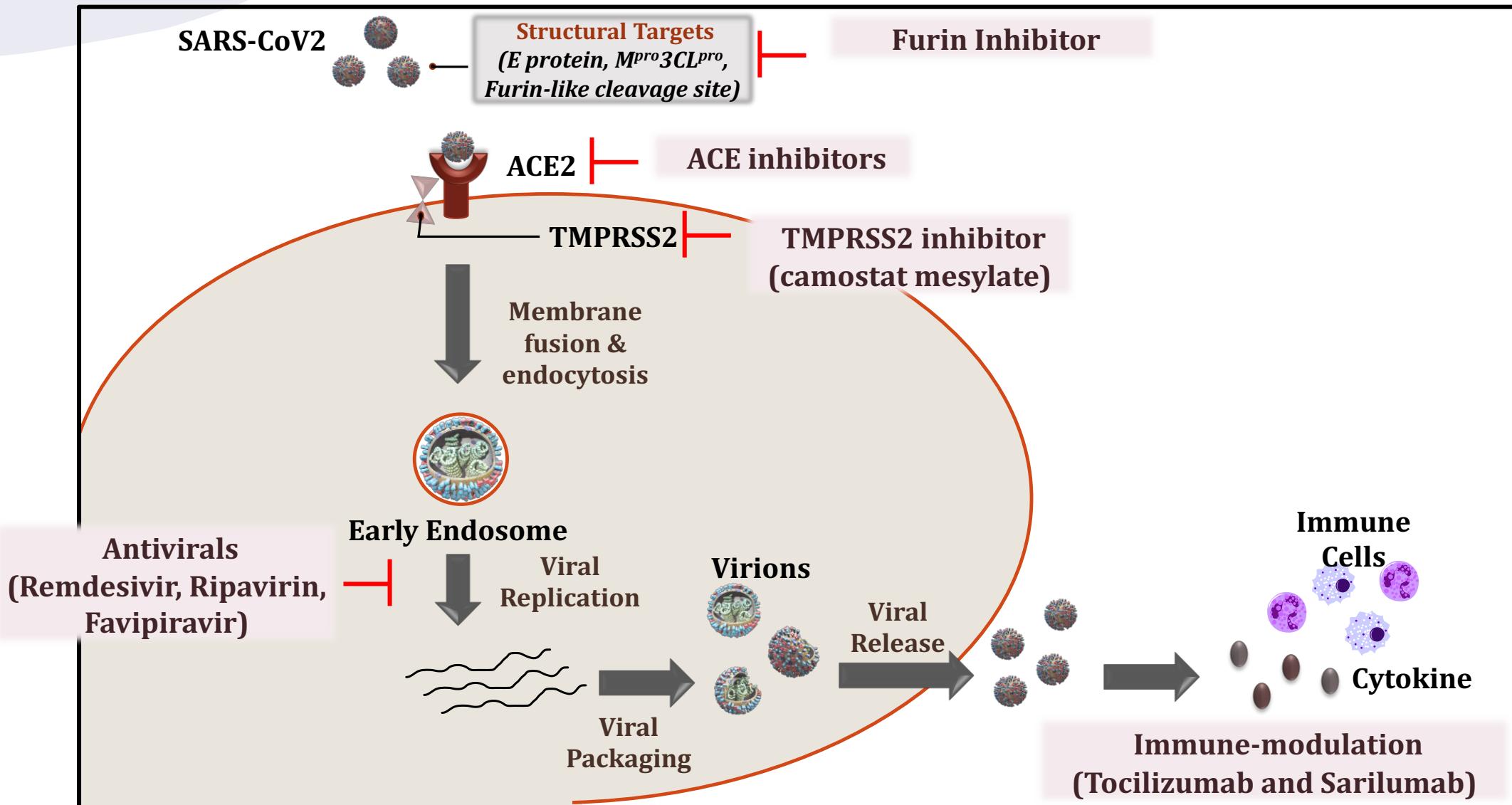
Has polybasic cleavage site, that can be processed by furin-like proteases, is reason of pathogenicity.



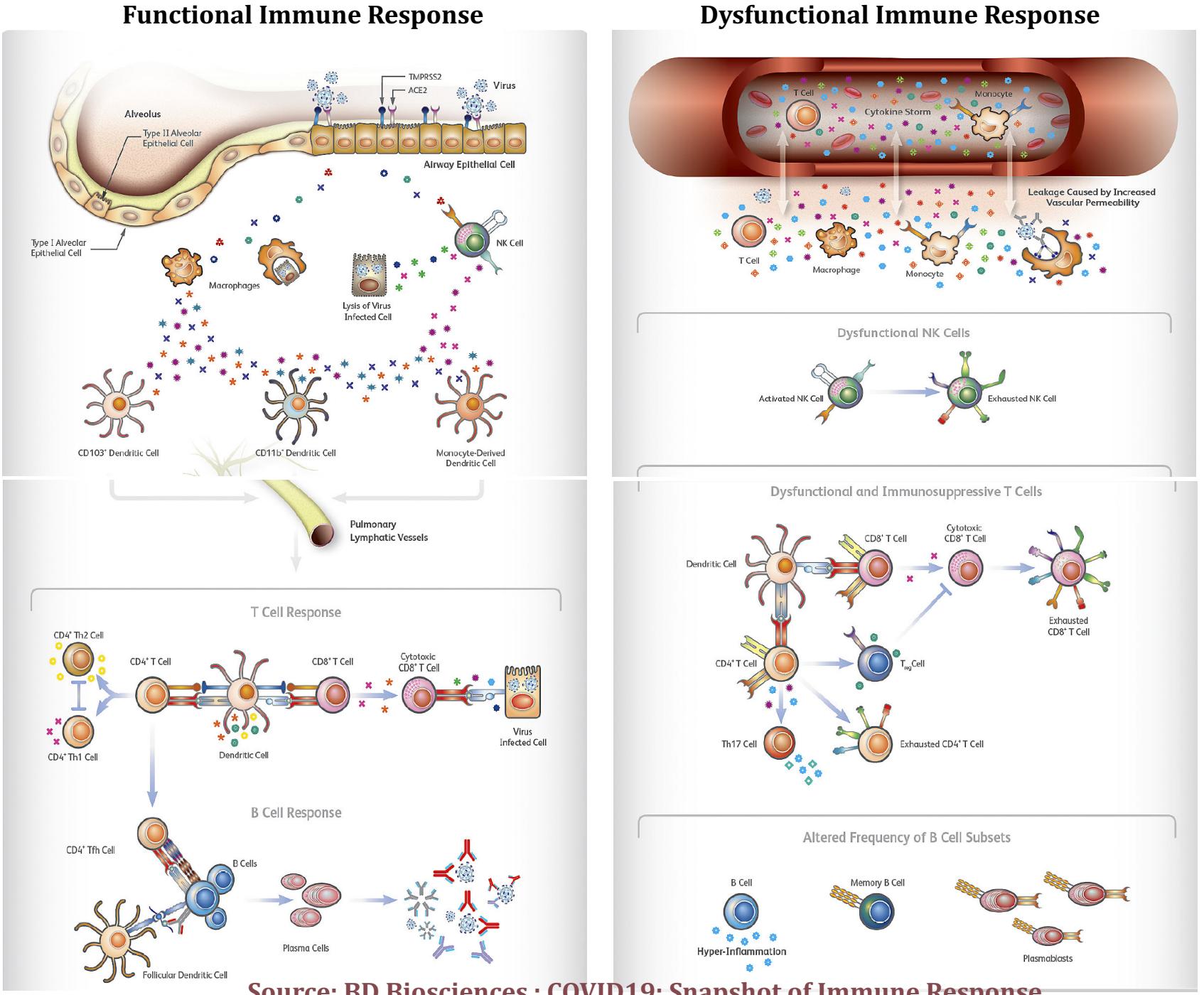
Source: Walls et al (2020), Cell.

# Entry into the cell and potential targets

Source: Adapted from Kaur et al (2020), J Inflamm



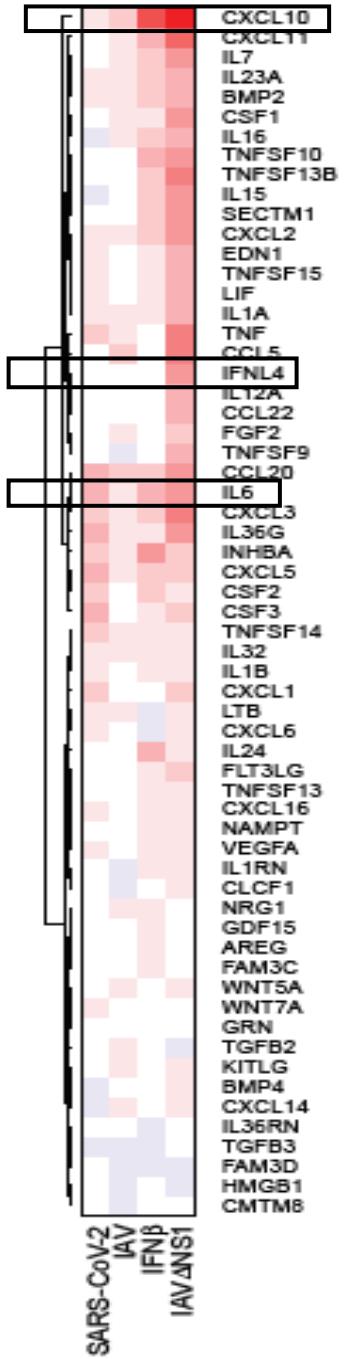
# Immune responses : Normal and Diseased



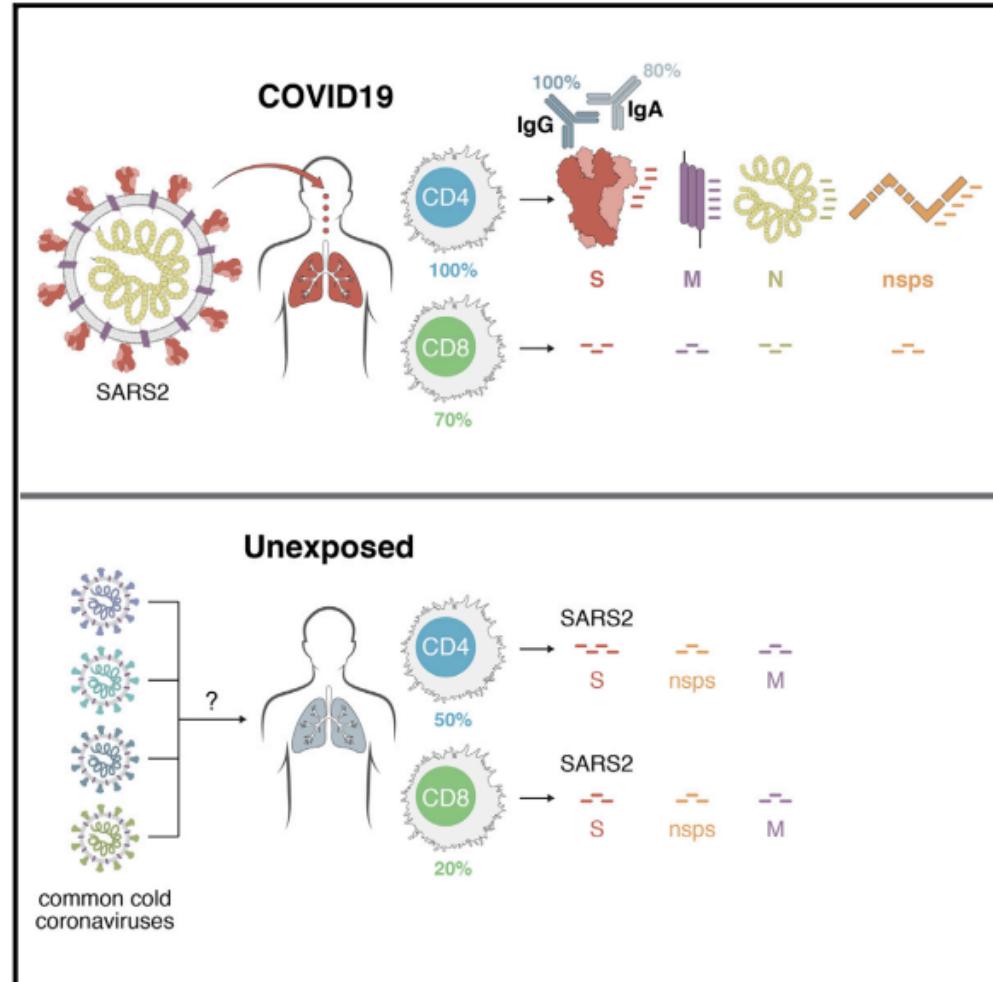
# Host-immune responses against SARS-CoV-2 infection ?

## Key Highlights:

- ✓ SARS-CoV-2 infection induces **low IFN-I and -III levels** with a moderate ISG response.
- ✓ **Strong chemokine expression** is consistent across in vitro, ex vivo, and in vivo models.
- ✓ Low innate antiviral defenses and high pro-inflammatory cues contribute to COVID-19.



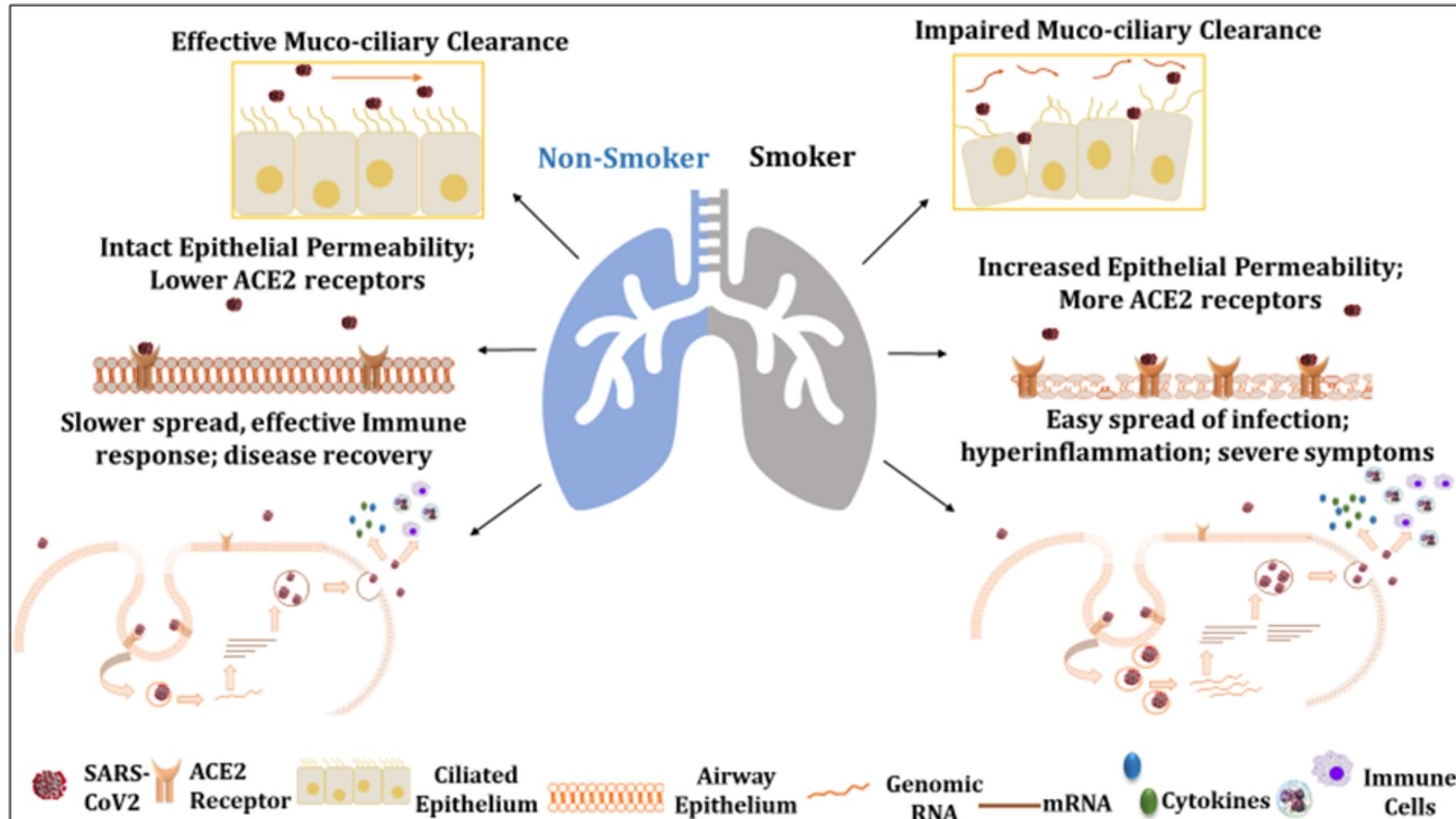
# T-cell mediated Adaptive Immunity?



## Key Findings:

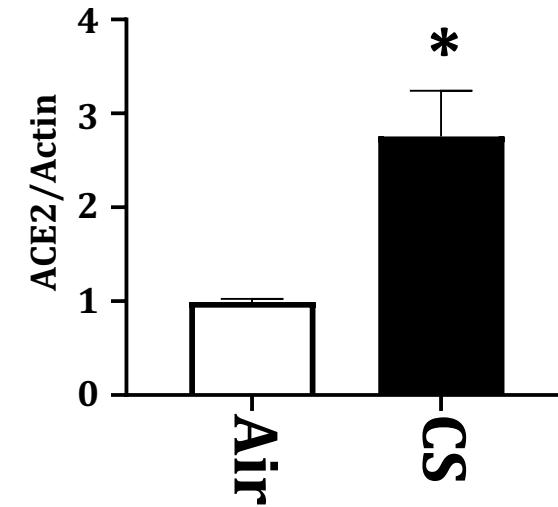
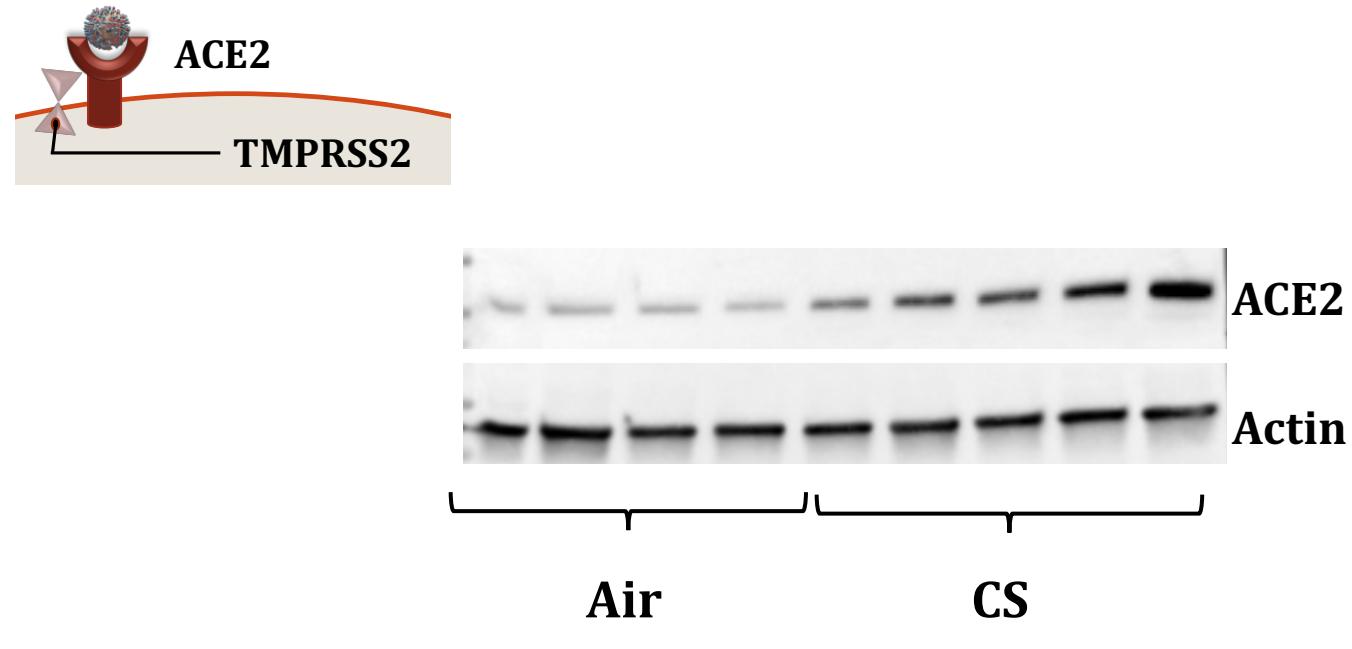
- ✓ CD4+ and CD8+ T cells detected in the epitope pools of 100% and 70% of convalescent COVID patients.
- ✓ T cell responses were focused not only on spike but also on M, N, and other ORFs
- ✓ T cell reactivity to SARS-CoV-2 epitopes was also detected in non-exposed individuals

# Susceptibility amongst Smokers



Source: Kaur et al (2020), J Inflamm.

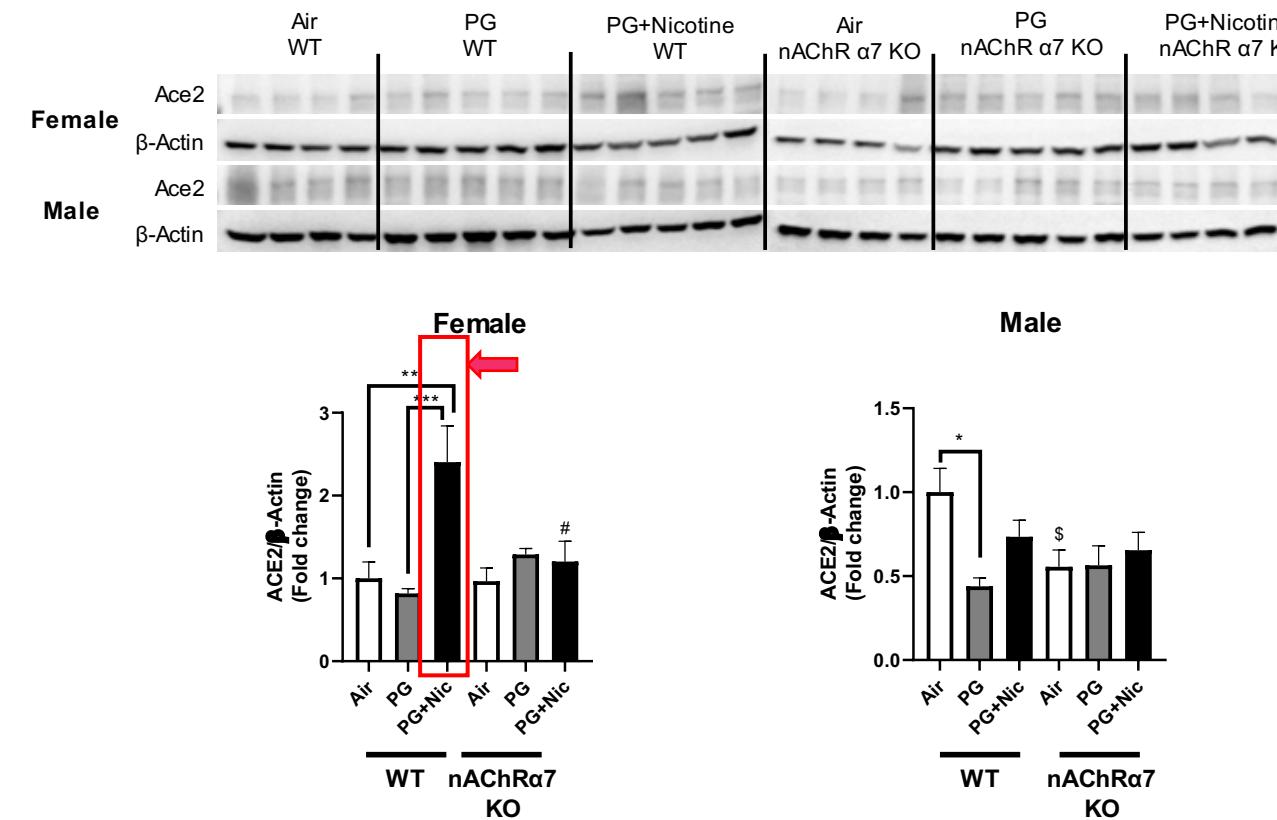
# Increased expression of ACE2 in the lungs of Cigarette smoke (CS) exposed p16-3MR mice.



Result from three independent experiments. Data is shown as a mean  $\pm$  SEM (n=4-5/group/experiment). SE: \* p<0.05 vs Air as determined using unpaired t-test.

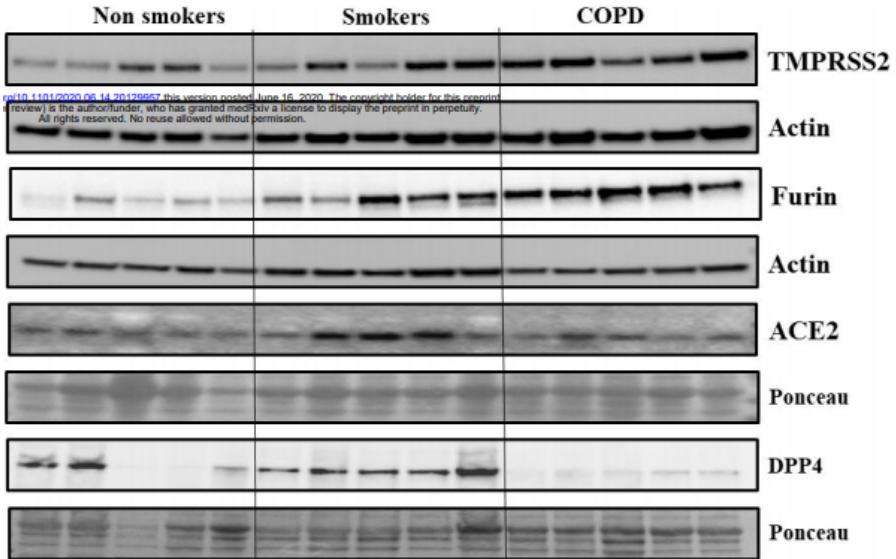
Source: Kaur (unpublished)

# Sub-chronic e-cig exposure differentially affects the protein abundance of ACE2 in mouse lungs



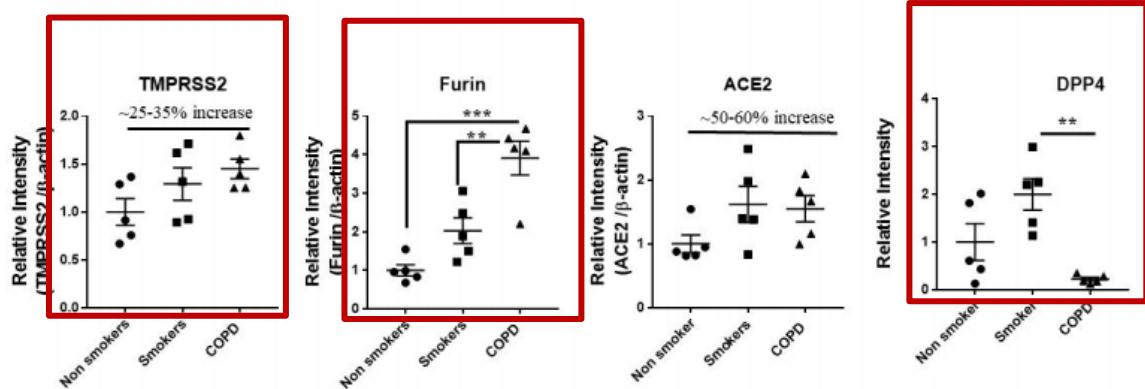
Source: Wang et al (2020), Respir Res.

# ACE2, Furin and TMPRSS2 are increased in patients with COPD.



## Key Findings:

Lung homogenates of smokers and COPD patients revealed increased protein abundance of important proteases and spike proteins like **TMPPRSS2 and furin** in association with a slight increase in SARS-CoV-2 receptor **ACE2 levels**.

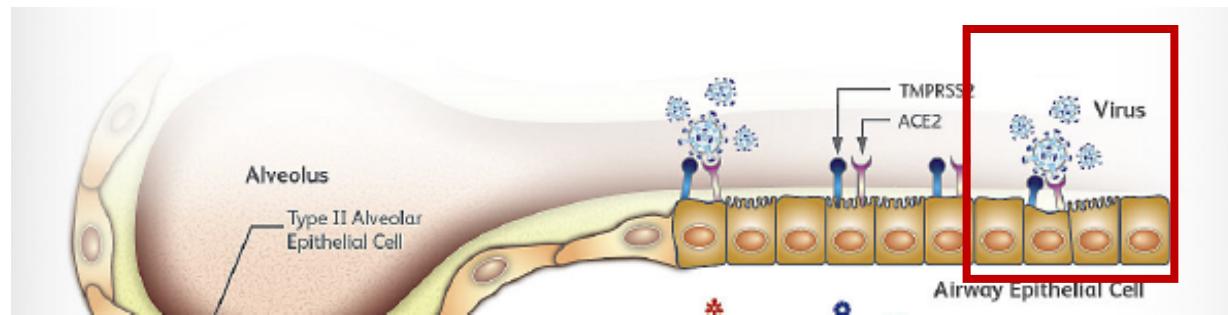


# ACE2 Activity in Serum samples from Covid19 Positive and Recovered patients

*Unpublished data by our group:*

ACE2 activity was significantly lowered in Covid-19 positive patients with a smoking history compared to patients who never smoked.

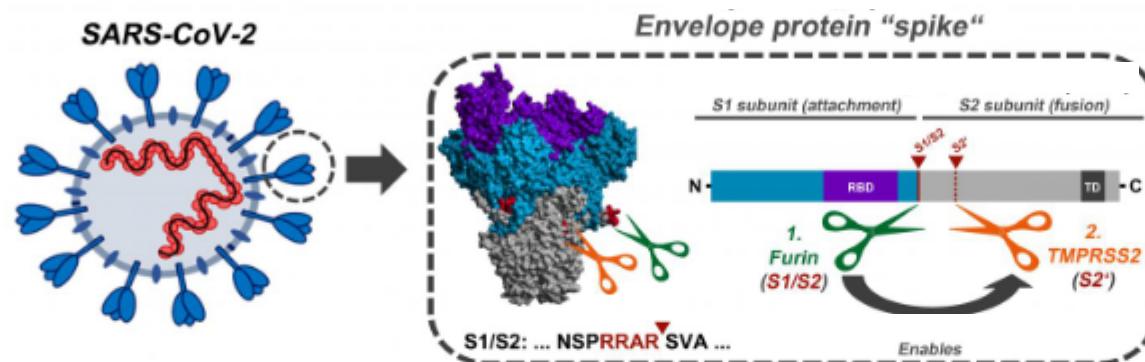
↑ Viral Invasion = ↓ ACE2 Activity



# Furin Activity in Serum samples from Covid19 Positive and Recovered patients

*Unpublished data by our group:*

- Furin activity is relatively higher amongst Covid19 positive and recovered patients as compared to Covid19 negative samples.
- The Furin activity amongst Covid19 positive patients with a smoking history was subtly higher than patients who never smoked.



# Questions to be addressed in Future

- **Link between air pollution and COVID-19 susceptibility (Wu et al, 2020).**
- **Effect of pre-existing pulmonary conditions on COVID-19 severity?**
- **Gender-based variations in disease severity and why?**
- **Effect of infection on pre-natal care?**
- **Phenotypic switching of macrophages amongst Covid19 positive patients?**
- Contribution of **NETs in alveolar inflammation** in SARS-Cov2 epithelial entry?
- Health implications of **recovered population?**
- Role of **genetic and epigenetic factors** in governing the disease?

# *Acknowledgements*

- Dr. Irfan Rahman
- Dr. Rahman lab colleagues and collaborators

# *Funding Sources*

- NIEHS
- NHLBI