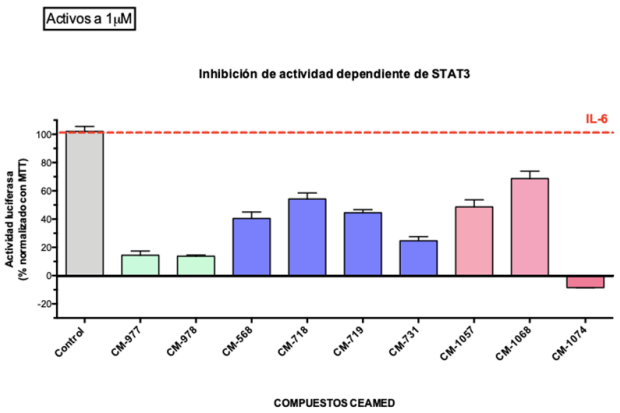
# Novel STAT3 inhibitors designed by CEAMED

- CEAMED has been developing small molecule inhibitors of STAT3 as potential treatments for Triple Negative Breast Cancers (TNBCs).

- CEAMED has at its disposition several families of compounds that potently reduce IL-6 activated STAT3 levels with IC50 values 50 - 1000 nM (compounds are >100-fold more potent than Silibinin).




# Lead STAT3 inhibitor designed by CEAMED

CM-978:

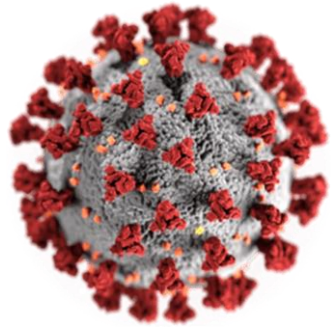
- is a potent inhibitor of IL-6 induced STAT3 activation (IC50 ~ 0.6 μM)

- is well tolerated (low toxicity) in both mice and rats after oral dosing.

- pharmacokinetic studies in both rats and mice indicate it has a good half-life, high volume of distribution and high bioavailability.

Given its *in vitro* & *in vivo* characteristics CM-978 is a good candidate for further studies to assess its potential use as a treatment to prevent / reduce cytokine storm induced ARDS.

# Investigational compounds to treat severe COVID-19



## Contact

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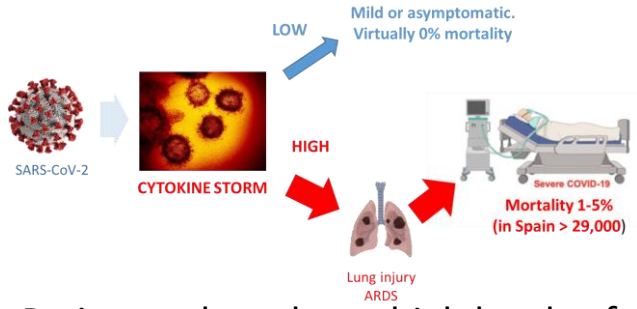
## SARS-CoV-2 and COVID-19

- COVID-19, is caused by infection with the novel severe acute respiratory syndrome-associated coronavirus 2 (SARS-CoV-2).
- Neither a vaccine, nor antiviral drugs are yet available with proven efficacy for SARS-CoV-2 prevention or treatment.

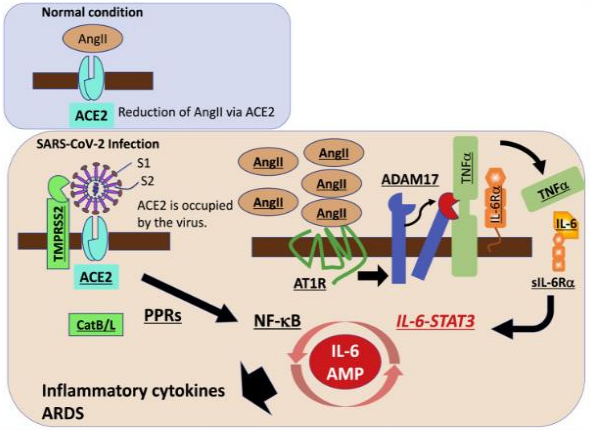
## Why do some people die, while others survive?




- Patients who release high levels of cytokines are more likely to suffer a severe form of COVID-19.
- A high level of cytokine release can cause ARDS and multi-organ failure.

## How does SARS-CoV-2 induce a cytokine storm?

- SARS-CoV-2 uses the membrane enzyme ACE2 to infiltrate and infect cells.
- Reduced enzymatic action of ACE2, increases the levels of Angiotensin II (AngII).
- High levels of AngII result in the activation of the IL-6/JAK/STAT3 pathway that culminates in amplifying interleukins and causing a cytokine storm




## Possible treatments to reduce /prevent a cytokine storm

- Inhibitors of the IL-6/JAK/STAT3 pathway may therefore be useful in treating these patients.
- Clinical trials are in progress with an IL-6 antibody (Siltuximab) and a JAK1-2 inhibitor (Ruxolitinib).
- Recruiting has begun in Spain for a trial using the natural product Silibinin, a reported STAT3 inhibitor.