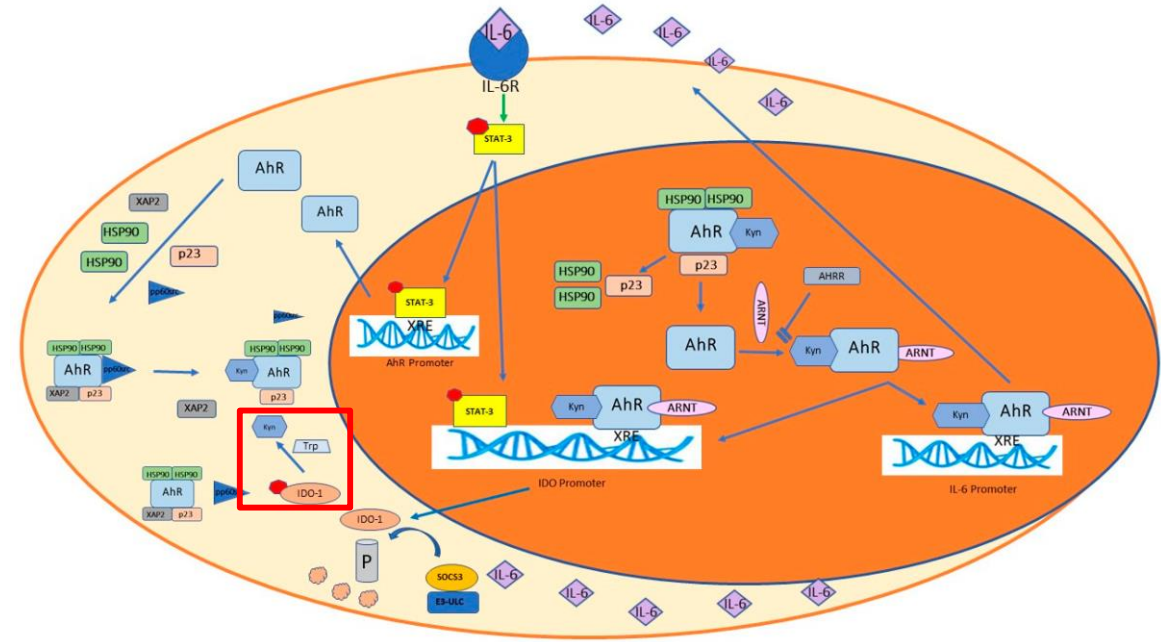# Journal meeting

23.05.31

Chae Dong Hoon

# Introduction

- **AhR(aryl hydrocarbon receptor)**
- Activated by several **ligand(aromatic hydrocarbon, Kyn, etc....)**

  -> participate in various signaling

    : **AhR repression** (AHRR)

    **antioxidant** (NRF2)

    **chemical defense**(CYP1A1, CYP1A2, etc...)

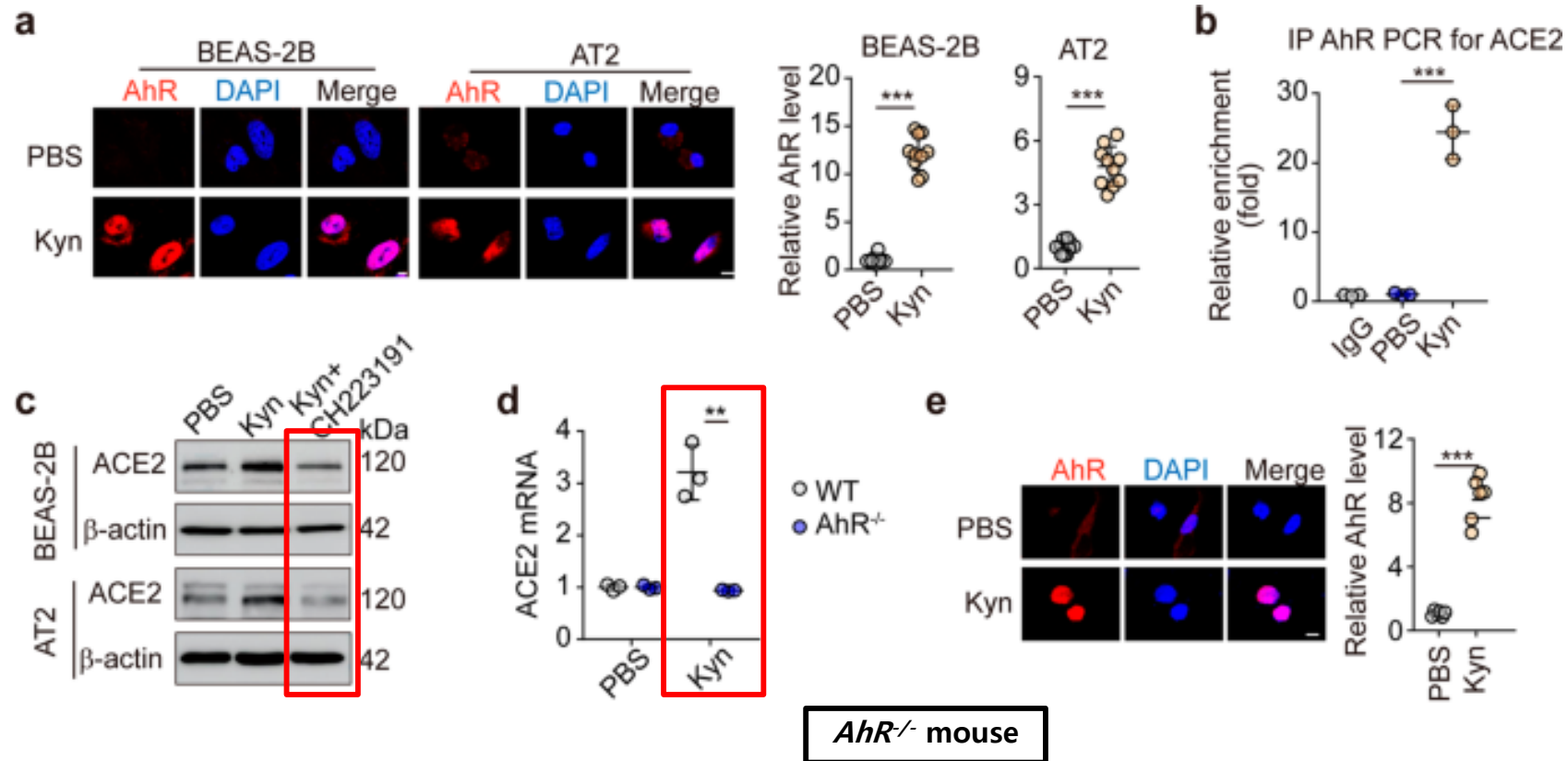    **immunomodulation**(IL-1b, IL-6, IDO, etc...)

    ....

- **activity of IDO** in virus condition(abundant IFN-r, IL-1b, IL-6, TNF-a, etc...) produce **Kyn**, **which lead activation of AhR**

# ACE2 expression is regulated by AhR in SARS-CoV-2-infected macaques



**In vitro**

*CH223191 – AhR inhibitor

*AT2 cell – lung epithelial cell

*AhR⁻/⁻ mouse*
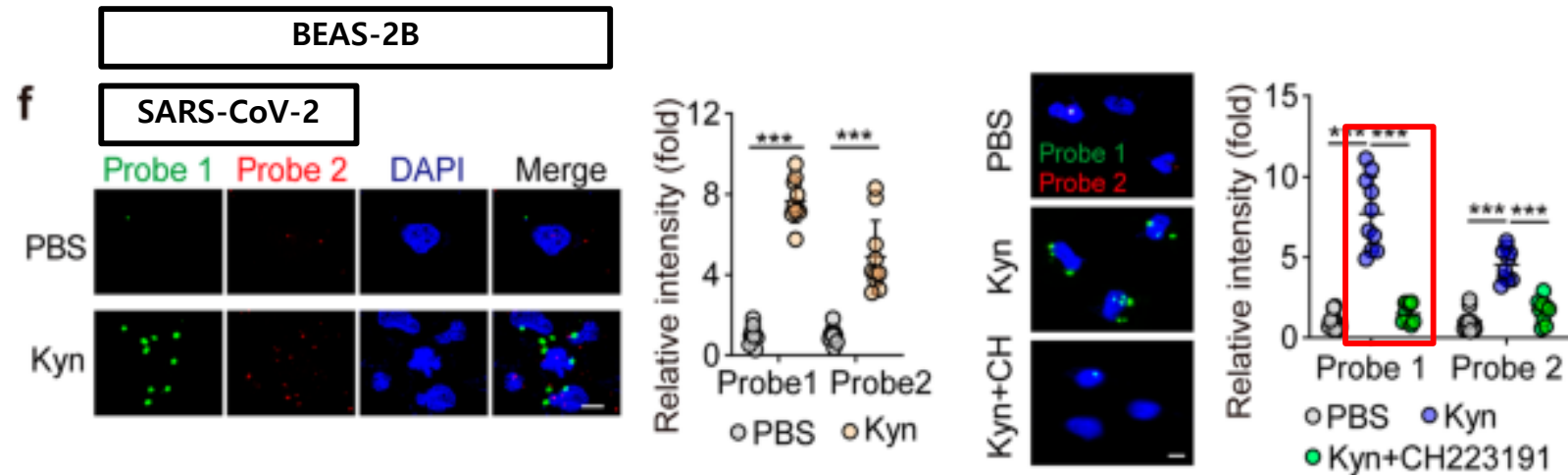
✓ Activation of AhR increase protein level of ACE2

✓ Kyn did not have an effect on ACE2 upregulation in AhR⁻/⁻ AT2 cell

# ACE2 expression is regulated by AhR in SARS-CoV-2-infected macaques

In vitro

*viral treatment for 48hr

*Kyn, CH223191 pretreated for 48hr



BEAS-2B

SARS-CoV-2

✓ **The viral load was enhanced in BEAS-2B cells pretreated with Kyn.**

✓ **Inhibition of AhR by CH223191 indeed decreased the viral load and suppressed replication in pretreated BEAS-2B cells**

# ACE2 expression is regulated by AhR in SARS-CoV-2-infected macaques

In vivo
(macaques)

*CH223191 – AhR inhibitor

*AT2 cell – lung epithelial cell

h  AhR

i  ACE2

j

k
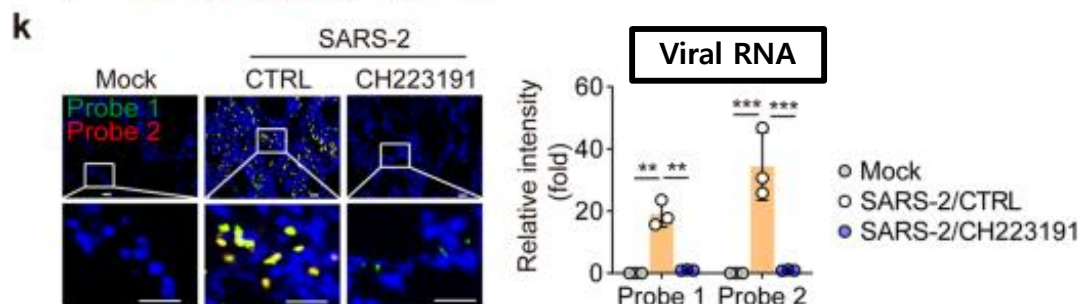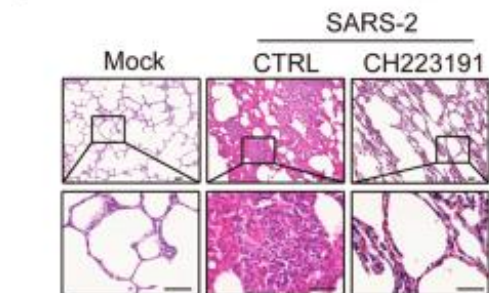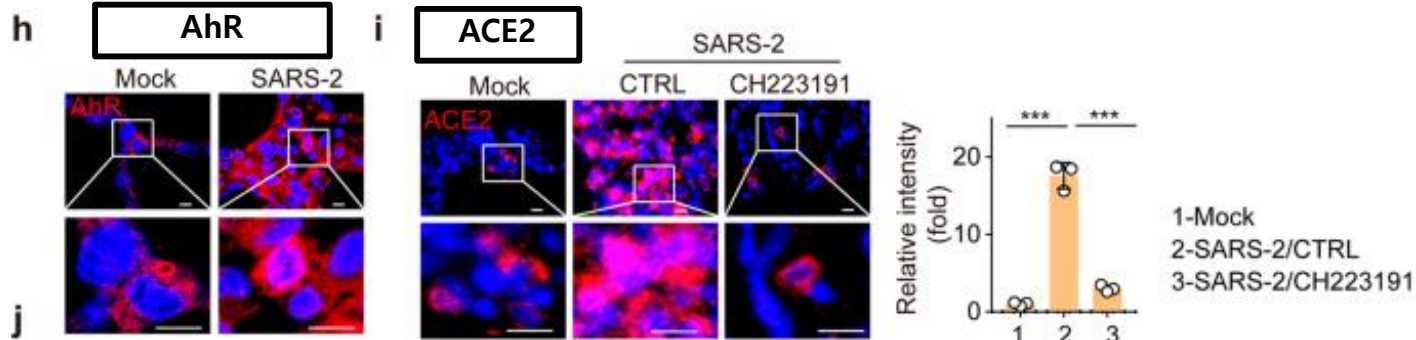


✓ **macaques were infected with SARS-CoV-2 and were then treated with the AhR inhibitor CH223191 for 7 days**

✓ **In macaques' lung tissue, they show same result of in vitro test -> increase ACE2 expression and viral by AhR**

# Cigarette smoke increases susceptibility of alveolar macrophages to SARS-CoV-2 infection through inducing reactive oxygen species-upregulated angiotensin-converting enzyme 2 expression



Non-smoking patient

*BAL : bronchoalveolar lavage
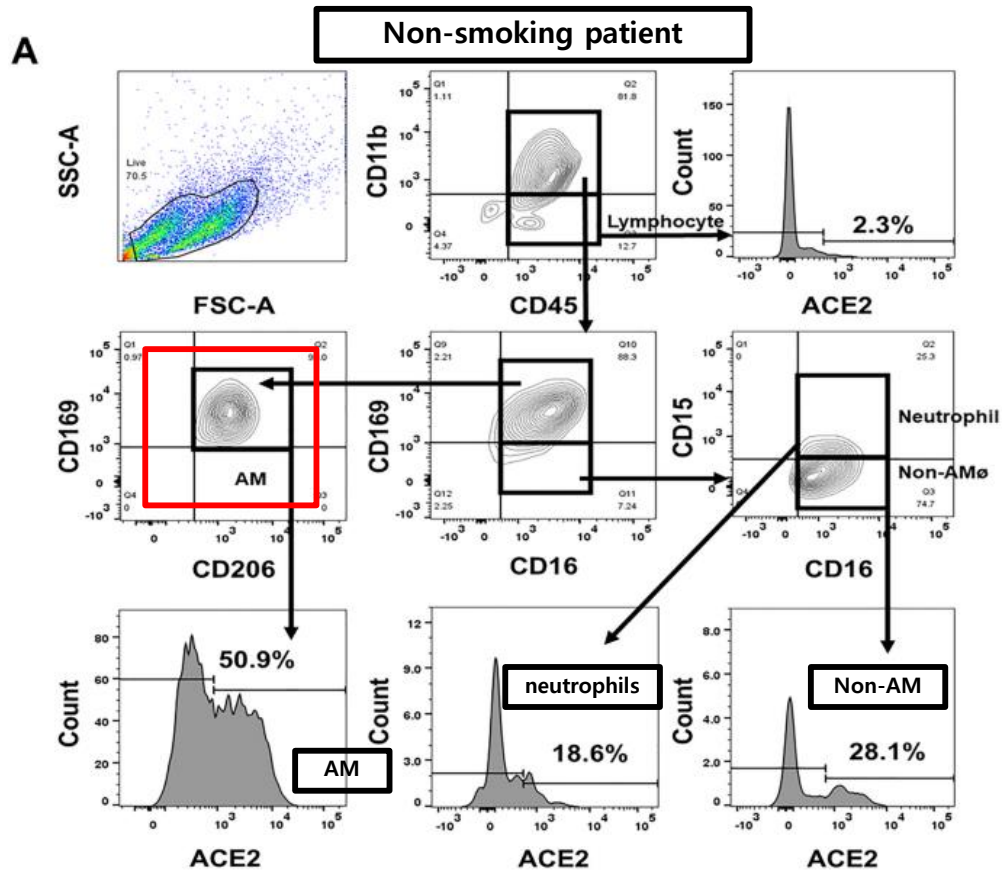
✓ According to BAL, AMs were the most abundant immune cells

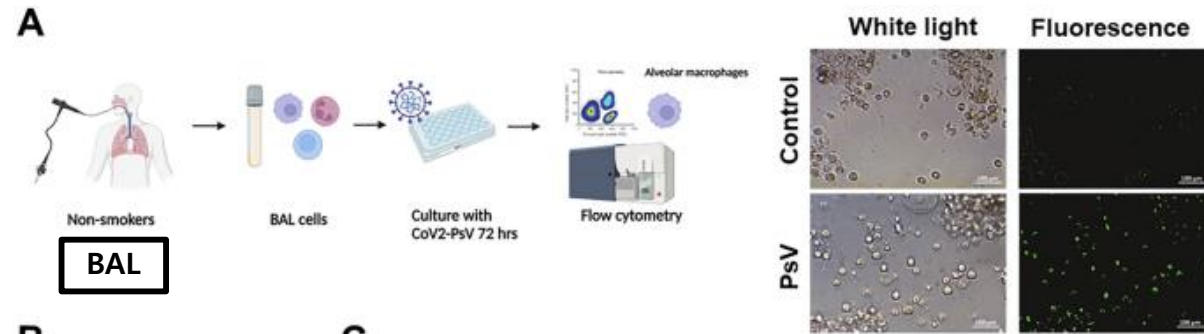✓ AMs expressed more ACE2 than other pulmonary immune cells
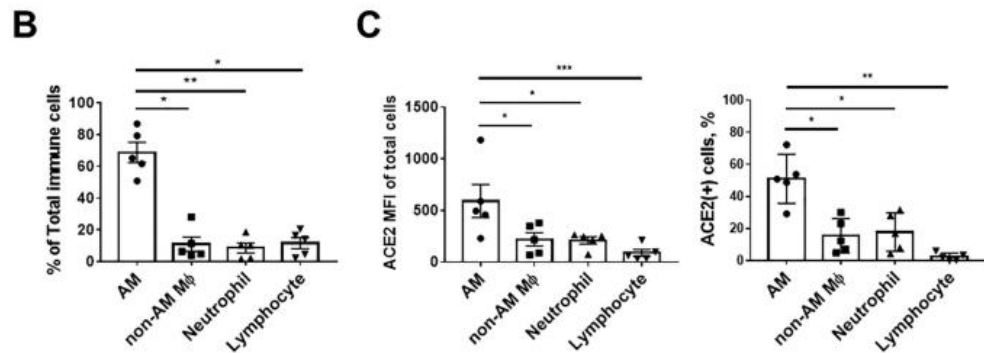
# Cigarette smoke increases susceptibility of alveolar macrophages to SARS-CoV-2 infection through inducing reactive oxygen species-upregulated angiotensin-converting enzyme 2 expression
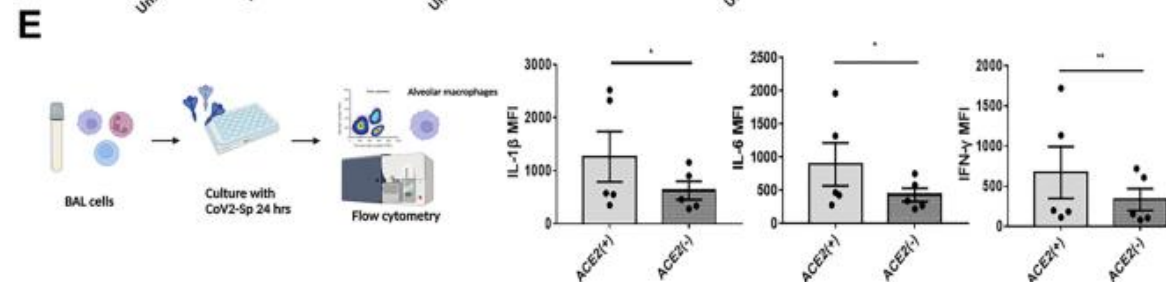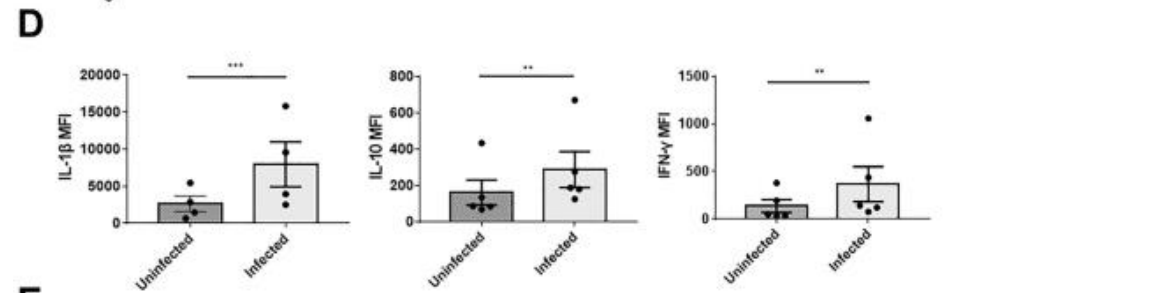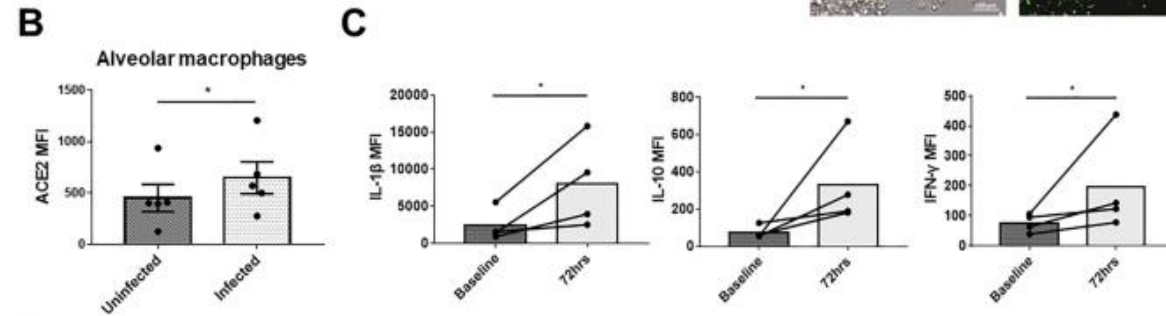


*BAL : bronchoalveolar lavage

✓ CoV-2 PsV-infected AMs had higher ACE2 expression and significantly increased production of IL-1β, IL–10, and IFN–γ

✓ ACE2-expressing AMs produced higher levels of IL-1β, IL-6, and IFN-γ compared to those without ACE2 expression

=>AMs with higher ACE2 expression are more susceptible to SARS-CoV-2 infection and produce more inflammatory cytokines upon infection.

# Cigarette smoke increases susceptibility of alveolar macrophages to SARS-CoV-2 infection through inducing reactive oxygen species-upregulated angiotensin-converting enzyme 2 expression
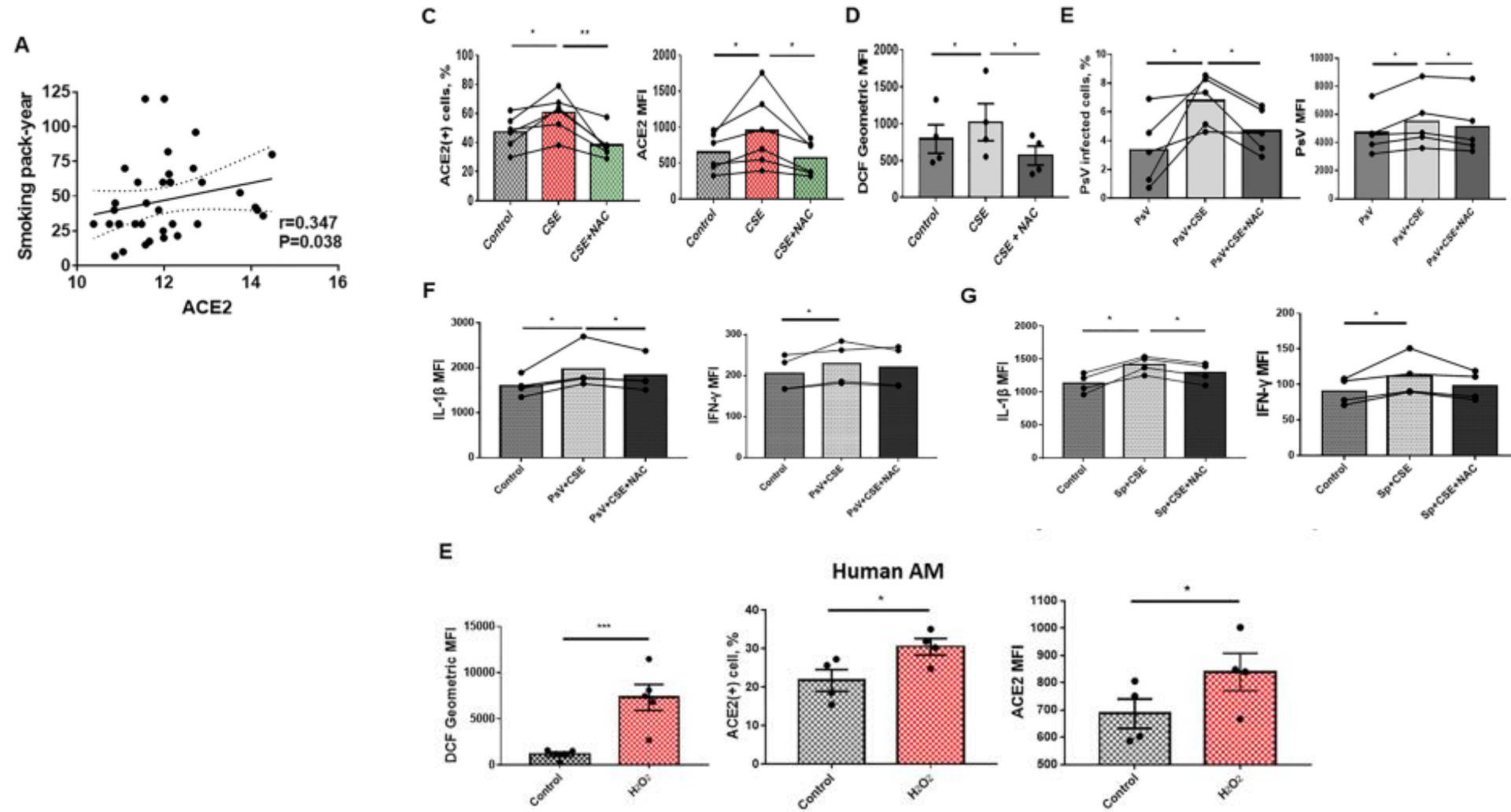


✓ Smoking is associated with increased ACE2 in Ams

-> The ACE2 expression in AMs was positively correlated with smoking pack-year

✓ After smoking, ROS production, ACE2 expression and virus sensitiveness are increased

# Summary

- **Activation of AhR** in coronavirus-infected primates shows **up-regulating ACE2 expression**

- In alveolar macrophage, CSE smoking is stimulated AhR activation through ROS production and it leads to increase ACE2 expression

 =>As a result, ACE2 is activated, increasing sensitivity to coronavirus and activating inflammation

- The virus infection itself activates AhR, which raises ACE2,
resulting in higher sensitivity and enhanced immune response
to the virus

**The AhR management of inflammation in COVID-19**