

# ***Pathogenesis and therapy of COVID-19***



<https://streetartnews.net/2020/05/now-forever-by-tristan-eaton-in-new-york.html>

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**Albert Einstein College of  
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# COVID-19: A new disease and humanitarian catastrophe

## Coronavirus pandemic

Coronavirus whistleblower doctor dies in Wuhan hospital

Passing of Li Wenliang sparks outpouring of grief and anger in China



LI Wenliang raised the alarm over some new pneumonia cases in an online chat group with medics that was shared widely

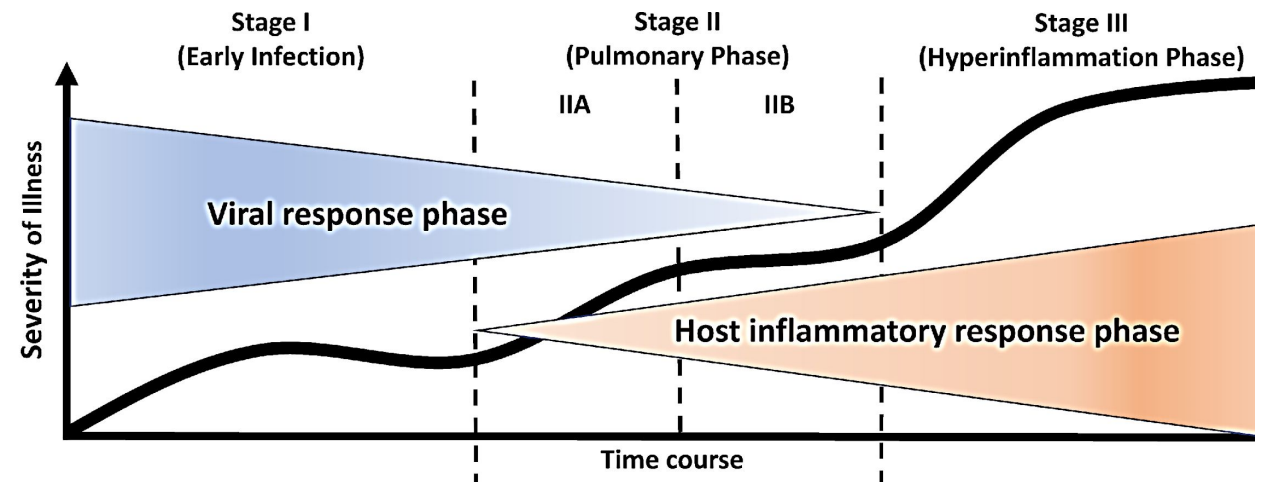
James Kynge in Hong Kong and Nian Liu in Beijing FEBRUARY 6 2020

## Control virus

Remdesivir  
SARS-CoV-2 antibody (Mab)  
Covid-19 convalescent plasma (CCP)

## Control inflammation

Steroids  
Anti-inflammatory  
agents (e.g., anti-IL-6)



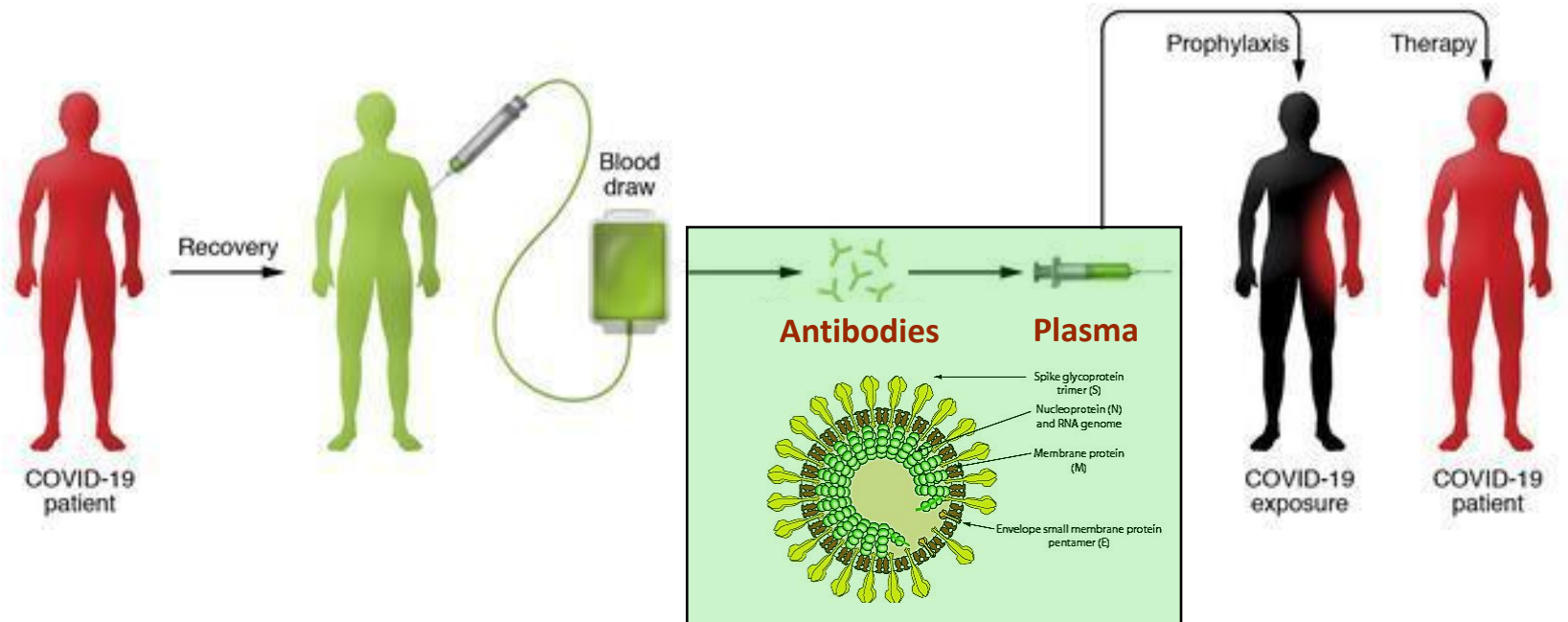
[https://www.jhltonline.org/article/S1053-2498\(20\)31473-X/fulltext](https://www.jhltonline.org/article/S1053-2498(20)31473-X/fulltext)

# The convalescent sera option for containing COVID-19

Arturo Casadevall, Liise-anne Pirofski

*J Clin Invest.* 2020;**130**(4):1545-1548. <https://doi.org/10.1172/JCI138003>. Published online March 13, 2020

- Early 20<sup>th</sup> century
  - Meningitis
  - Influenza
  - Polio
  - Measles
- Early 21<sup>st</sup> century
  - SARS
  - MERS
  - H1N1
  - **COVID-19**





# *The convalescent plasma donor program at Montefiore*



**'It's time to save people': Young Israel members who had coronavirus donate blood to help others**

[David Propper](#), Rockland/Westchester Journal News Published 4:49 p.m. ET  
March 31, 2020 | Updated 9:55 a.m. ET April 2, 2020

**The New York Times** <https://nyti.ms/2yNJpei>

May 12, 2020

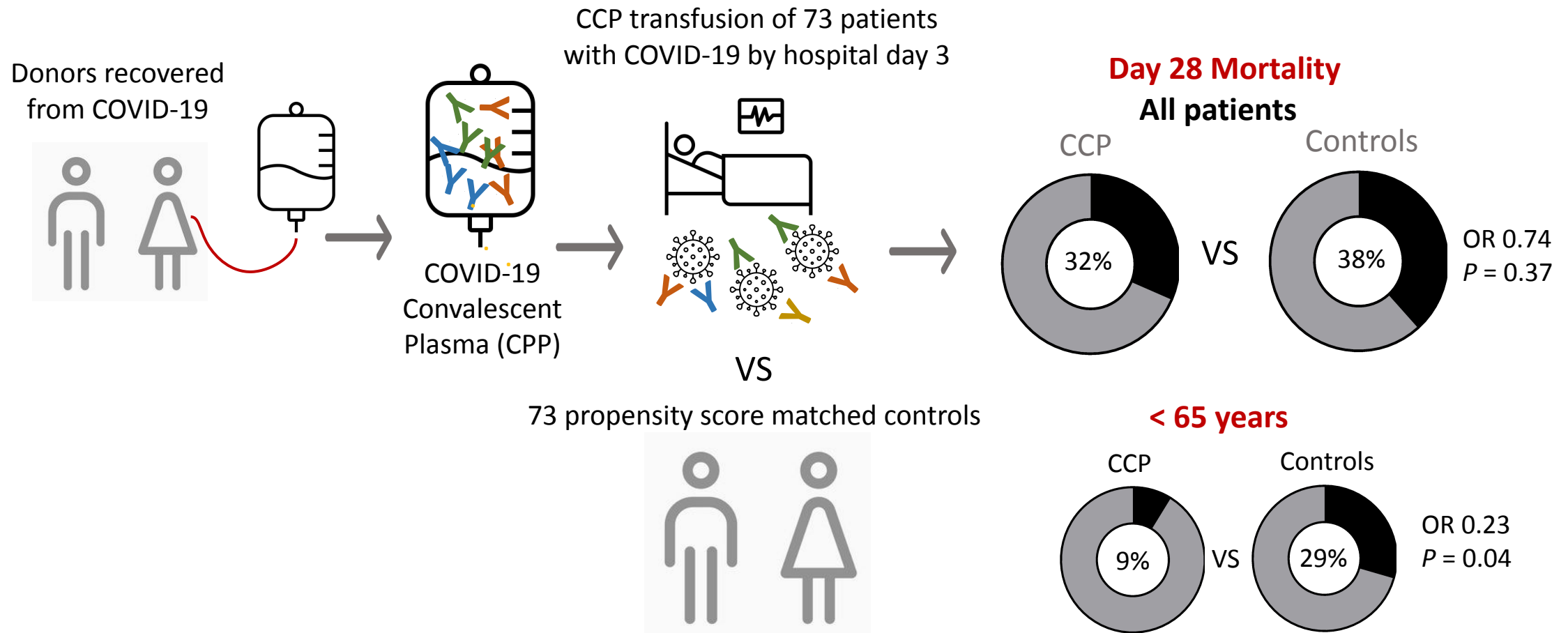
***Hasidic Jews, Hit Hard by the Outbreak, Flock to Donate Plasma***

"The community has taken a tragedy and turned it into a superpower," said an expert on using plasma to treat people after virus exposure.

# Treatment of severe COVID-19 with convalescent plasma in Bronx, NYC



Hyunah Yoon MD



# *One year into the pandemic*

## *What we know about CCP*

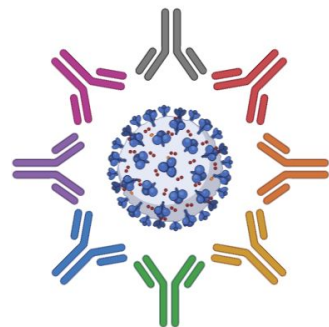
- It is as safe as standard plasma.
- It shows signals of efficacy:
  - Faster symptom resolution.
  - Reduced inflammatory markers.
  - Anti-viral clearance.
  - **Reduced mortality**
    - When high/er titer CCP given early.
    - Ineffective later in disease.
  - **Viral clearance in humoral deficiency.**

## *What we don't know*

- Its efficacy versus a control.
- Its efficacy as a function of:
  - **Age**
  - **Sex**
  - **Race/ethnicity**
  - **Co-morbidities**
  - **Concomitant therapies**
- Characteristics of effective CCP
  - **SARS-CoV-2 quantity**
  - **SARS-CoV-2 specificity**
  - **Antibody function/s**

<sup>1</sup> <https://www.fda.gov/media/141477/download>, <sup>2</sup> <https://www.pnas.org/content/117/17/9490>,  
<sup>3</sup> <https://jamanetwork.com/journals/jama/fullarticle/2766943>, <sup>4</sup> <https://www.nature.com/articles/s41591-020-1088-9>,  
<sup>5</sup> [https://ajp.amjpathol.org/article/S0002-9440\(20\)30370-9/fulltext](https://ajp.amjpathol.org/article/S0002-9440(20)30370-9/fulltext), <sup>6</sup> <https://insight.jci.org/articles/view/142270/pdf>,  
<sup>7</sup> <https://www.bmj.com/content/371/bmj.m3939>, <sup>8</sup> <https://pubmed.ncbi.nlm.nih.gov/33232588/>, <sup>9</sup> <https://pubmed.ncbi.nlm.nih.gov/33232588/>,  
<sup>10</sup> <https://www.nejm.org/doi/full/10.1056/NEJMoa2031893>, <sup>11</sup> <https://www.medrxiv.org/content/10.1101/2020.08.26.20182444v2>,  
<sup>12</sup> <https://www.medrxiv.org/content/10.1101/2020.07.01.20139857v1>, <sup>13</sup> <https://ashpublications.org/blood/article/136/20/2290/463806/Convalescent-plasma-therapy-for-B-cell-depleted>





**CONTAIN COVID-19**

clinicaltrials.gov NCT04364737

Hyunah Yoon MD



Mila Ortigoza MD PhD



## Study design

- Randomized double blinded placebo-controlled trial of *convalescent plasma* versus *saline* in hospitalized patients.
- Moderately to severely ill -  $\leq 7$  days since symptom onset - hospitalized  $\leq 72$ hrs.
- Goal 1000 participants - **874 enrolled**

## Multicenter trial

- NYC/Bronx/Brooklyn/Long Island (7), Connecticut (2), Miami (2), Texas (6)

## Outcome measures

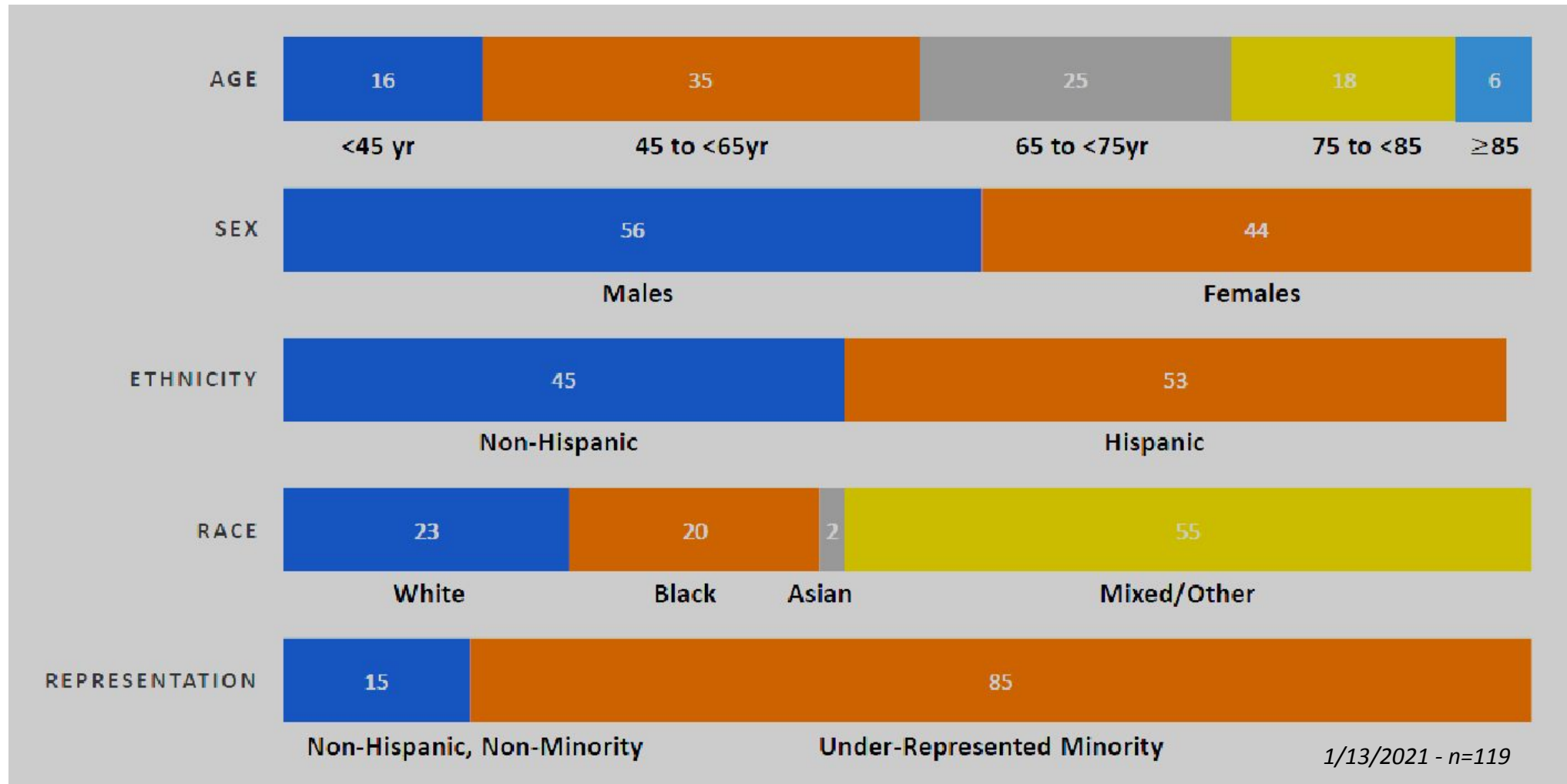
- Primary: Status @ 14 days - WHO scale
- Secondary: Status @ 28 days, mortality, convalescent plasma SARS-CoV-2 titer

Patient State	Score	Descriptor
Uninfected	0	Uninfected; no viral RNA detected
Ambulatory	1	Asymptomatic; viral RNA detected
	2	Symptomatic; Independent
	3	Symptomatic; assistance needed
Hospitalized: Mild disease	4	Hospitalized; no oxygen therapy
	5	Hospitalized; oxygen by mask or nasal prongs
Hospitalized: Severe disease	6	Hospitalized; oxygen by NIV or High flow
	7	Intubation & Mechanical ventilation; $pO_2/FIO_2 \geq 150$ or $SpO_2/FIO_2 \geq 200$
	8	Mechanical ventilation $pO_2/FIO_2 < 150$ ( $SpO_2/FIO_2 < 200$ ) or vasopressors
	9	Mechanical ventilation $pO_2/FIO_2 < 150$ and vasopressors, dialysis or ECMO
Death	10	Dead

## Funding

- Mathers Foundation - April 1, 2020
- Montefiore Medical Center
- NYU Langone Medical Center
- NIH - NCATS - OWS - July 8, 2020

# Montefiore-Einstein CONTAIN enrollment





# ***Research amid the pandemic***

- Celebrates science, medicine, and humanity and brings hope.
- CCP has demonstrated signals of efficacy, including reduced Covid-19 mortality, and may have a place in the treatment armamentarium.
- Now is the moment to definitively establish its efficacy scientifically.
  - To inform clinical guidelines for its use.
  - To inform the use of antibody therapies for the next pandemic.



# *It takes a metropolis ...*

- Albert Einstein College of Medicine & Montefiore Medical Center
  - Division of infectious diseases faculty and fellows
  - Pirofski laboratory and extended laboratory family
  - Department of Medicine chair - Yaron Tomer
  - Dean Gordon Tomaselli
  - Montefiore Medical Center leadership
- National convalescent plasma leadership group (ccpp19.org)
- CONTAIN-19 leadership and teams
  - Einstein/Montefiore - **Hyunah Yoon MD**
  - NYU - **Mila Ortigoza MD, PhD**
  - Yale Medical Center, University of Miami, University of Texas Health
  - NIH/NCATS/CTSAs
- Funding
  - Mathers Foundation
  - Montefiore/Einsteine
  - NYU Langone
  - NIH - NCATS - OWS



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