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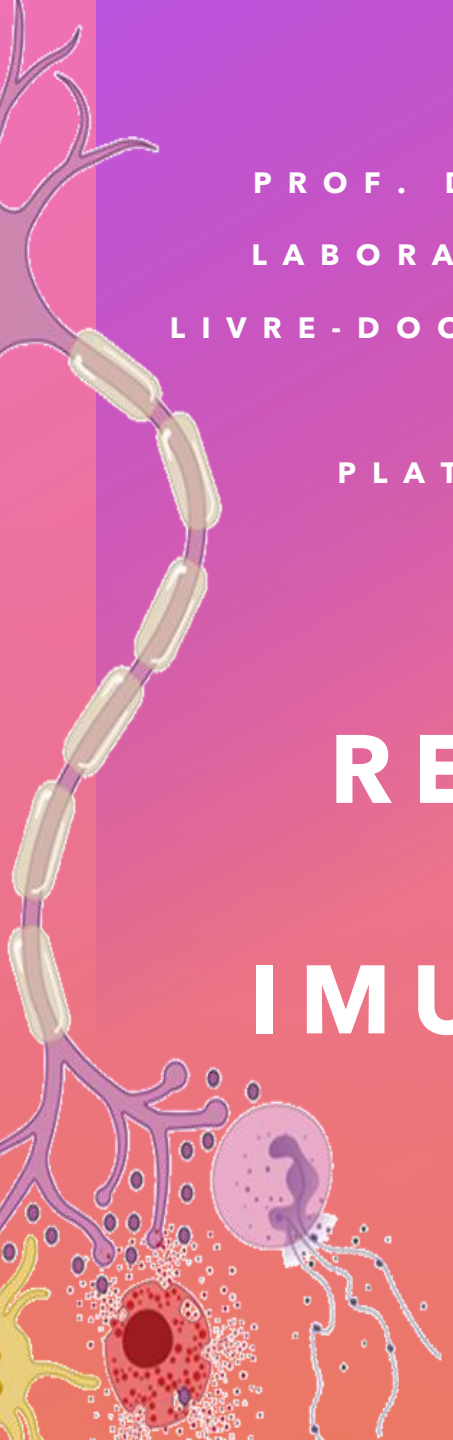
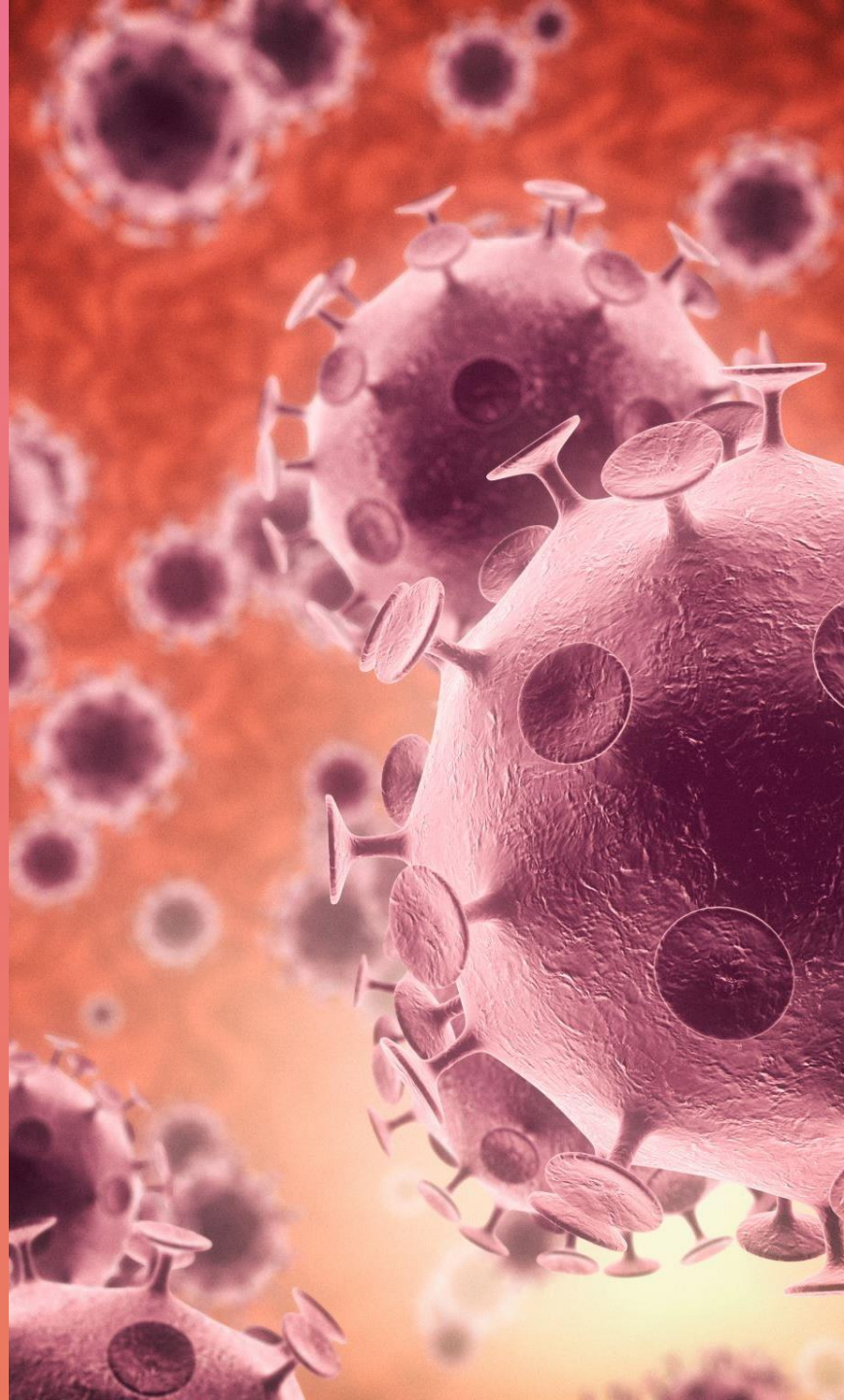
PLATAFORMA CIENTÍFICA PASTEUR-USP

COVID-19: RESPOSTA IMUNE E IMUNOPATOGÊNESE





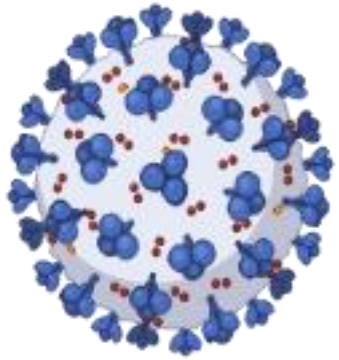
Laboratory of Neuroimmunology of Arboviruses

DEPARTAMENTO DE Imunologia
INSTITUTO DE CIÊNCIAS BIOMÉDICAS | USP

Institut Pasteur USP
Scientific Platform Pasteur USP

Neuroimmune Interactions Laboratory

OBJETIVOS



- Resposta imune inata
  - Receptores de padrão – TLRs, NLRs, inflamassomas...
- Resposta imune adaptativa
  - Linfócitos T e Linfócitos B, anticorpos neutrlizantes, CD8 citotóxicos
- Imunopatogênese
  - *Cytokine storm,* imunocomplexos, coagulopatia.

World Health Organization

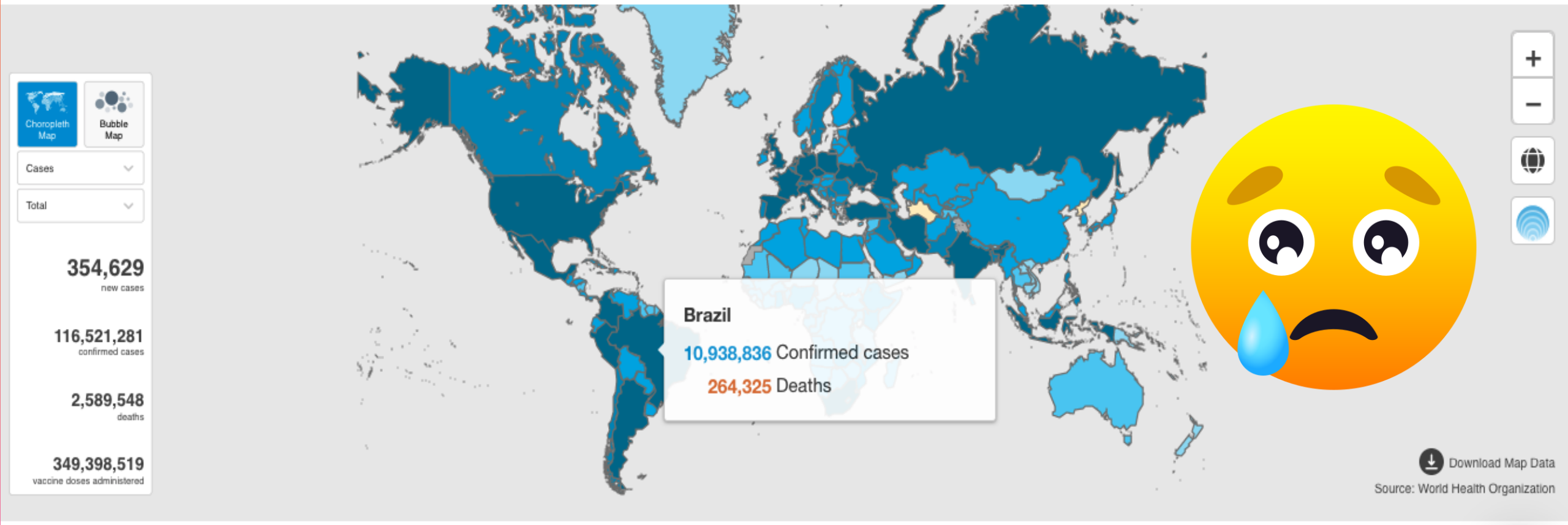
Search by Country, Territory, or Area

Covid-19 Response Fund

Donate

WHO Coronavirus (COVID-19) Dashboard

Overview | Data Table | Explore



Globally, as of **6:02pm CET, 8 March 2021**, there have been **116.521.281 confirmed cases** of COVID-19, including **2.589.548 deaths**, reported to WHO. As of **8 March 2021**, a total of **349.398.519 vaccine doses** have been administered.

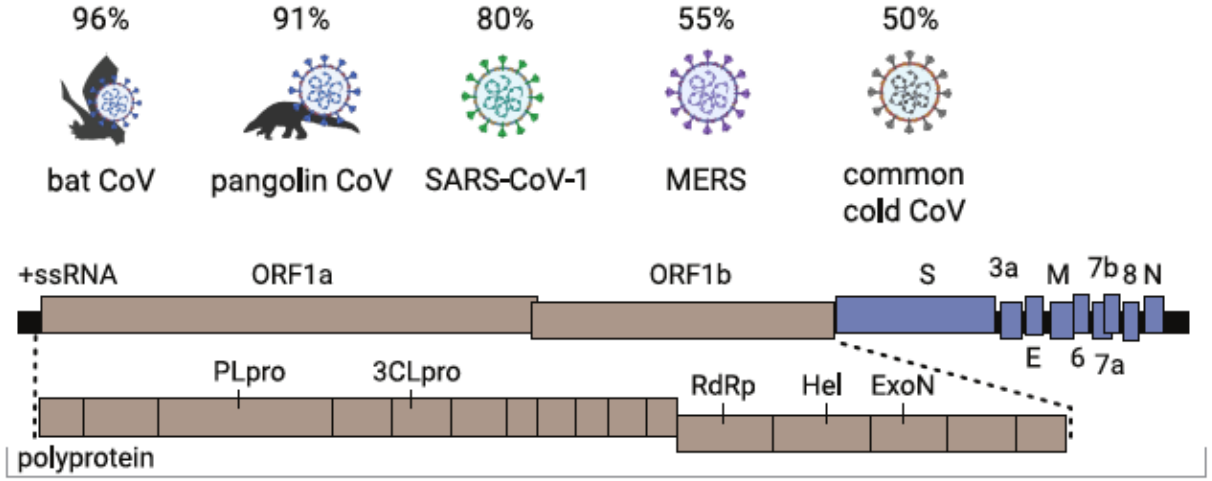
SARS-CoV-2 (COVID-19) by the numbers

Yinon M. Bar-On[1], Avi Flamholz[2], Rob Phillips[3,4], and Ron Milo[1*]
[1]Weizmann Intitute of Science, Rehovot 7610001, Israel [2]University of California, Berkeley, CA 94720, USA
[3]California Institute of Technology, Pasadena, CA 91125, USA [4]Chan Zuckerberg Biohub, San Francisco, CA 94158, USA
*Corresponding author: ron.milo@weizmann.ac.il.
Comments are welcome; this article is being updated on an ongoing basis at: https://bit.ly/2WOeN64

eLife
published in eLife, March 31st, 2020
https://elifesciences.org/articles/57309

Genome

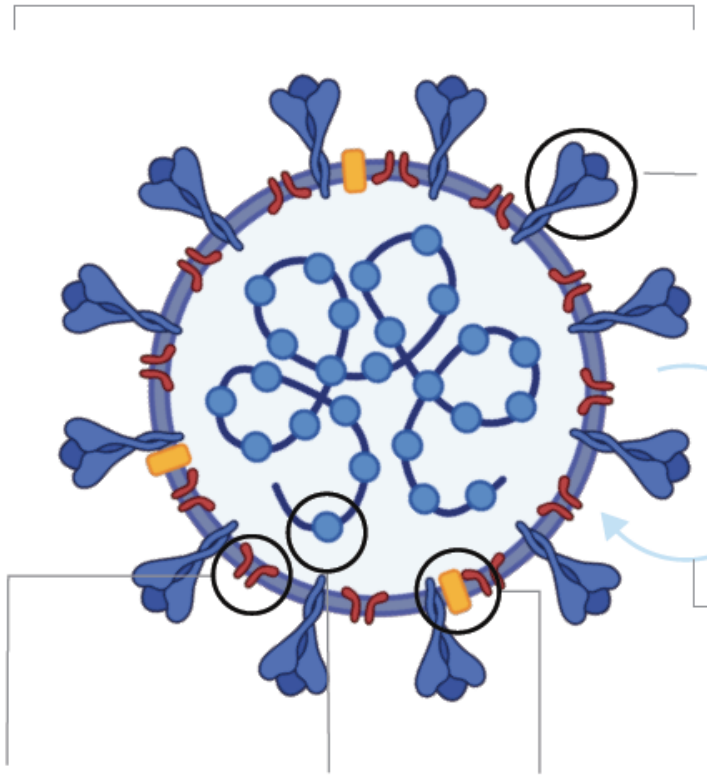
Nucleotide identity to SARS-CoV-2



Length: ≈30kb; β-coronavirus with 10-14 ORFs (24-27 proteins)

Size & Content

Diameter: ≈100 nm
Volume: ~10^6 nm^3 = 10^{-3} fL
Mass: ~10^3 MDa ≈ 1 fg



Spike trimer
Length: ≈10 nm
Copies per virion: ≈100
(300 monomers, measured for SARS-CoV-1)
Affinity to ACE2 receptor K_d: ≈1-30 nM
primed by TMPRSS2

Membrane protein
≈2000 copies
(measured for SARS-CoV-1)

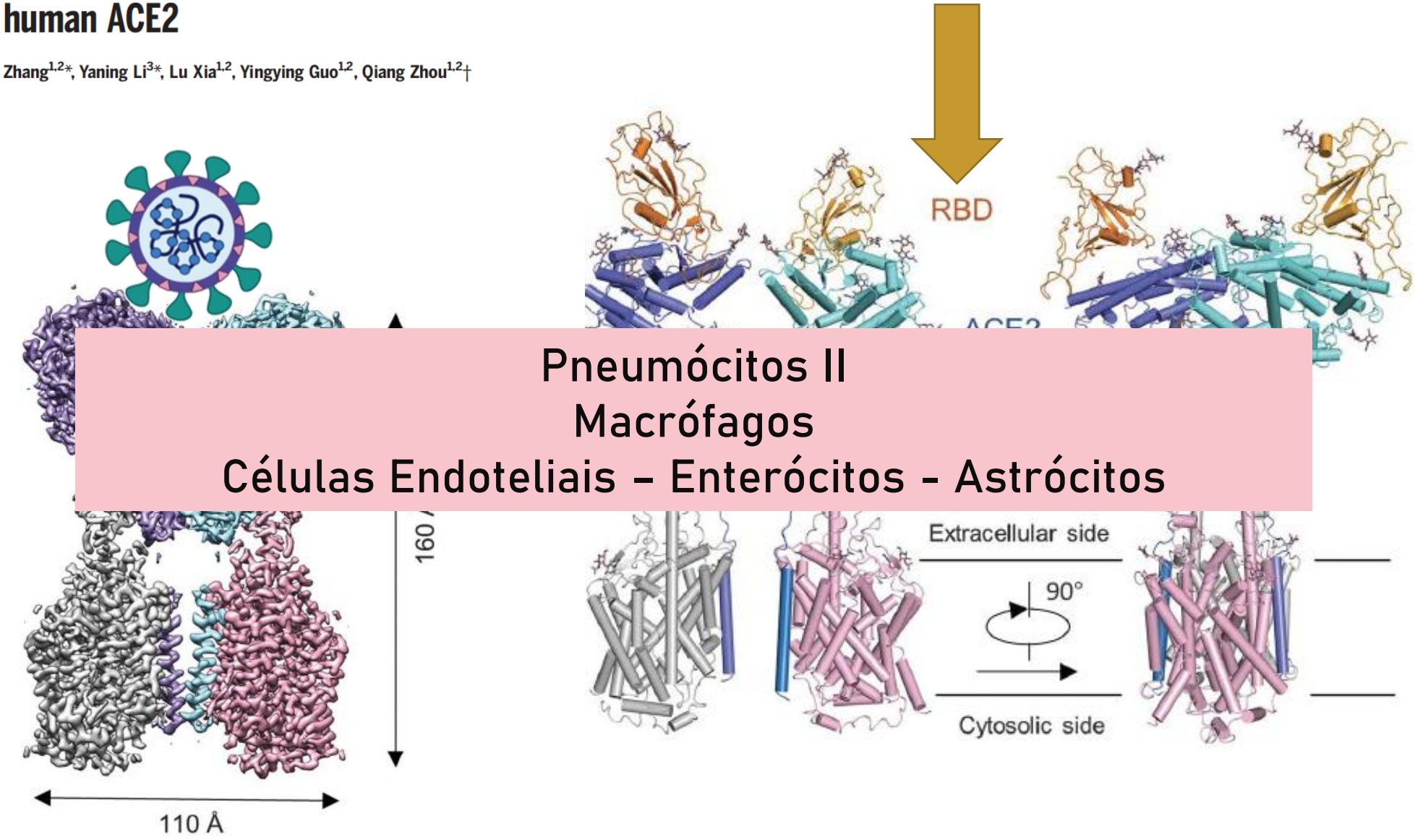
Nucleoprotein
≈1000 copies
(measured for SARS-CoV-1)

Envelope protein
≈20 copies
(100 monomers, measured for TGEV coronavirus)

CORONAVIRUS

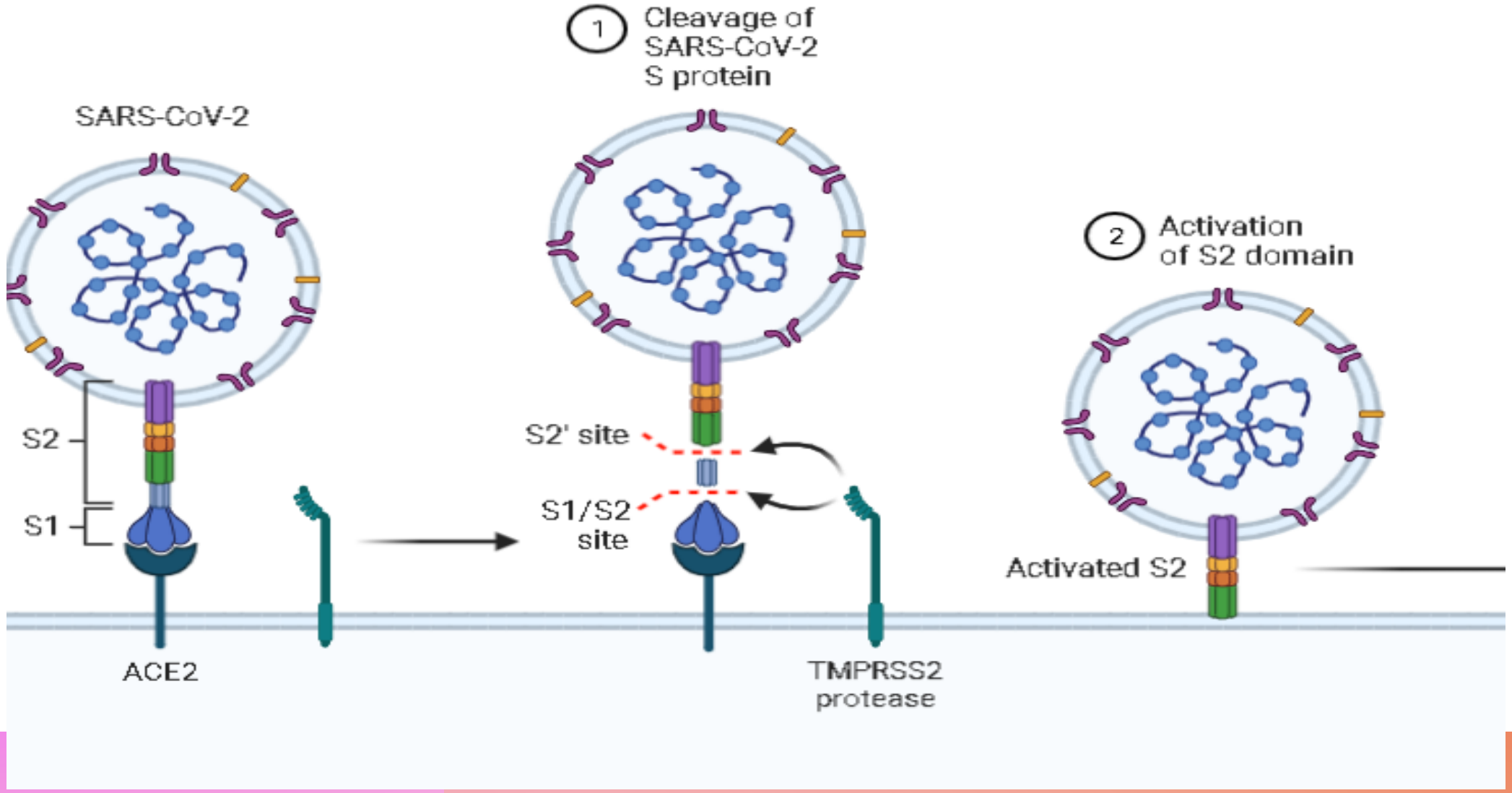
Structural basis for the recognition of SARS-CoV-2 by full-length human ACE2

Renhong Yan[1,2], Yuanyuan Zhang[1,2]*, Yaning Li[3]*, Lu Xia[1,2], Yingying Guo[1,2], Qiang Zhou[1,2]†

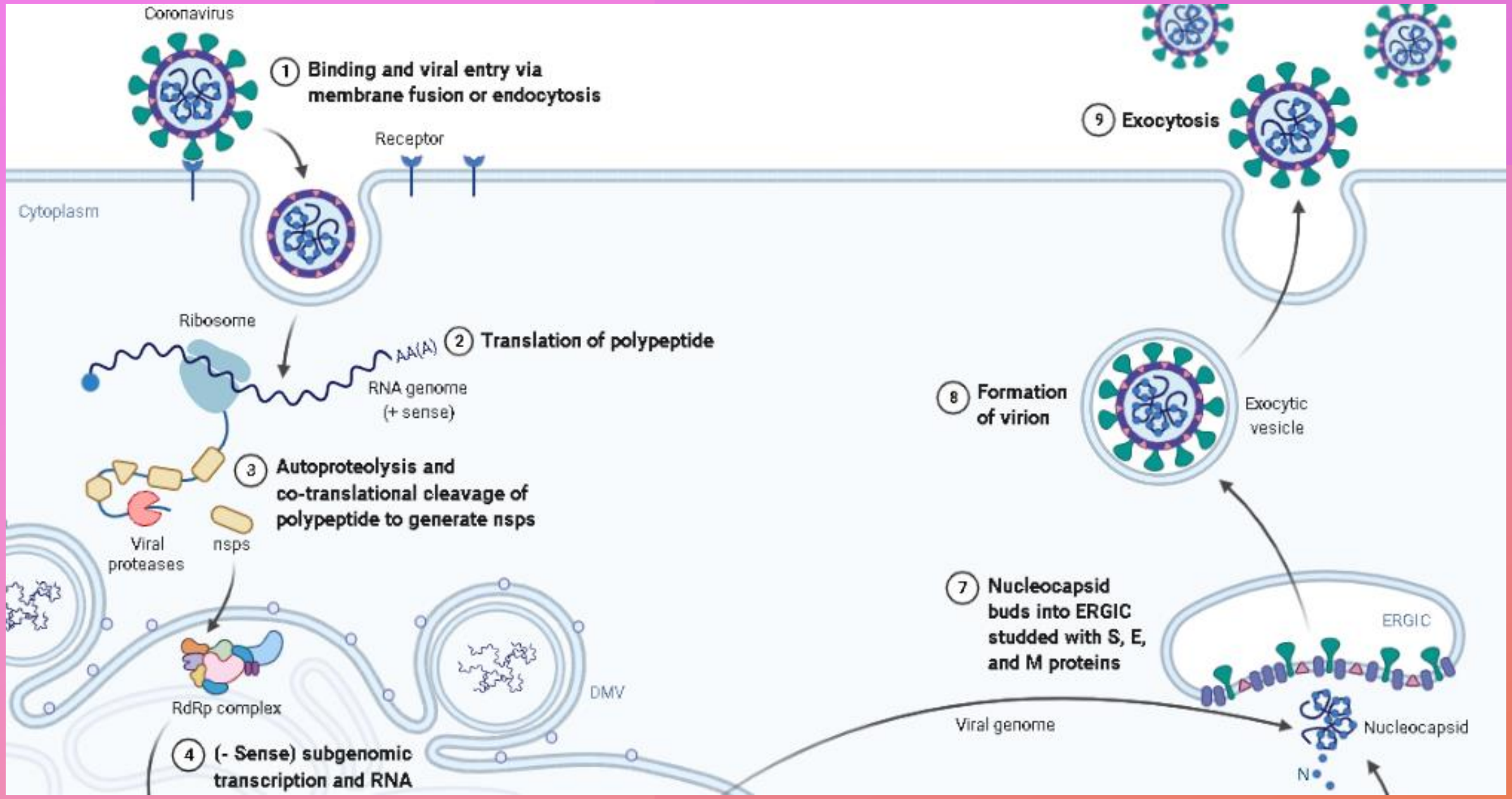


Pneumócitos II
Macrófagos
Células Endoteliais – Enterócitos - Astrócitos

ADESÃO E INVASÃO CELULAR
ACE-2 + TMPRSS2

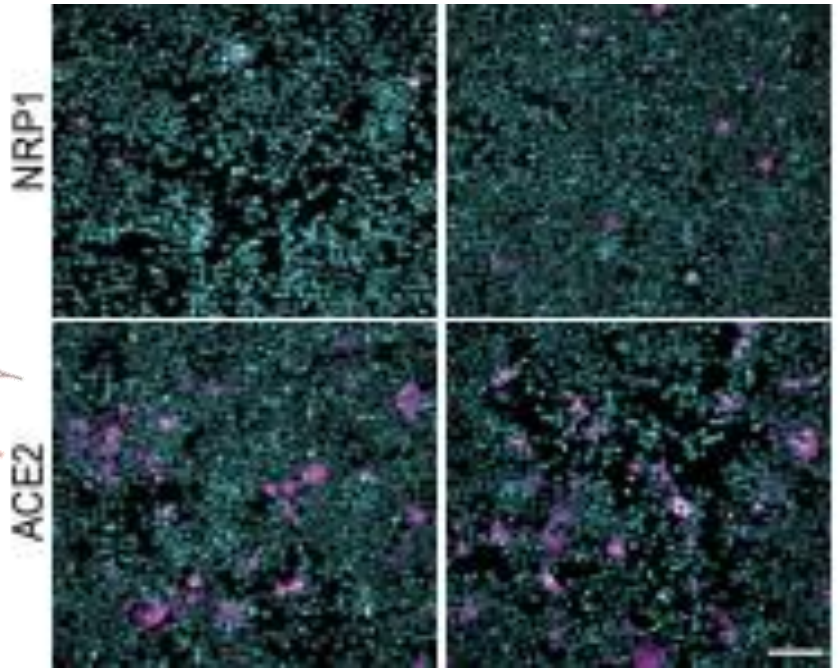


REPLICAÇÃO SARS-CoV2

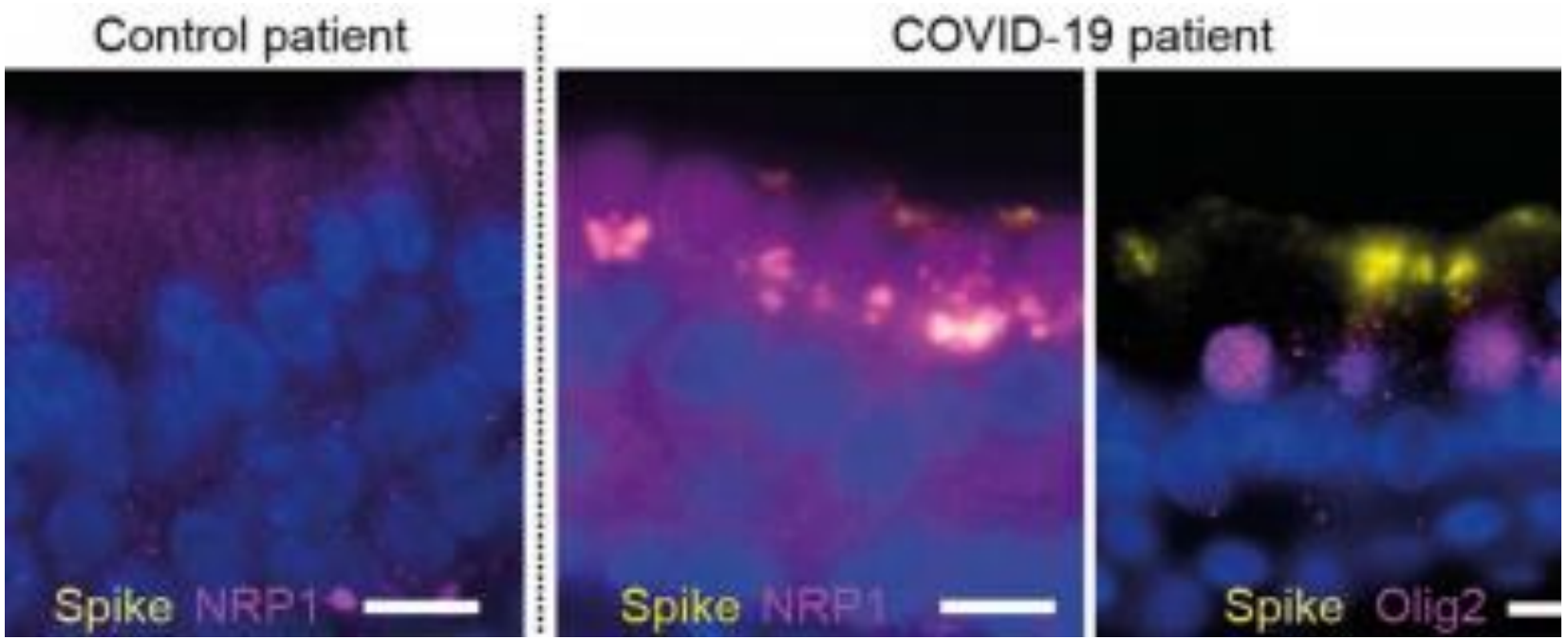


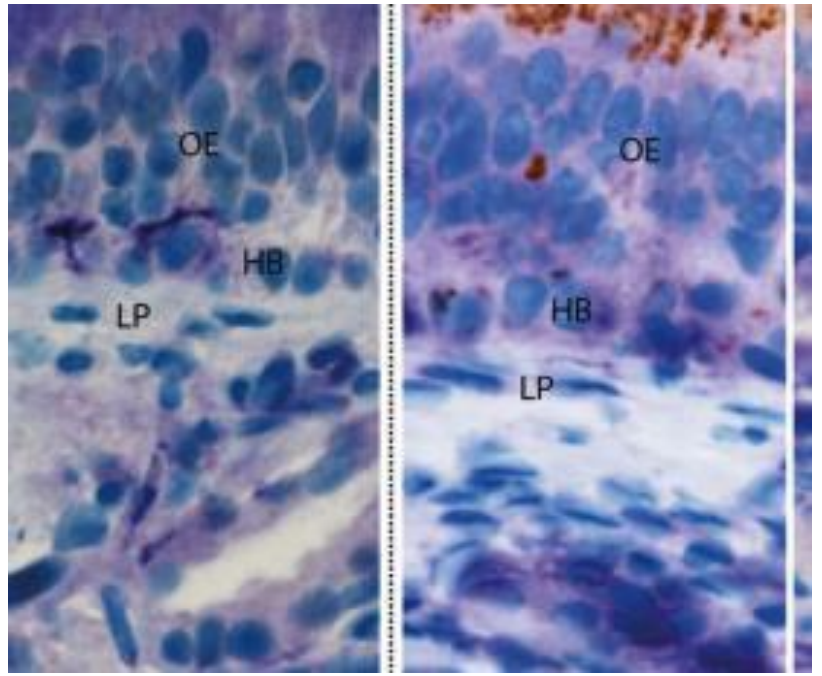
Neuropilin-1 facilitates SARS-CoV-2 cell entry and infectivity

Ludovico Cantuti-Castelvetri[1,2]*, Ravi Ojha[3]*, Liliana D. Pedro[1,2]*, Minou Djannatian[1,2]*, Jonas Fran
Suvi Kuivanen[7]*, Franziska van der Meer[4], Katri Kallio[3], Tuğberk Kaya[1,2,8], Maria Anastasina[3,9],
Teemu Smura[7], Lev Levanov[7], Leonora Szirovicza[7], Allan Tobi[10], Hannimari Kallio-Kokko[11],
Pamela Österlund[12], Merja Joensuu[13], Frédéric A. Meunier[13], Sarah J. Butcher[3,9],
Martin Sebastian Winkler[14], Brit Mollenhauer[15,16], Ari Helenius[17], Ozgun Gokce[8],
Tambet Teesalu[3,19,20], Jussi Hepojoki[5,21], Olli Vapalahti[7,11,22], Christine Stadelmann[4],
Giuseppe Balistreri[3,18]†, Mikael Simons[1,2,23]†



Epitélio Olfativo





Como é a resposta imune ao SARS-CoV2?

2 COMPONENTES

1 – imunidade Inata

2- Imunidade Adaptativa

Popular Latest

The

HEALTH

Immunology Is ... Die

Which is too bad bec... ...n reacts to the coronavirus.

ED YONG AUGUST 5, 2...

THE ATLANTIC

Editor's Note: The Atlantic *is making vit... ...so all readers. Find the collection here.*

Dinâmico

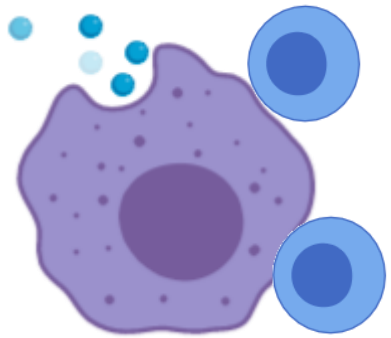
Imprevisível

Varia de Intensidade

DANGER

Resposta imune é uma resposta ao PERIGO

Endógeno ou Exógeno



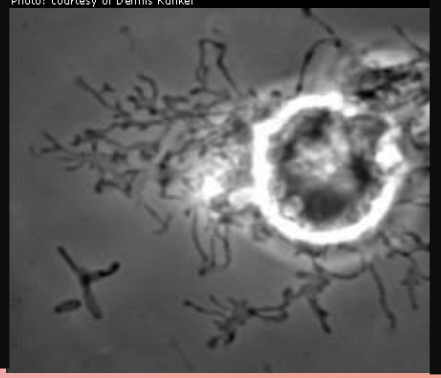
Padrões Moleculares

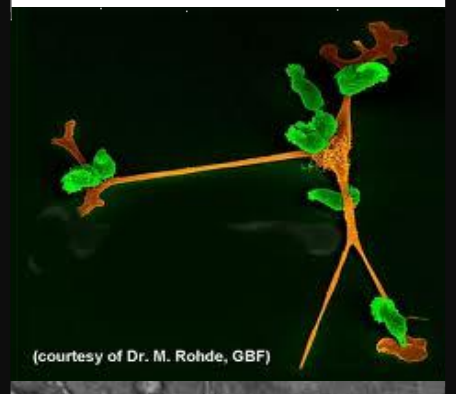
PAMPs – Pathogen Associated Molecullar Patterns

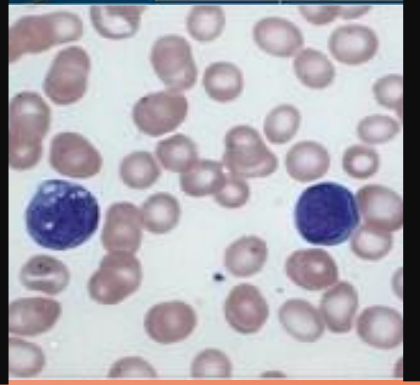
DAMPs – Danger Associated Molecular Pattern6

RESPOSTA IMUNE INATA E SUAS CÉLULAS

Tipo celular	Neutrófilo	Macrófago	Células dendríticas	Célula *natural killer*
Função	Fagocitose Espécies reativas de oxigênio e nitrogênio Peptídeos antimicrobianos	Fagocitose Mediadores inflamatórios Apresentação de antígenos Espécies reativas de oxigênio e nitrogênio Citocinas Proteínas do complemento	Apresentação de antígeno Sinais co-estimuladores Espécies reativas de oxigênio Interferon Citocinas	Lise da célula infectada por vírus Interferon Ativação de macrófagos







IMUNIDADE INATA

RECONHECIMENTO DE PADRÕES MOLECULARES !!!!!

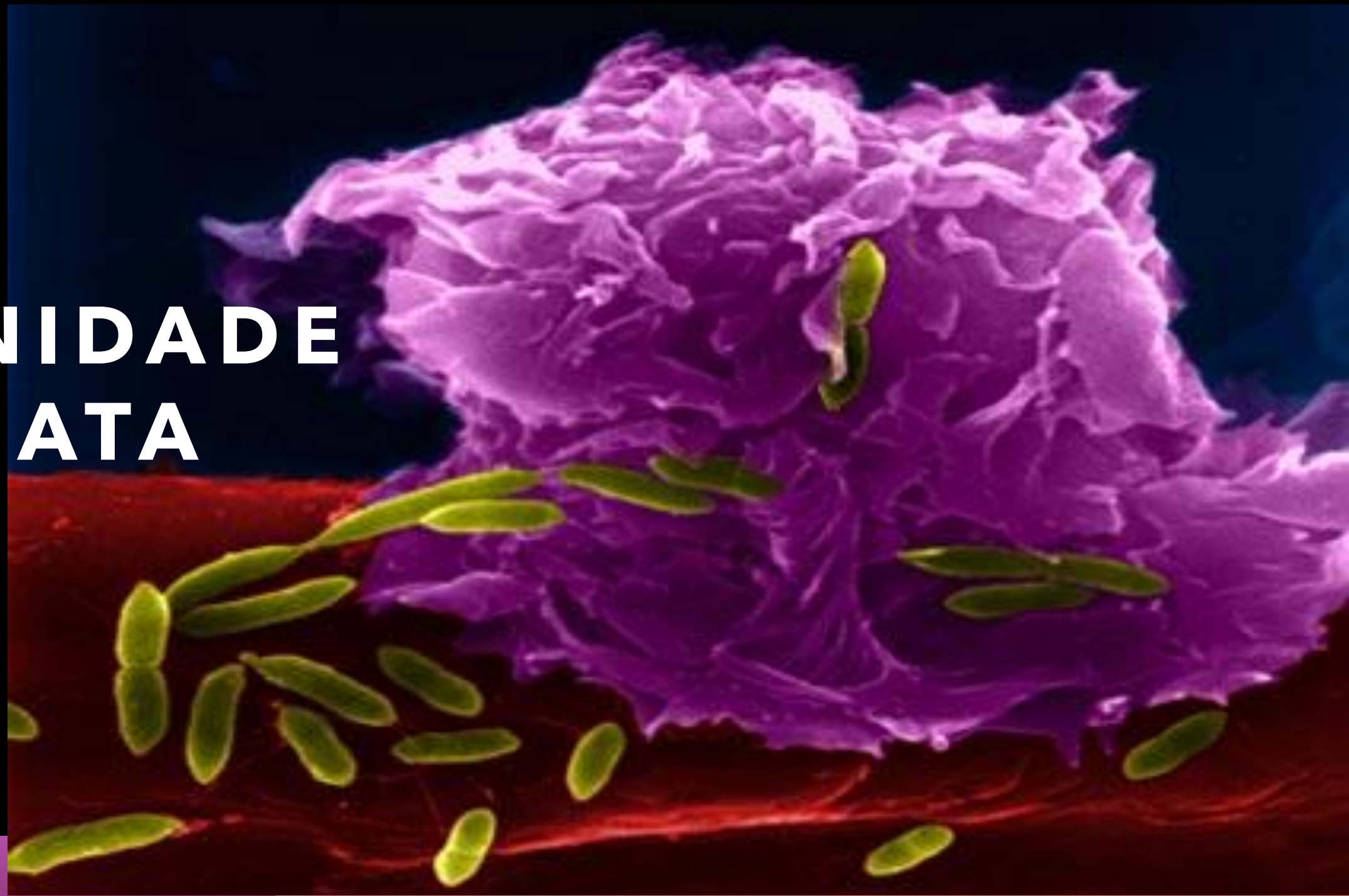
Carbohidratos
Pentoses -
Hexoses

Àcidos Graxos
SCFA / LCFA

Ácidos
Nucéicos
(DNA / RNA)

Proteínas
aa

IMUNIDADE INATA



Prêmio Nobel Medicina – Fisiologia - 2011

Photo: The Scripps Research Institute

Photo: CNRS Photo Library/Pascal Disdier

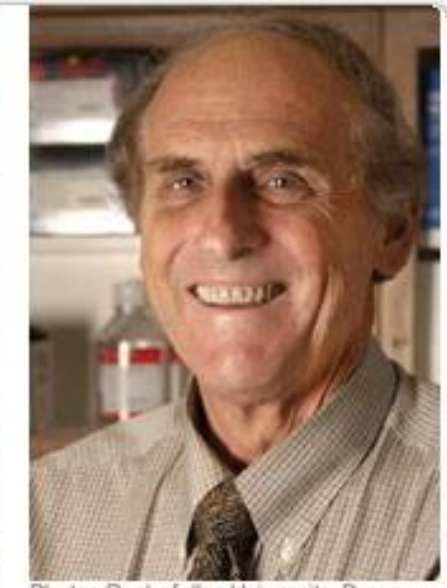


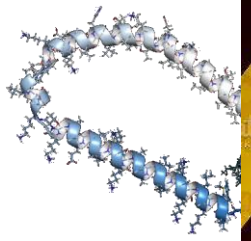
Photo: Rockefeller University Press

Bruce A. Beutler **Jules A. Hoffmann** **Ralph M. Steinman**

The Nobel Prize in Physiology or Medicine 2011 was divided, one half jointly to Bruce A. Beutler and Jules A. Hoffmann *"for their discoveries concerning the activation of innate immunity"* and the other half to Ralph M. Steinman *"for his discovery of the dendritic cell and its role in adaptive immunity"*.

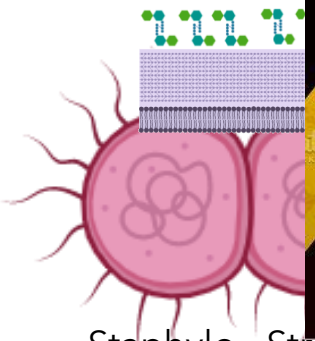
Charles Janeway **Ruslan Medzhitov**

"for their discoveries concerning the activation of innate immunity"



Alpha-synuc

TLR-2
Monocyte

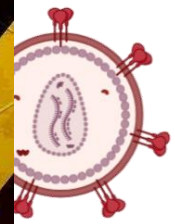


Staphylo - Strepto

DANGER

DNA

TLR-9
pDCs

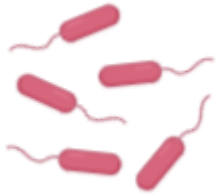


ZIKV

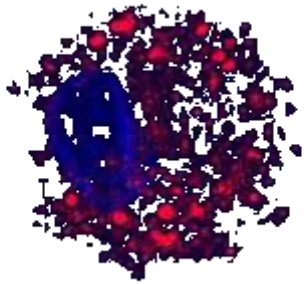
ZIKV

E. coli

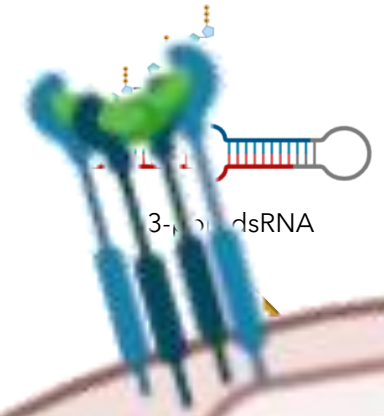
RECEPTORES TOLL-LIKE



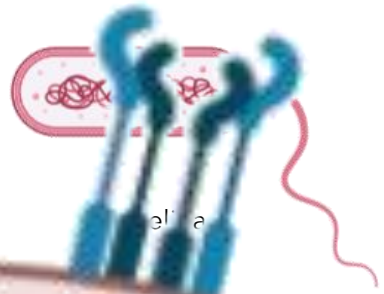
Sistema s de Secreção
SSTI/IIP



NLRP3
Monocytes



3-p dsRNA



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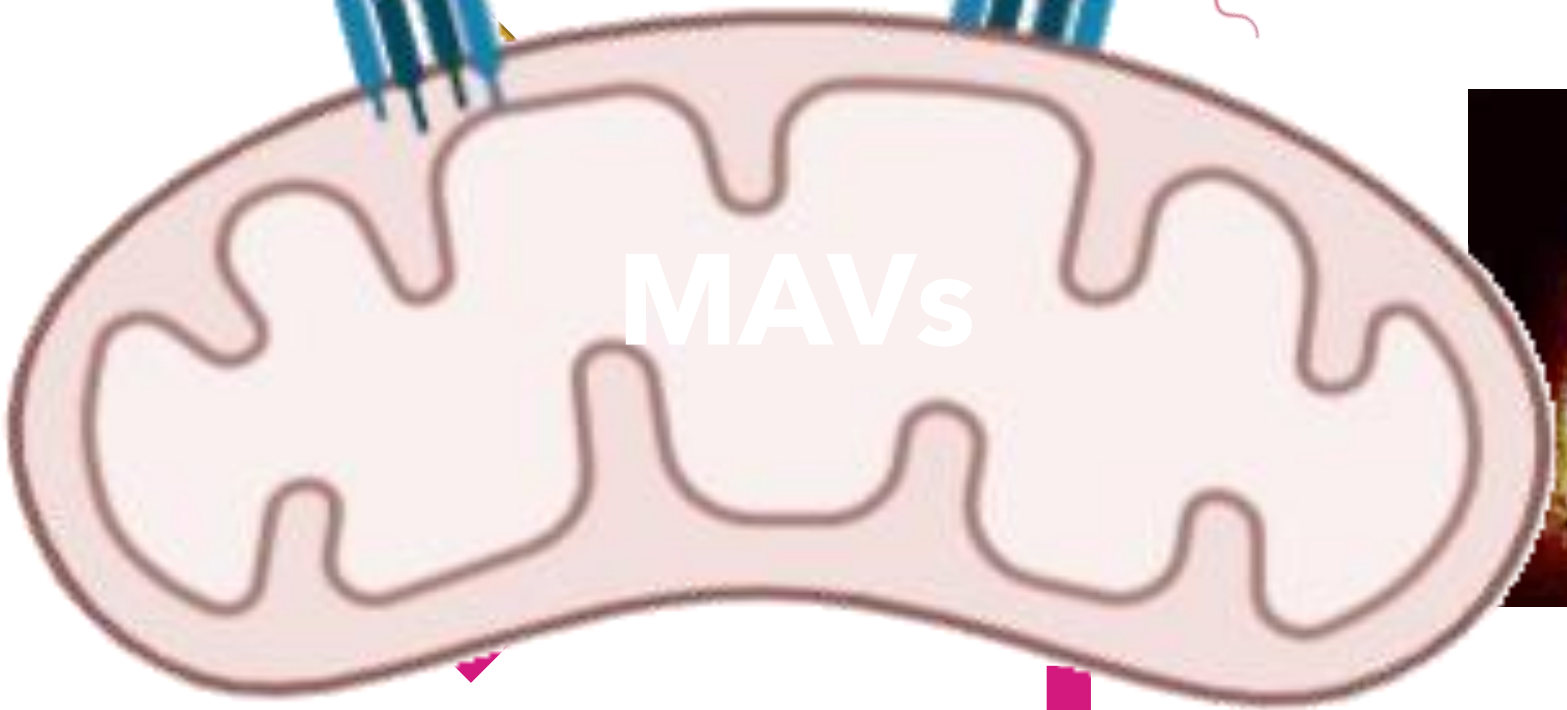
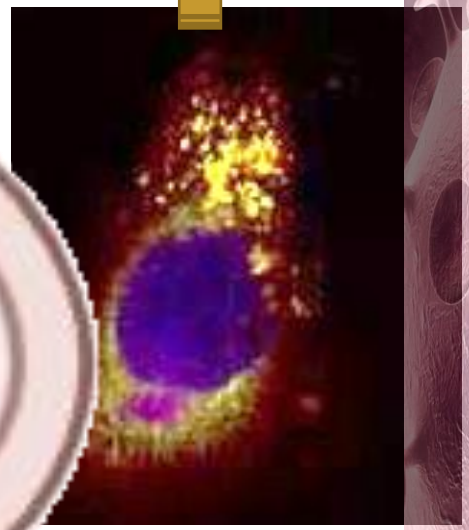


?

?

dsRNA



MDA-5
Monocytes

?

Imunidade Inata e seus RECEPTORES

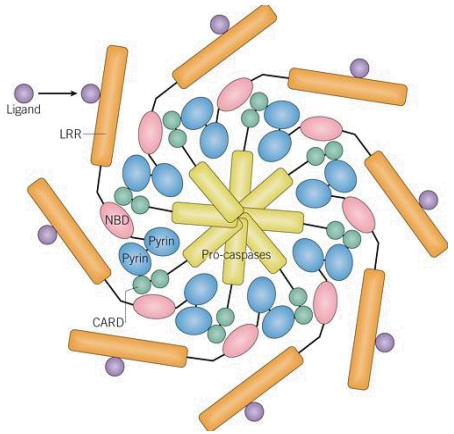
Receptores para PADRÕES DA NATUREZA (PRRs)

TOLL-LIKE RECEPTORS –
Ancorados na membrana

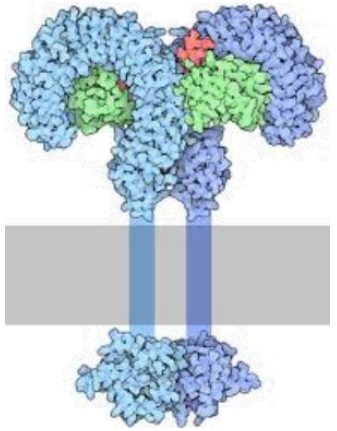
NOD RECEPTORS - Citoplasma
NOD/RIG-LIKE RECEPTORS – Citoplasma

Presentes em Muitas Células

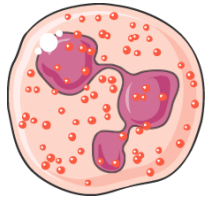
Sistema Imune Inato
e
Células Residentes



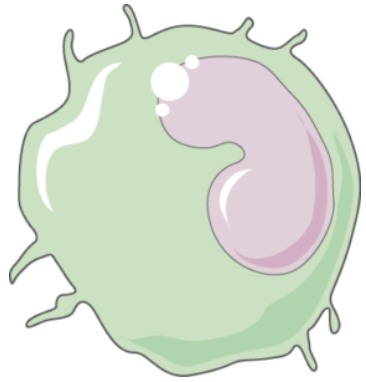
NLRs



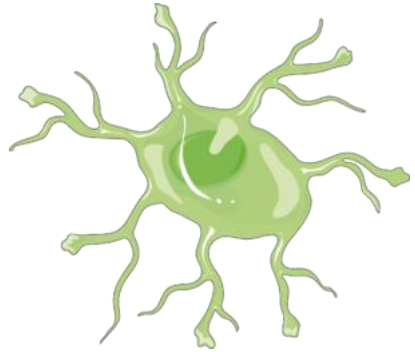
TLRs



Neutrófilo

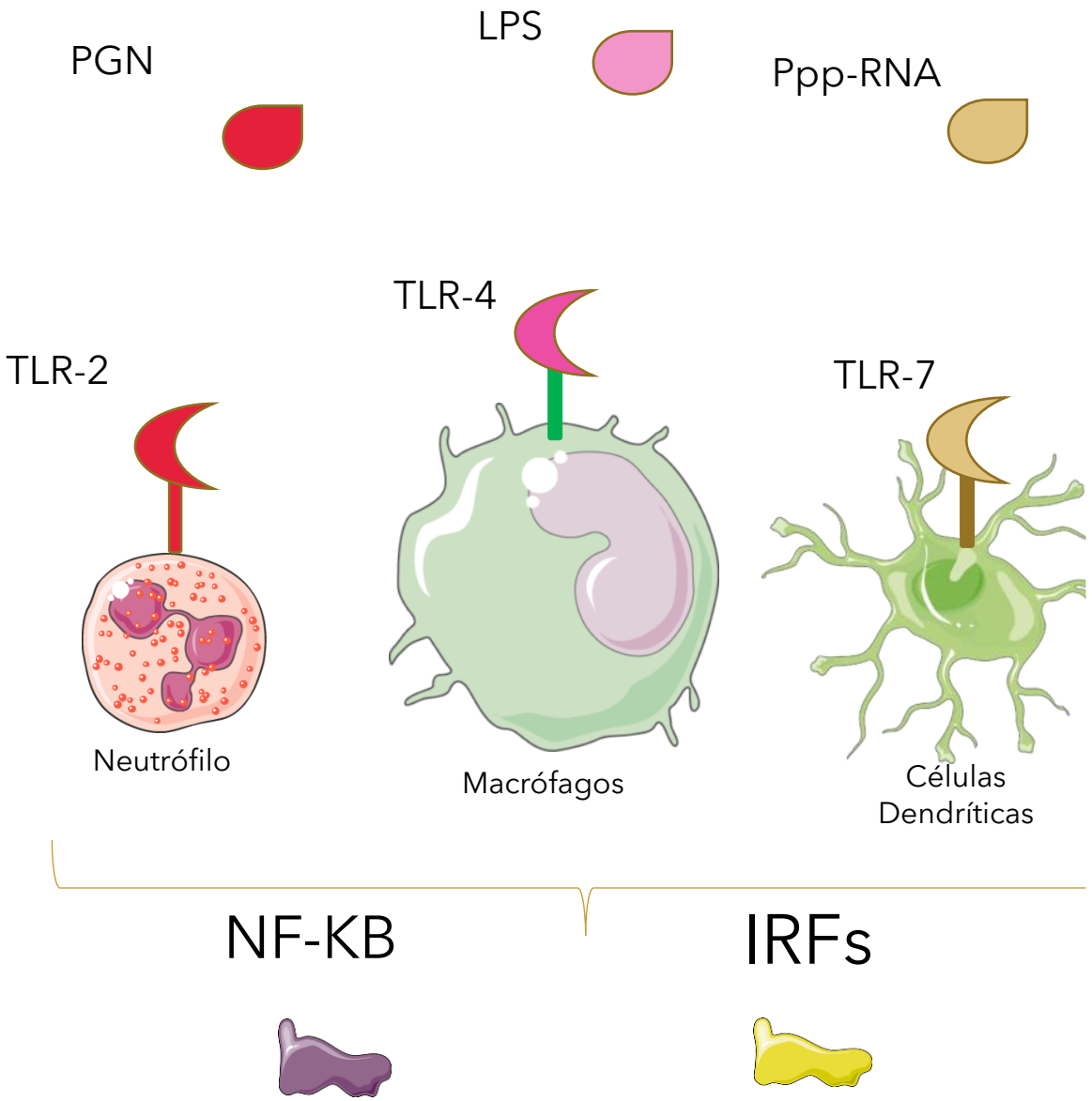


Macrófagos



Células Dendríticas

Ativação da Imunidade Inata
Sinaliza via NF-KB



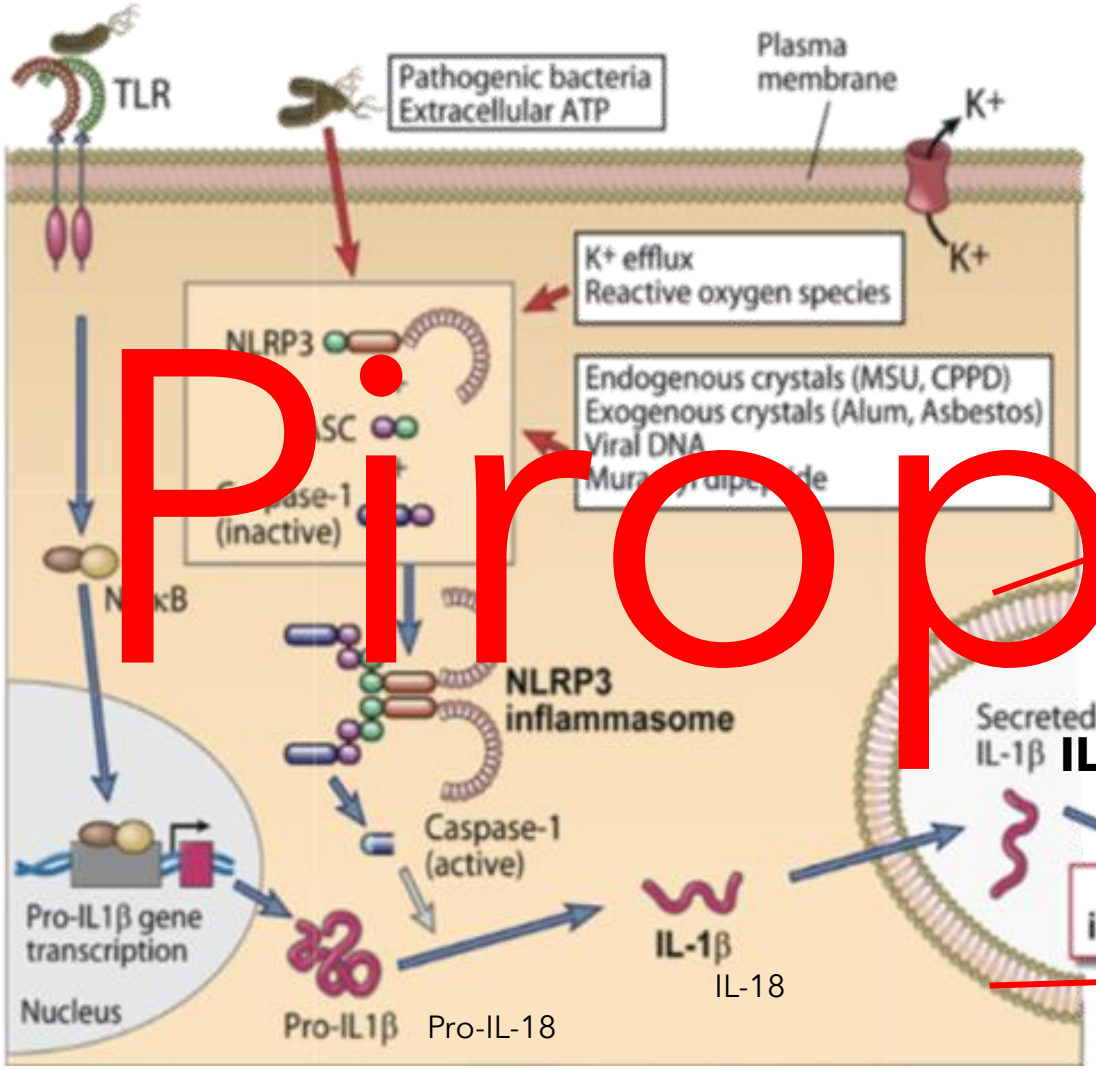
Citocinas inflamatórias-IL-6, TNF-α, IFN-a/b

Moléculas de Adesão – Integrinas, MHC I/II

Mediadores Lipídicos – Cox-2, 5-LO

Quimiocinas – CCL2, CXCL5, CXCL12

IL-1 – Inflamasoma e Piroptose

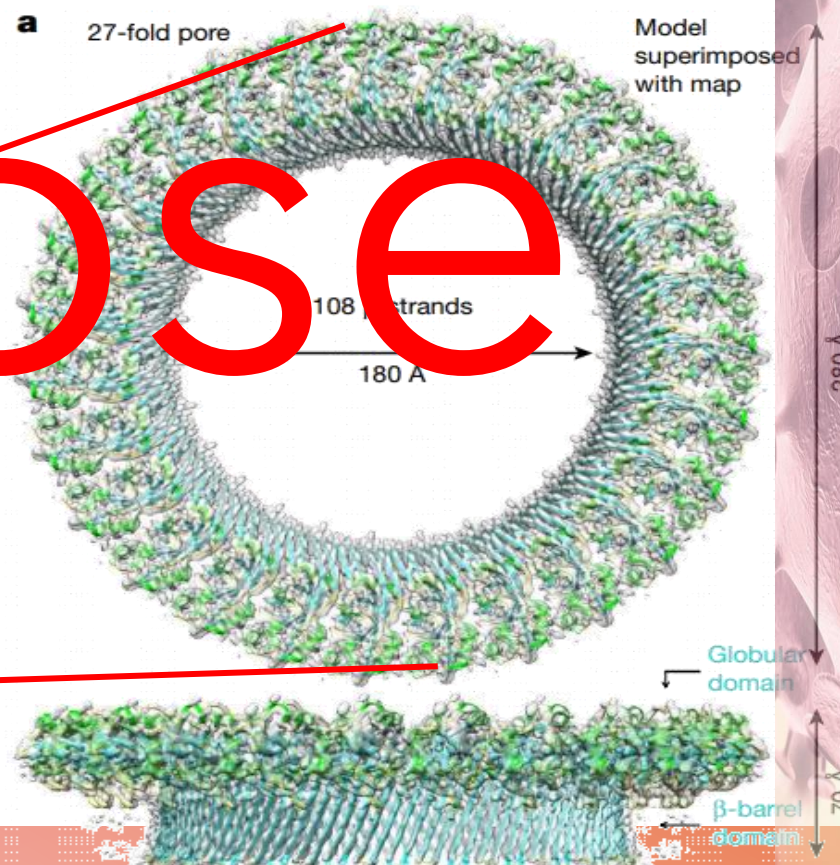


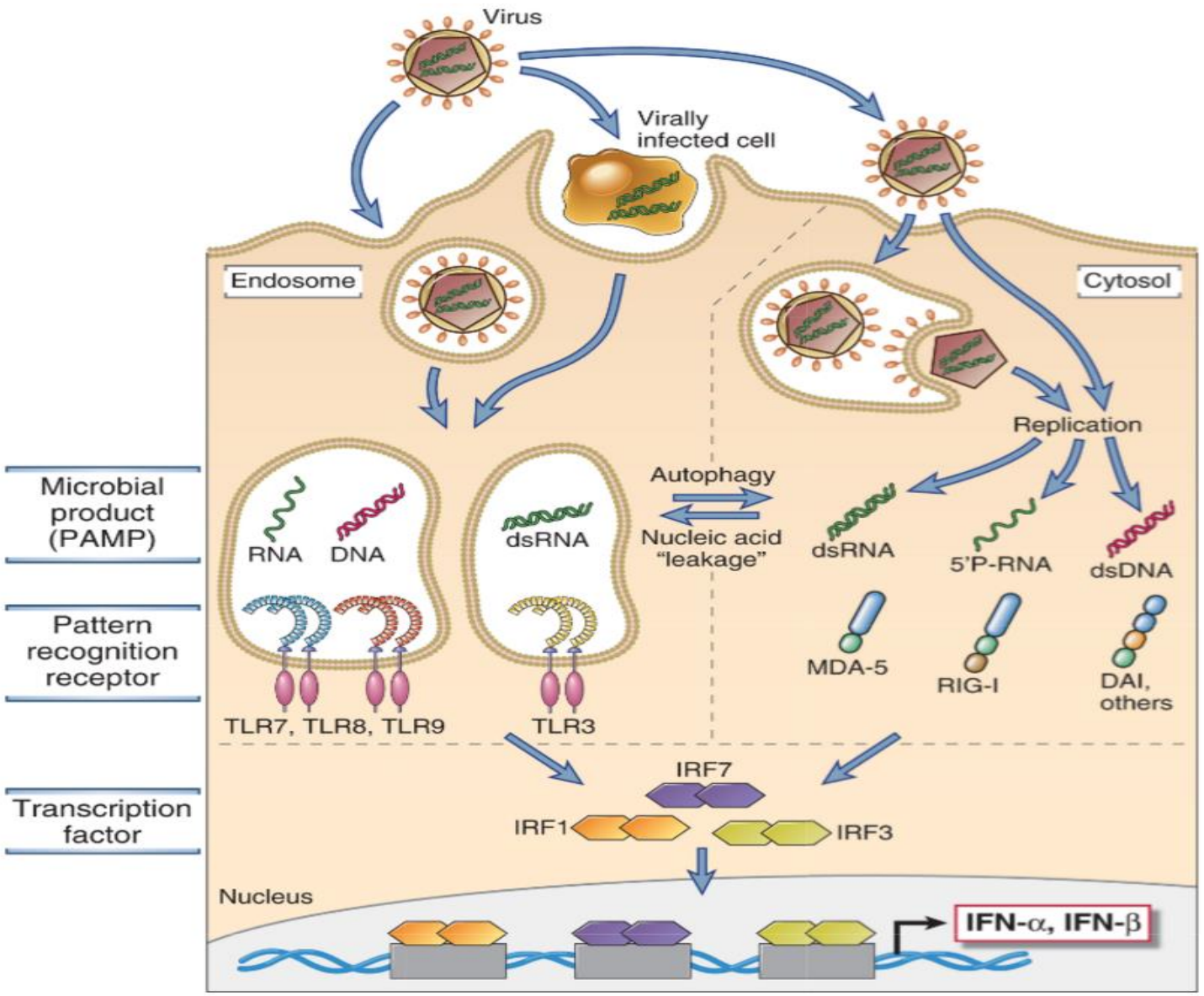
Piroptose

Cryo–EM structure of the gasdermin A3 membrane pore

Jianbin Ruan[1,2], Shiyu Xia[1,2], Xing Liu[1,3], Judy Lieberman[1,3] & Hao Wu[1,2]*

ten in mice, including three GSDMAs. GSDMs are cleaved by regulated processing that removes an inhibitory C-terminal fragment (GSDM-CT) to allow the N-terminal fragment (GSDM-NT) to bind to acidic lipids in the inner leaflet of mammalian cell membranes or on bacterial membranes to form pores. GSDMD is a substrate of inflam-





Sensores de Ácidos Nucléicos no Citoplasma

TLR-3
TLR-7
TLR-8
TLR-9

MDA-5

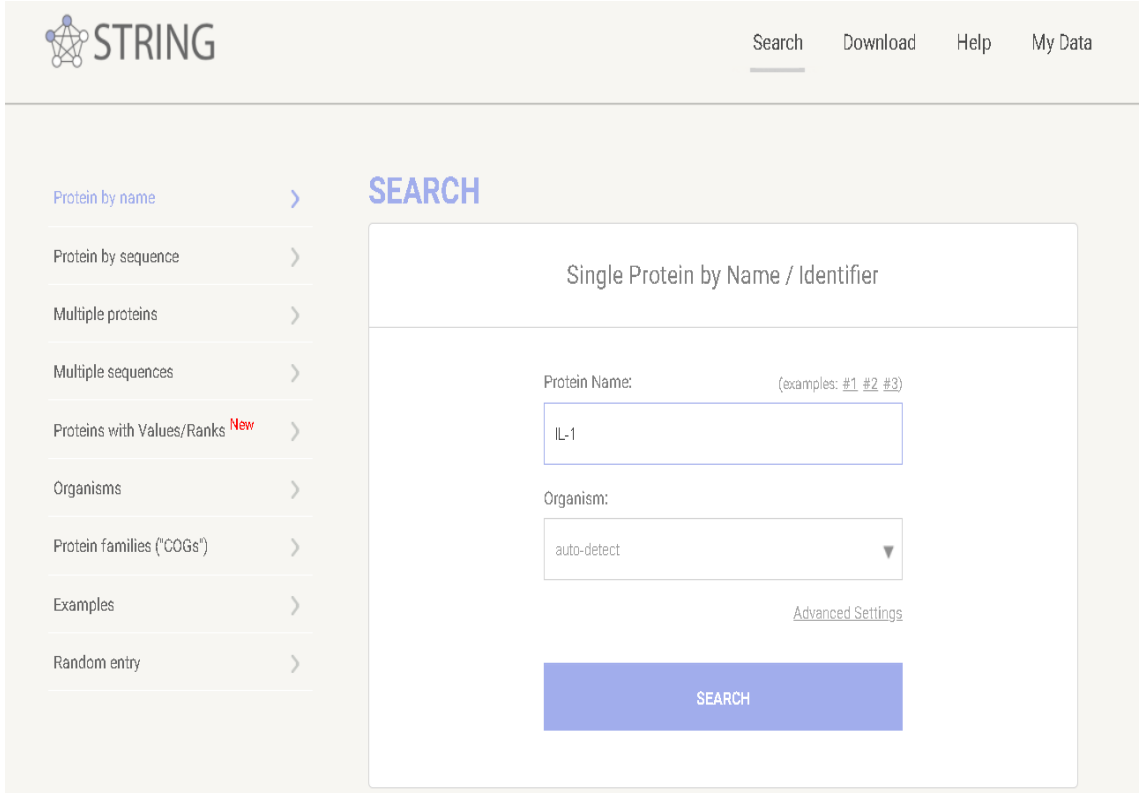
RIG-I

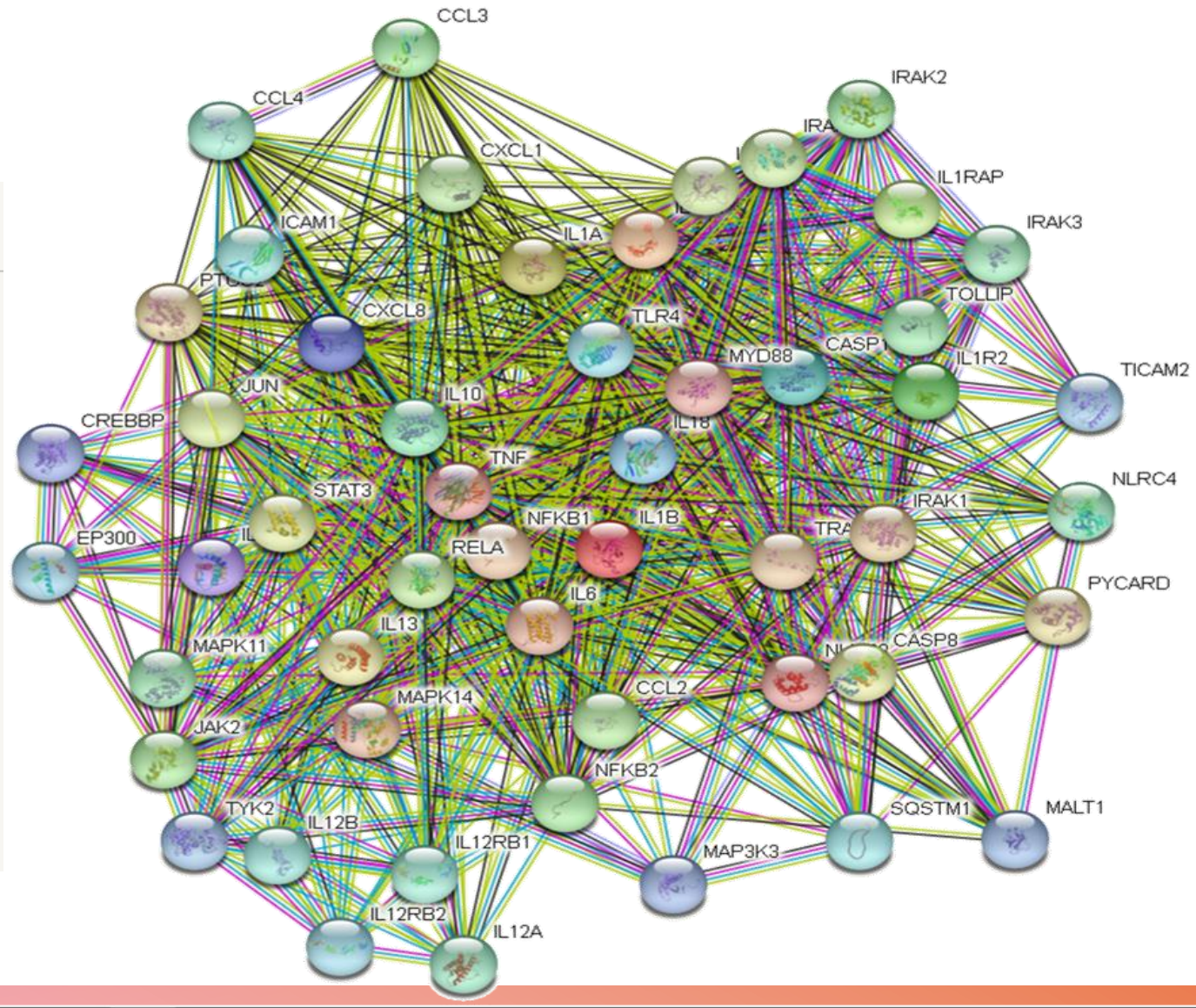
MAVs

INTERFERONS TIPO I

REDE DE CITOCINAS LOOP POSITIVO

www.string-db.org





Mas qual a importância dessas vias de sinalização intracelular?

E dessas citocinas ?

Quais são seus efeitos
BIOLÓGICOS ?

The NEW ENGLAND JOURNAL of MEDICINE

REVIEW ARTICLE

Dan L. Longo, M.D., *Editor*

Cytokine Storm

David C. Fajgenbaum, M.D., and Carl H. June, M.D.

IL-1

IL-6

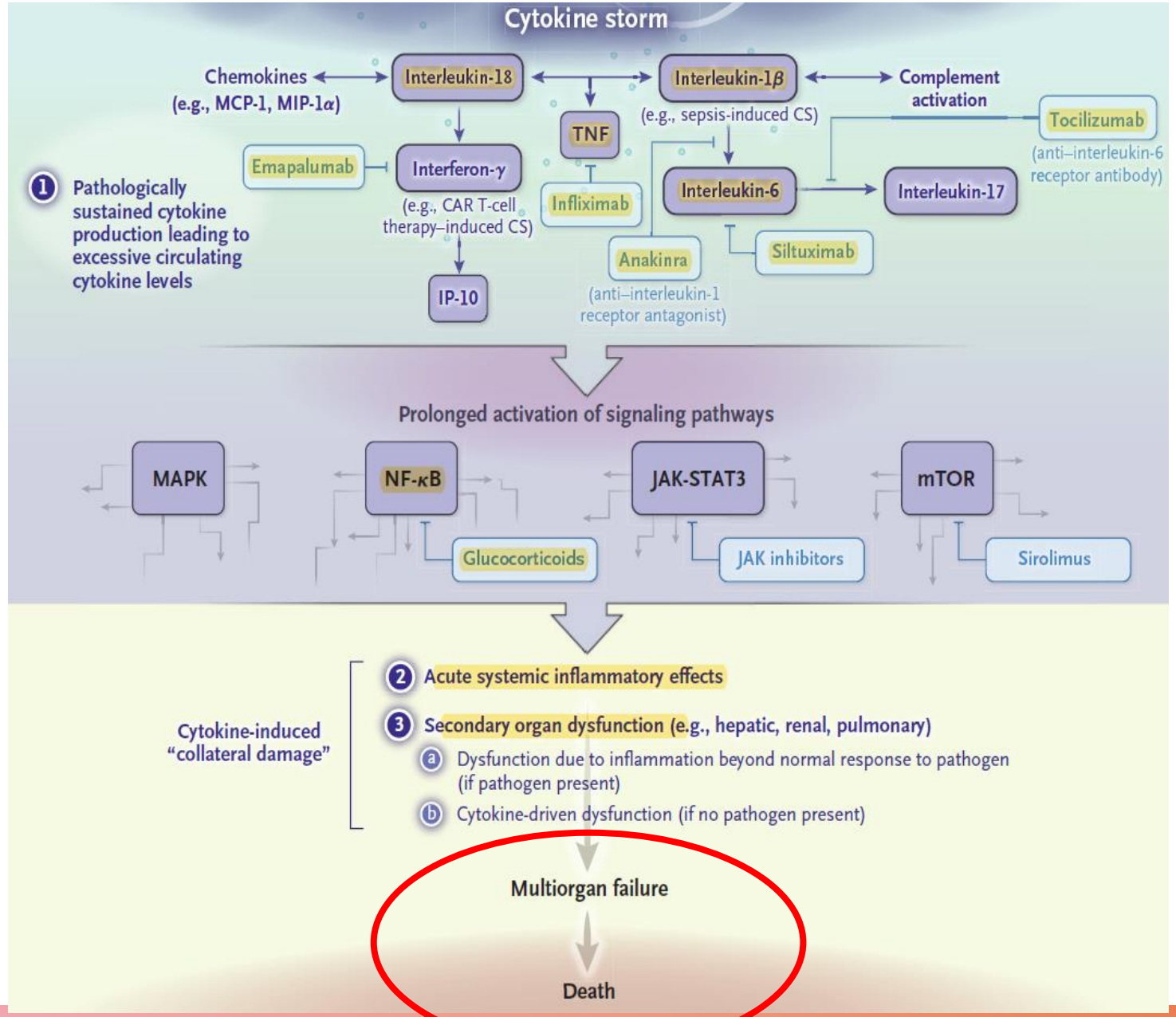
TNF-alpha

Interferons Tipo I

IFN-alpha
IFN-beta

Interferon Tipo II

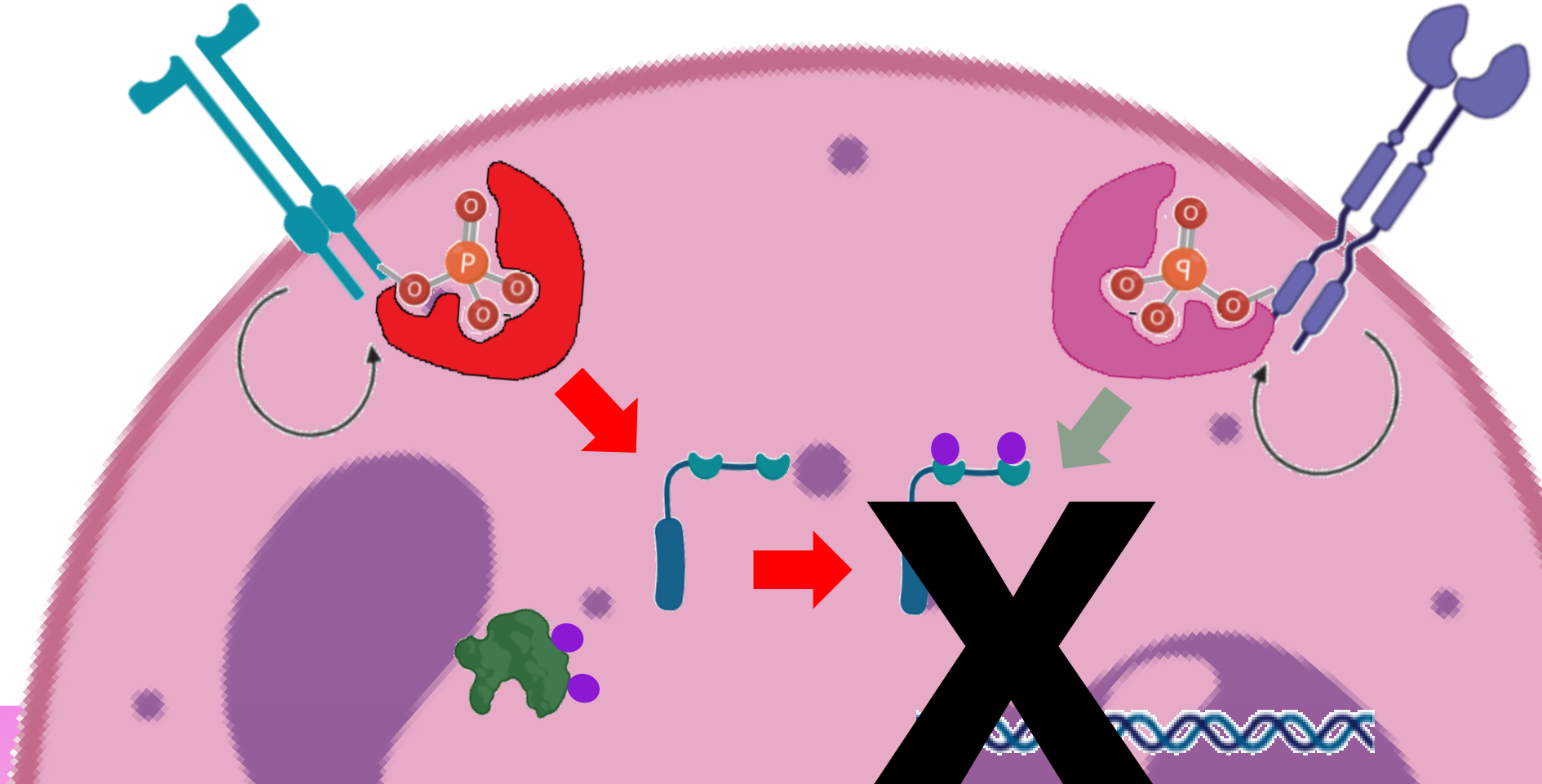
IFN-gamma



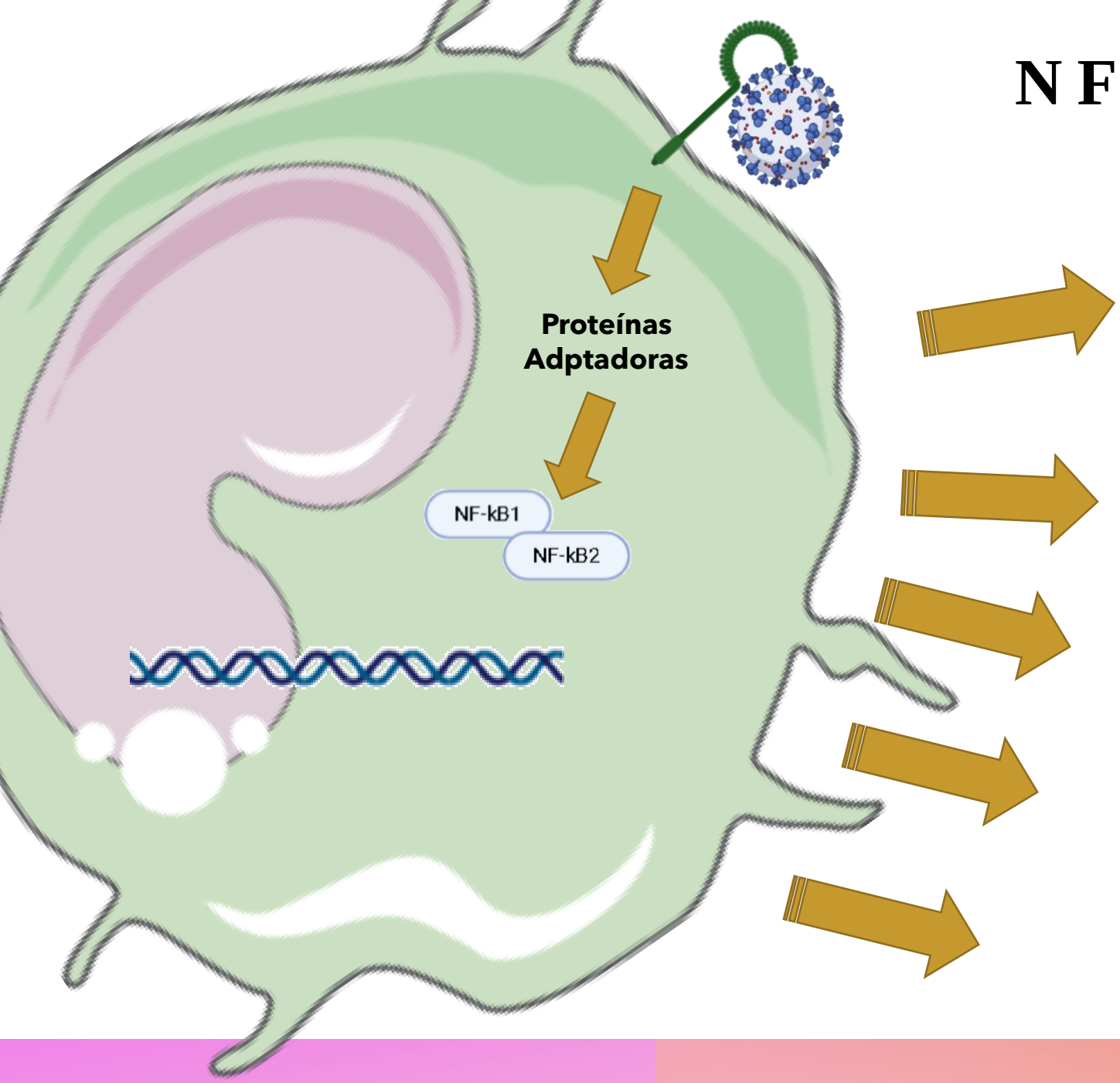
QUINASES VS. FOSFATASES

RECEPTORES ATIVATÓRIOS VS INIBITÓRIOS

FOSFORILAÇÃO VS DESFOSFORILAÇÃO



NF-KB E SEUS GENES ALVO



Citocinas inflamatórias
IL-6, IL-12, TNF-α

Moléculas de Adesão
Integrinas, selectinas, proteoglicanas.

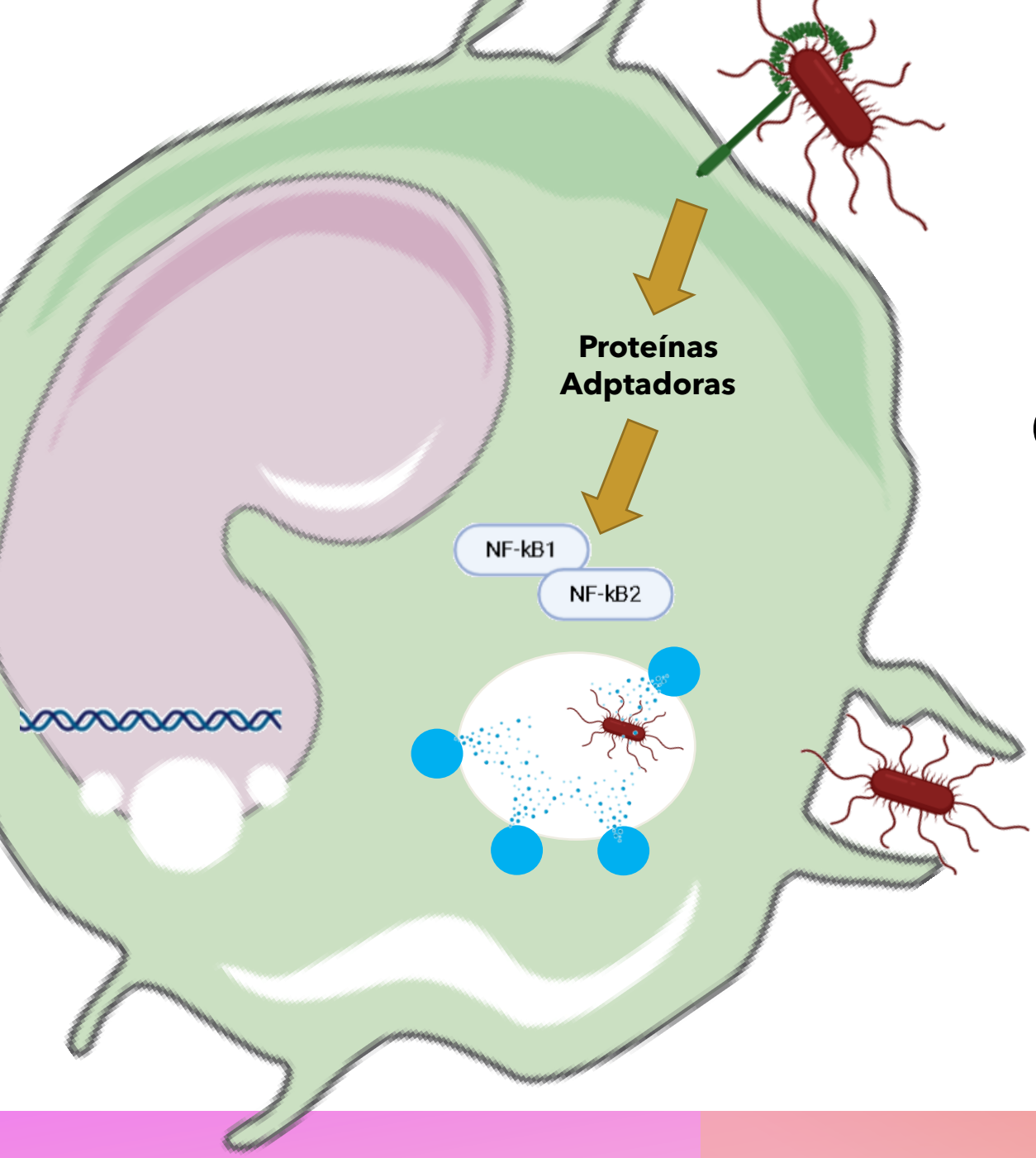
Moléculas de Apresentação de Ags MHC I/II

Mediadores Lipídicos
Cox-2, 5-LO

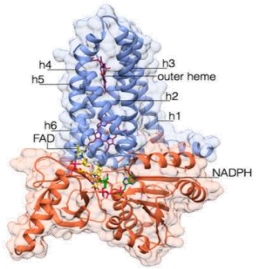
Quimiocinas
CCL2, CXCL5, CXCL12

Proteínas de FASE AGUDA
PROTEÍNAS DA COAGULAÇÃO

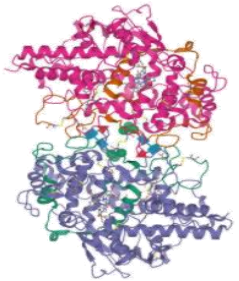
NF-KB – E SEUS GENES ALVO
SISTEMA NADPH OXIDASE
SUPERÓXIDO DISMUTASE
MIELOPEROXIDASE



O_2 → O_{2-} → H_2O_2 → H_2O + O_2



NADPHOx



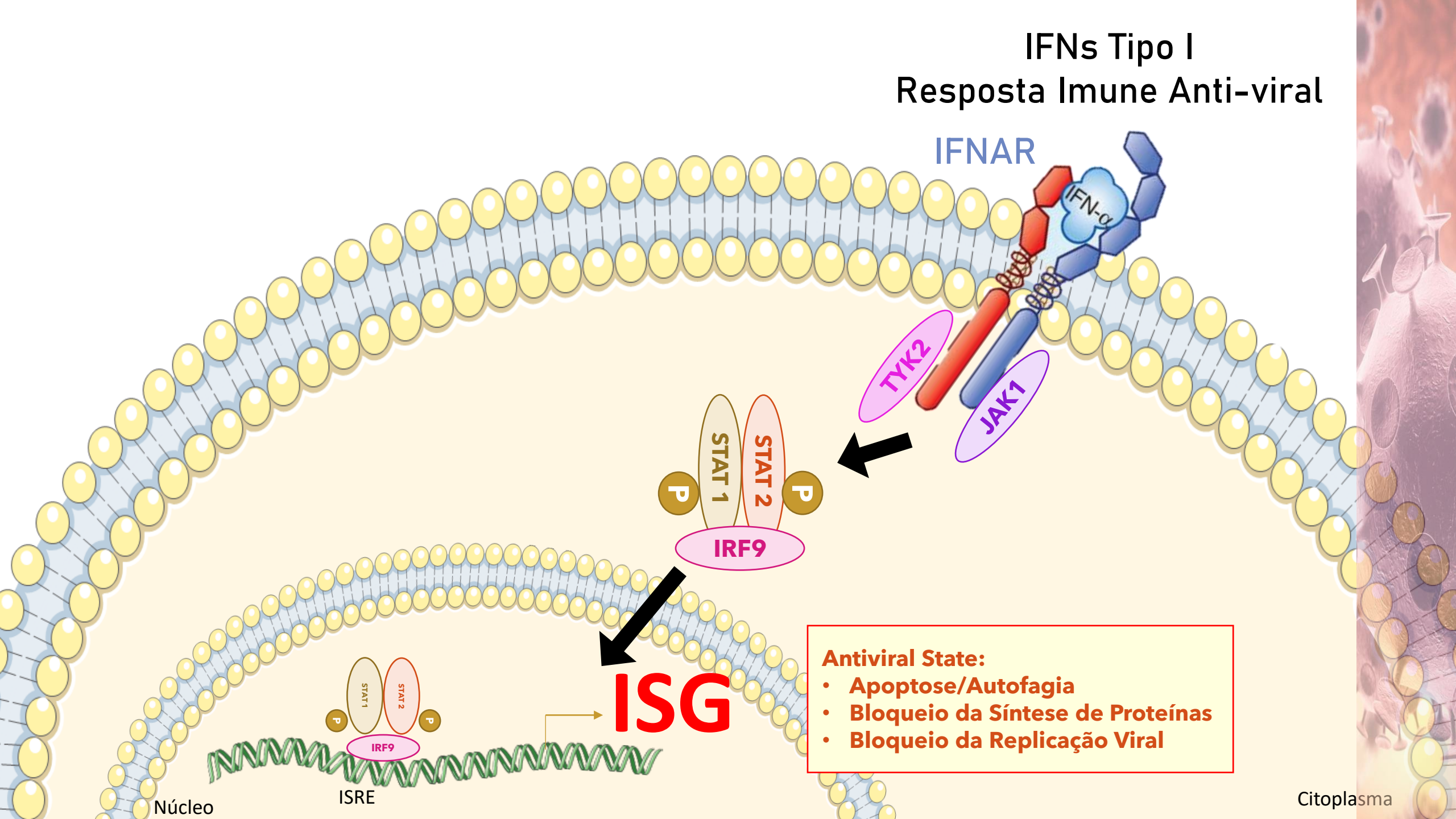
Mieloperoxidase

Crystal structures and atomic model of NADPH oxidase

Francesca Magnani, Simone Nenci, Elisa Millana Fananas, Marta Ceccon, Elvira Romero, Marco W. Fraaije, and Andrea Mattevi

PNAS June 27, 2017 114 (26) 6764-6769; first published June 12, 2017 https://doi.org/10.1073/pnas.1702293114

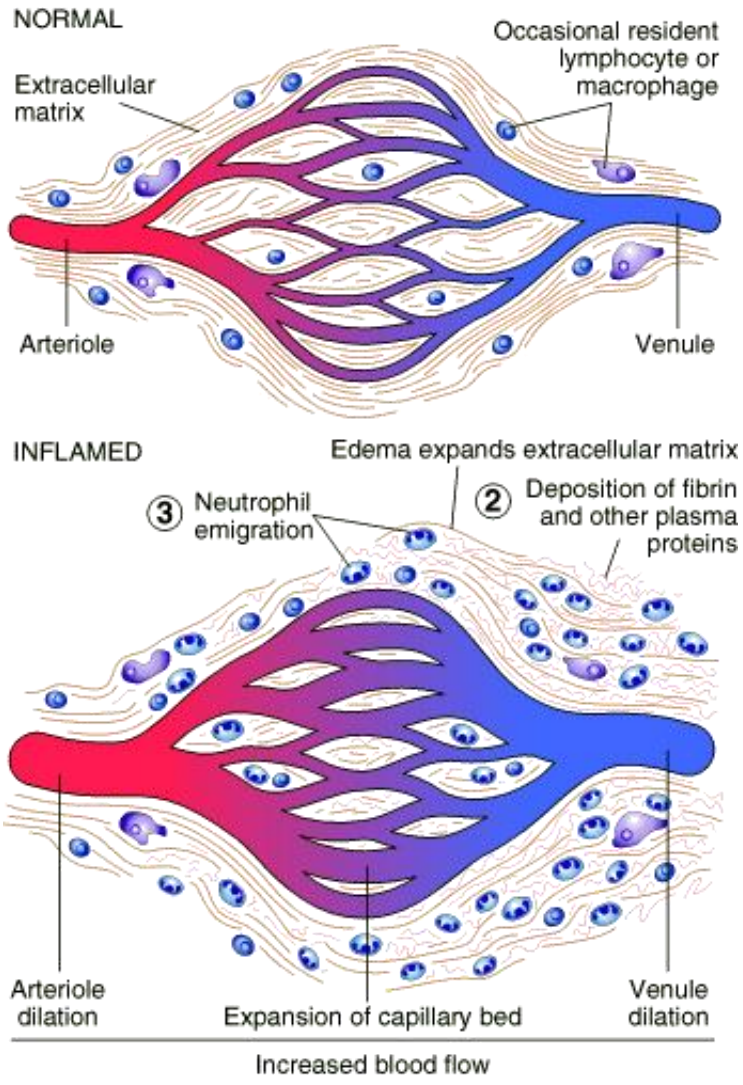
IFNs Tipo I
Resposta Imune Anti-viral

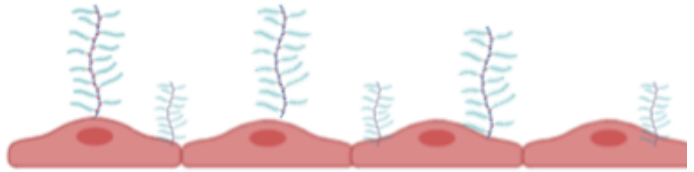


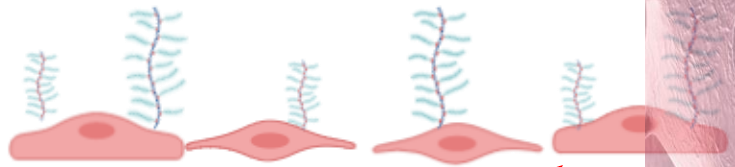
Antiviral State:

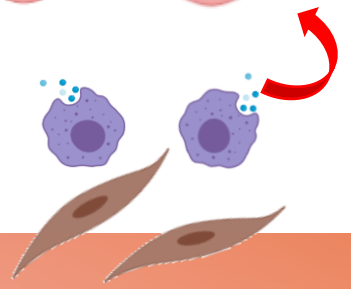
- **Apoptose/Autofagia**
- **Bloqueio da Síntese de Proteínas**
- **Bloqueio da Replicação Viral**

ALTERAÇÕES NO FLUXO SANGUÍNEO E MIGRAÇÃO DE LEUCÓCITOS

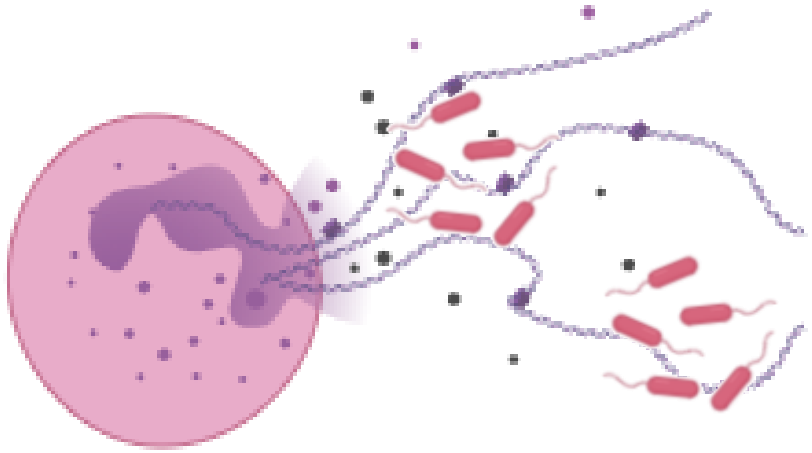






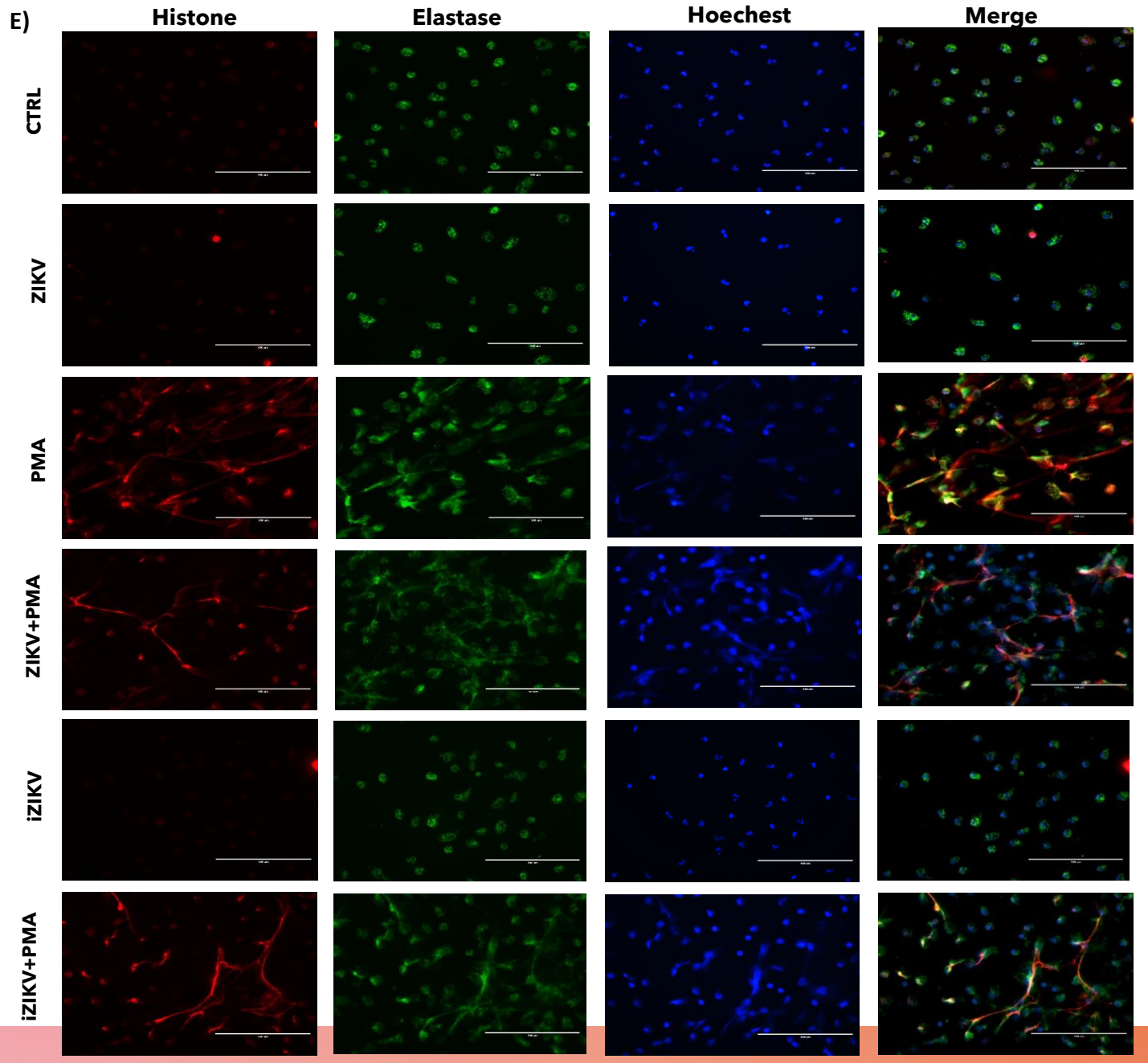


NETOSIS
OU *DNA TRAPS*

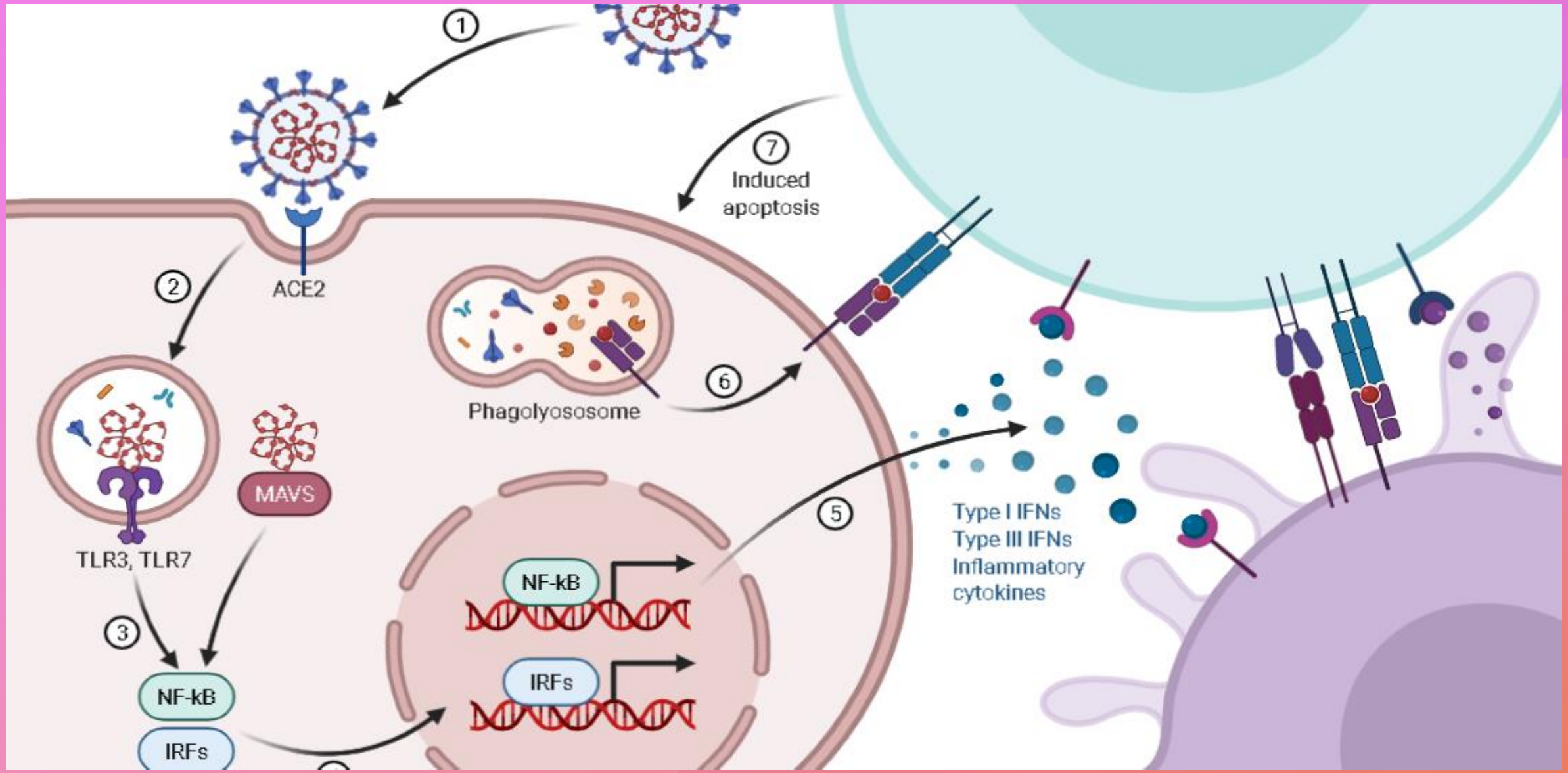


Extravasamento do material
Nuclear + Citoplasmático

PAD4 / ROS / MPO



RESUMINDO – SARS-COV2 ATIVA VIAS DA IMUNIDADE INATA PRODUTORAS DE CITOCINAS INFLAMATÓRIAS

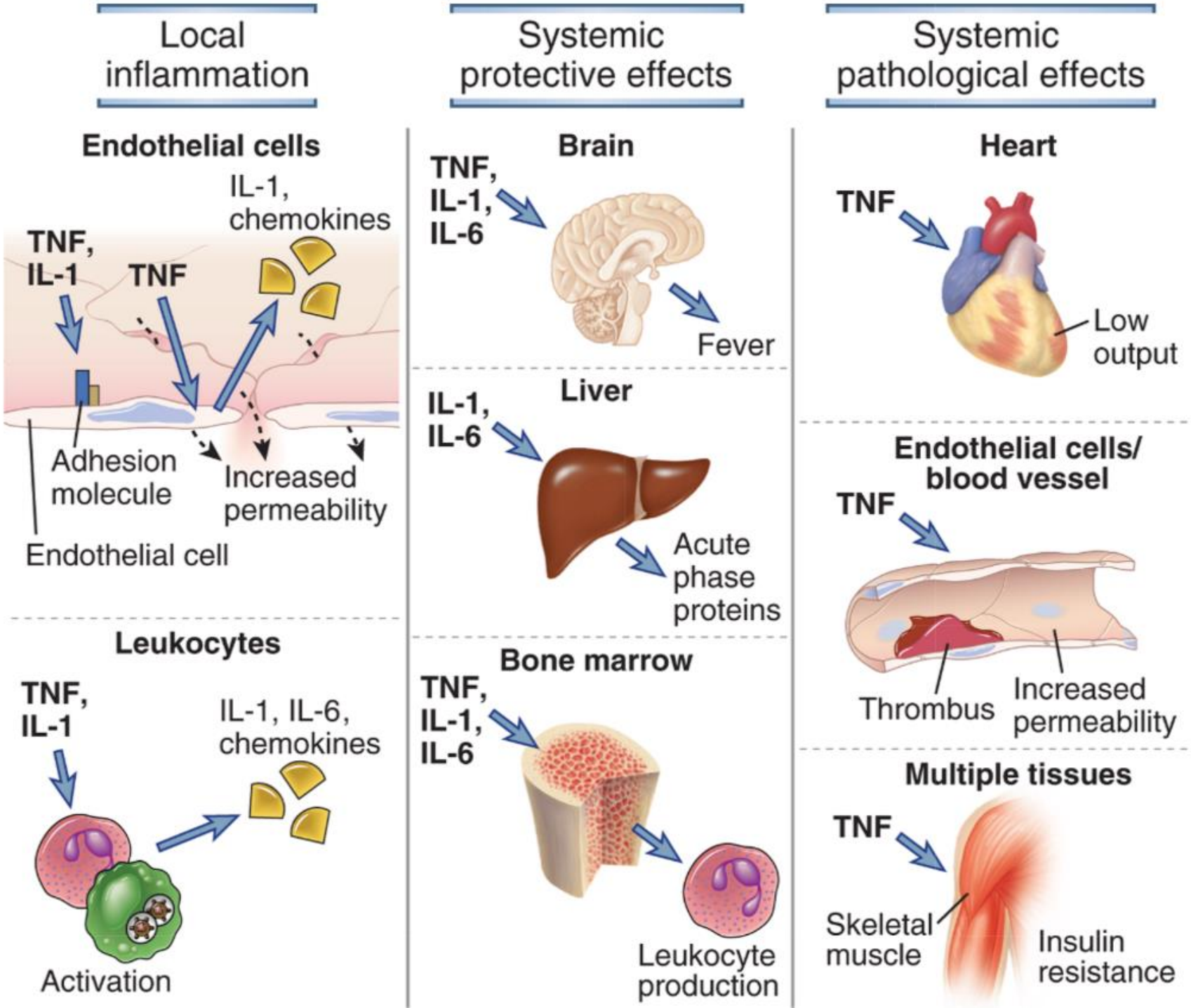


Efeitos

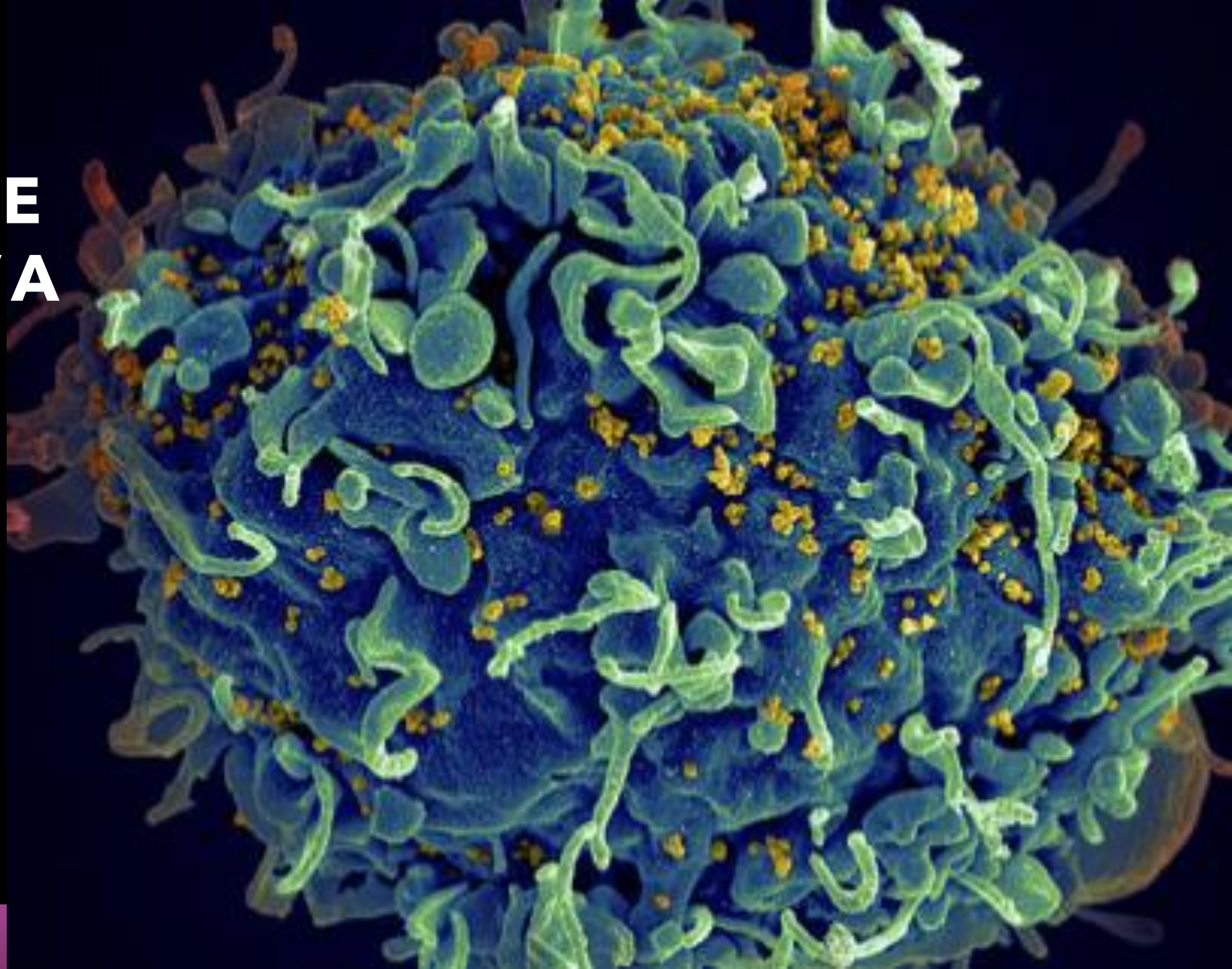
Locais

E

Sistêmicos



IMUNIDADE ADAPTATIVA

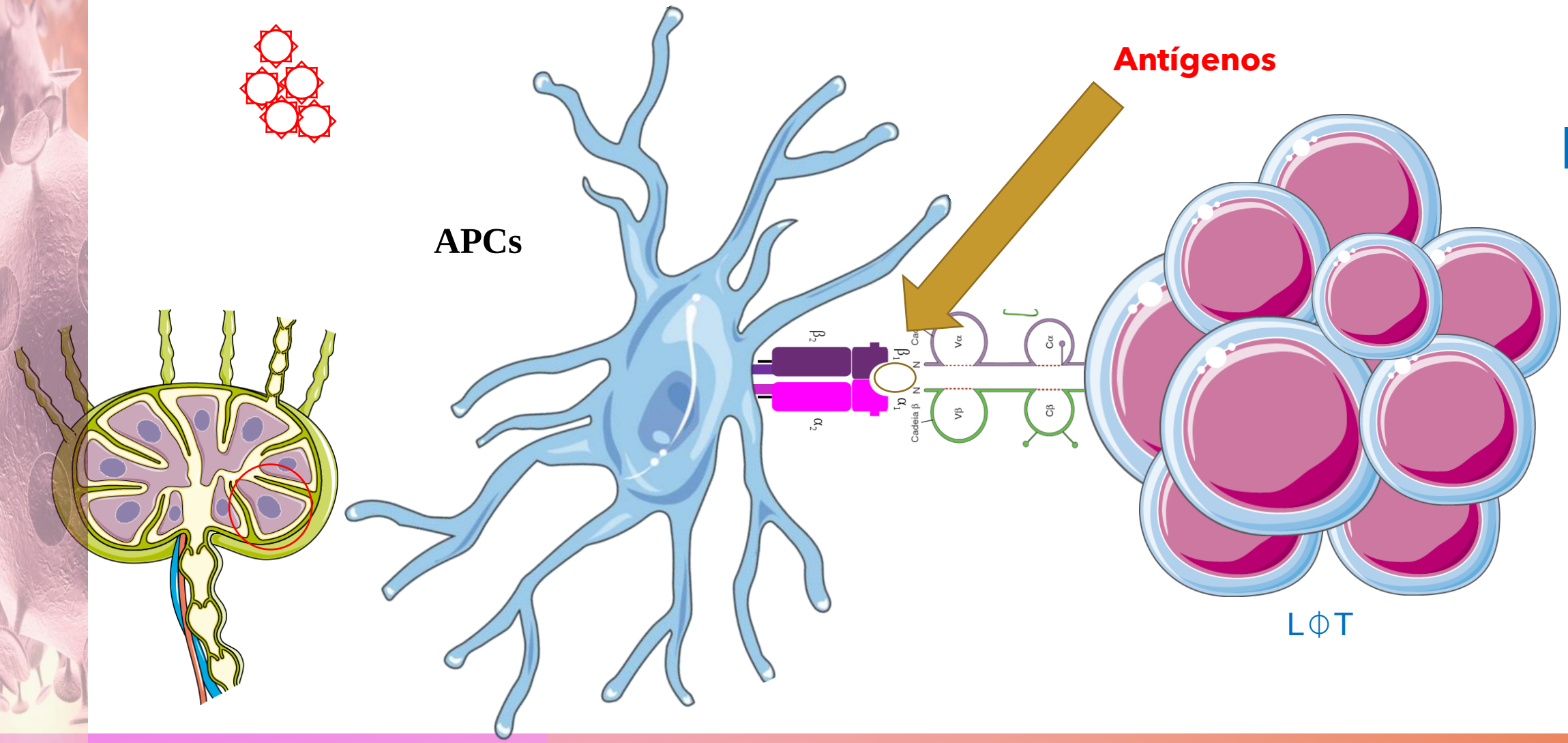


E QUAL O PAPEL DA IMUNIDADE ADAPTATIVA ?

LINFÓCITOS B

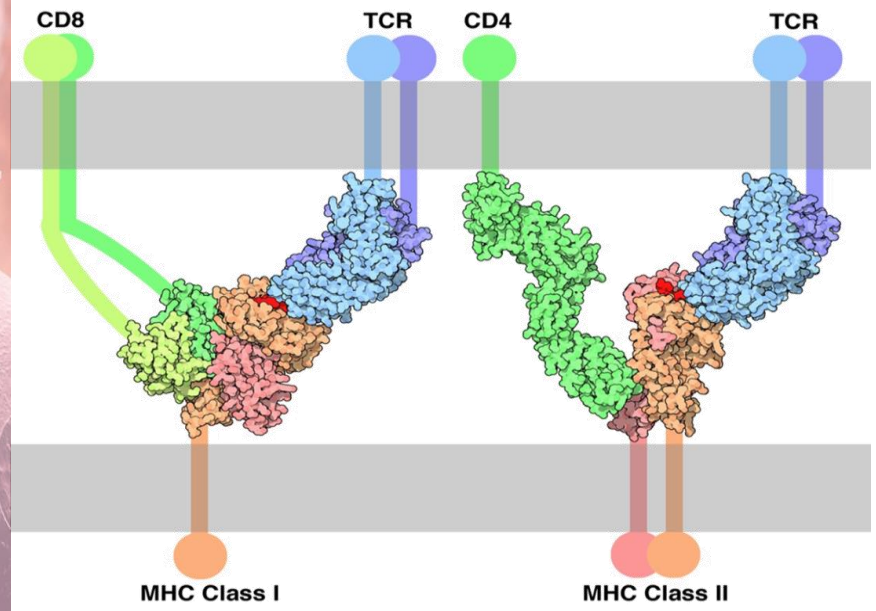
LINFÓCITOS T

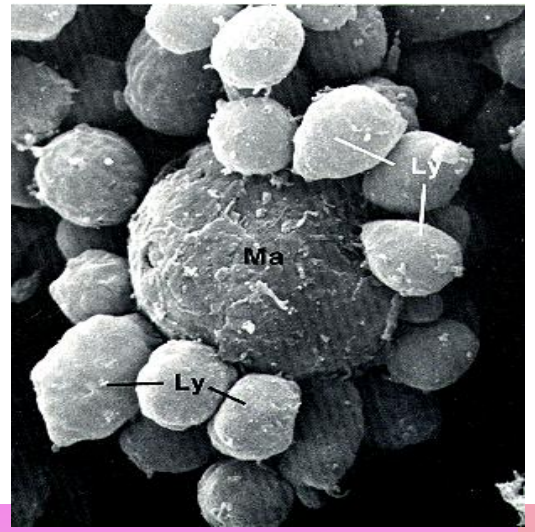
ATIVAÇÃO DA IMUNIDADE ADAPTATIVA
Apresentação de Antígenos

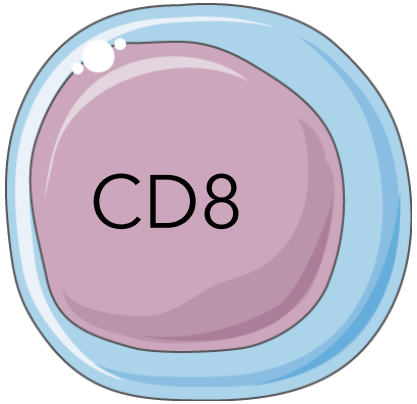


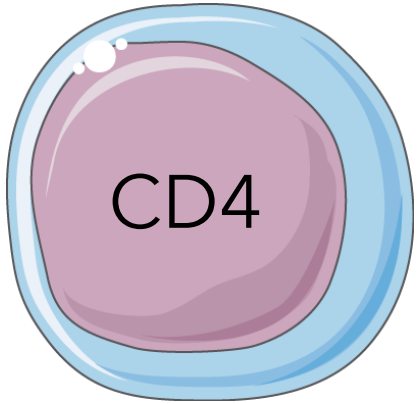
Van Kaer L et al 2019

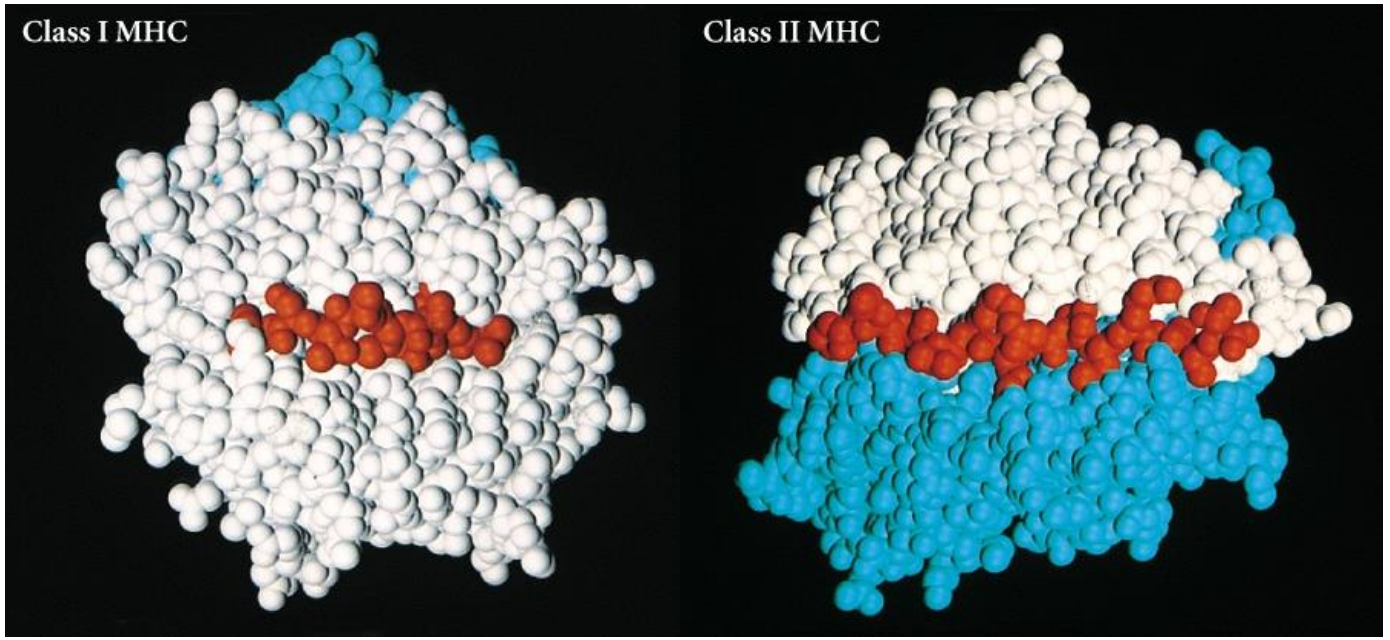
MHC + ANTÍ GENO + TCR





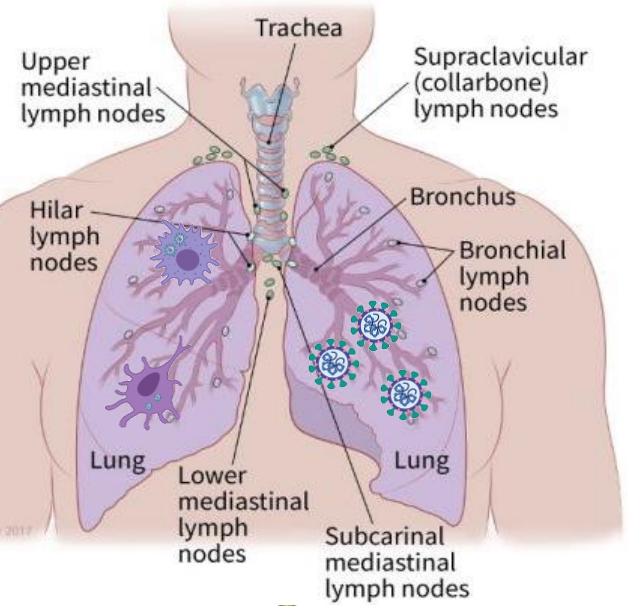


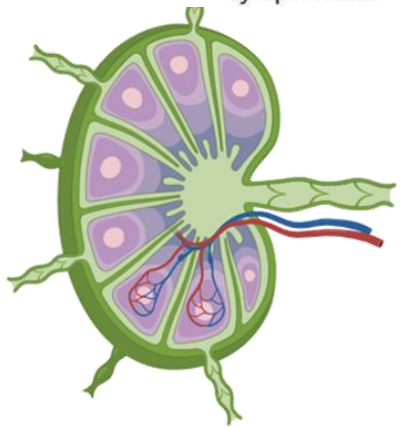


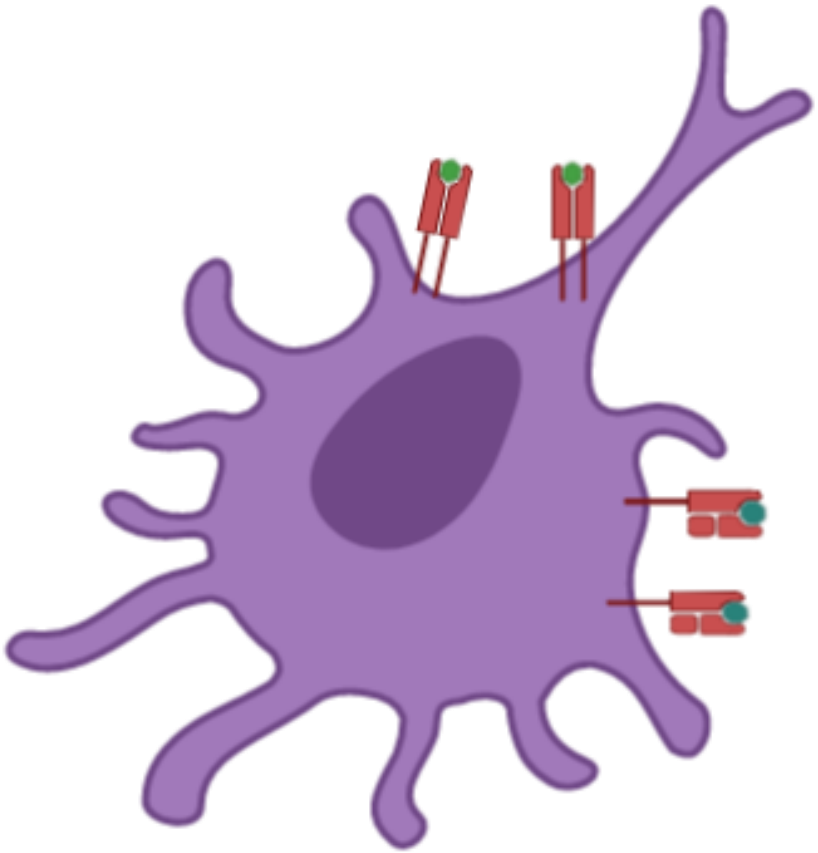


Abbas A:Imunologia celular e molecular. 8ª Ed.

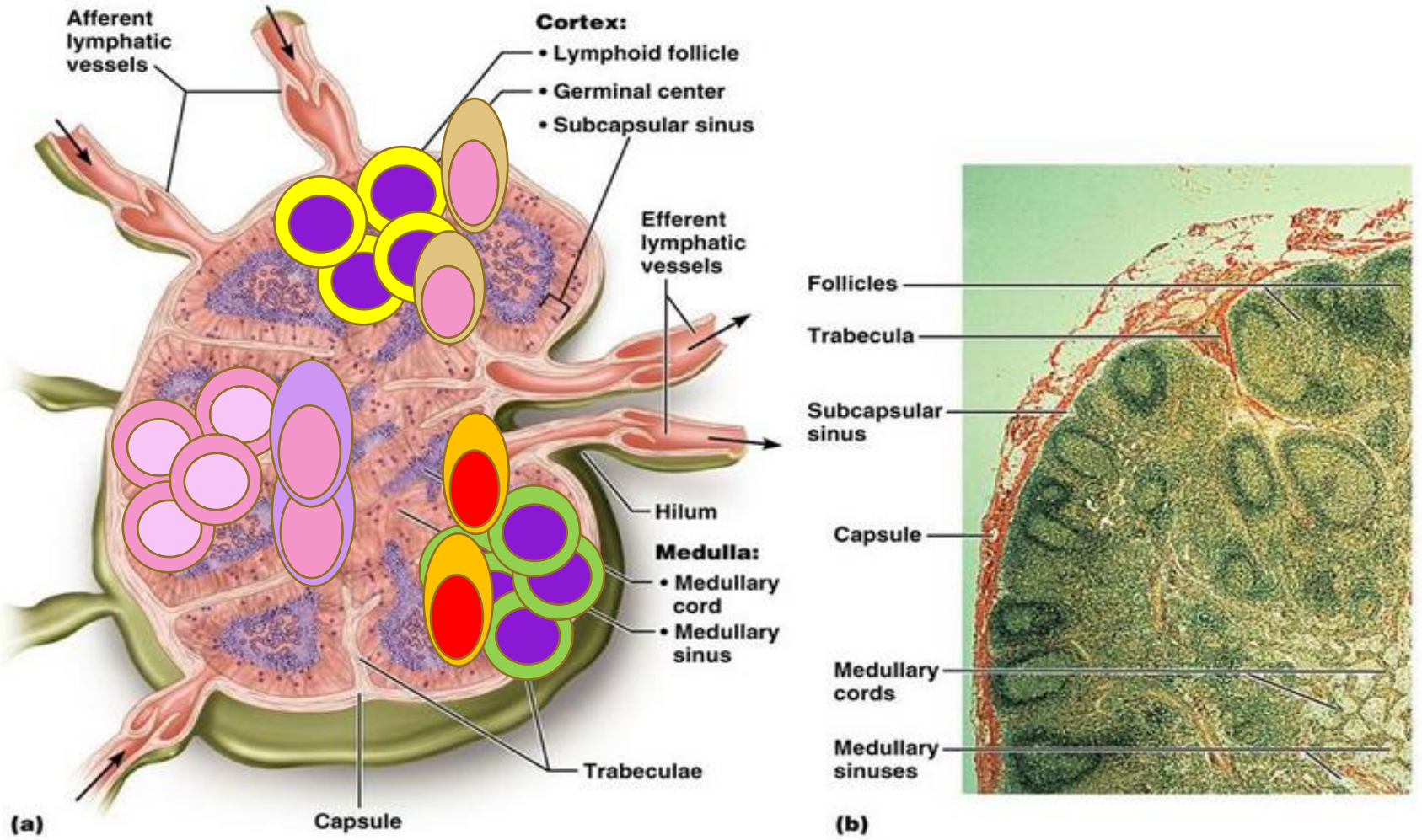
Ativação da Imunidade Adaptativa
Linfonodos, Baço e no Sítio da Infecção





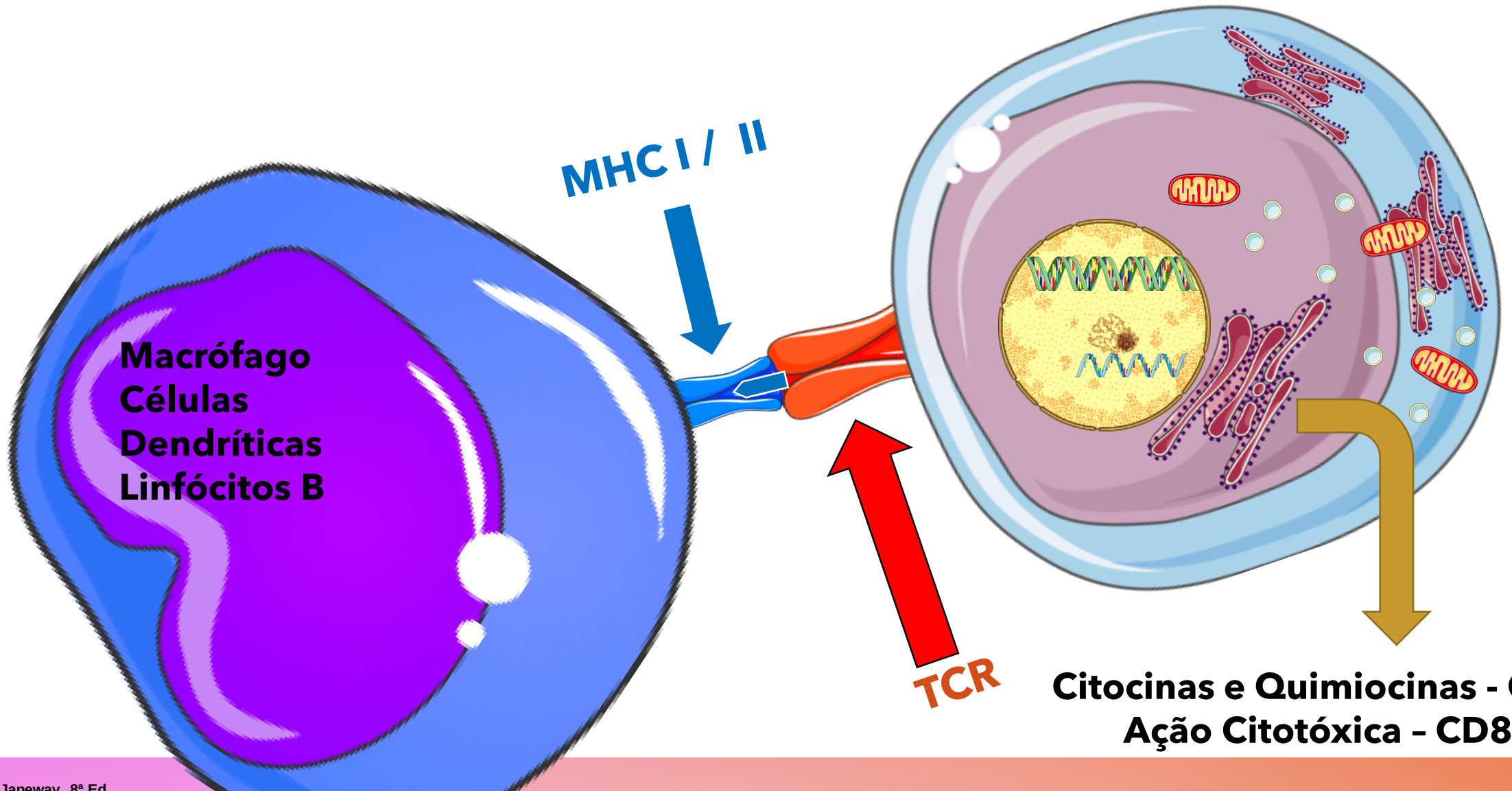


Drenagem Antígenos aos Linfonodos – Antígenos Proteicos



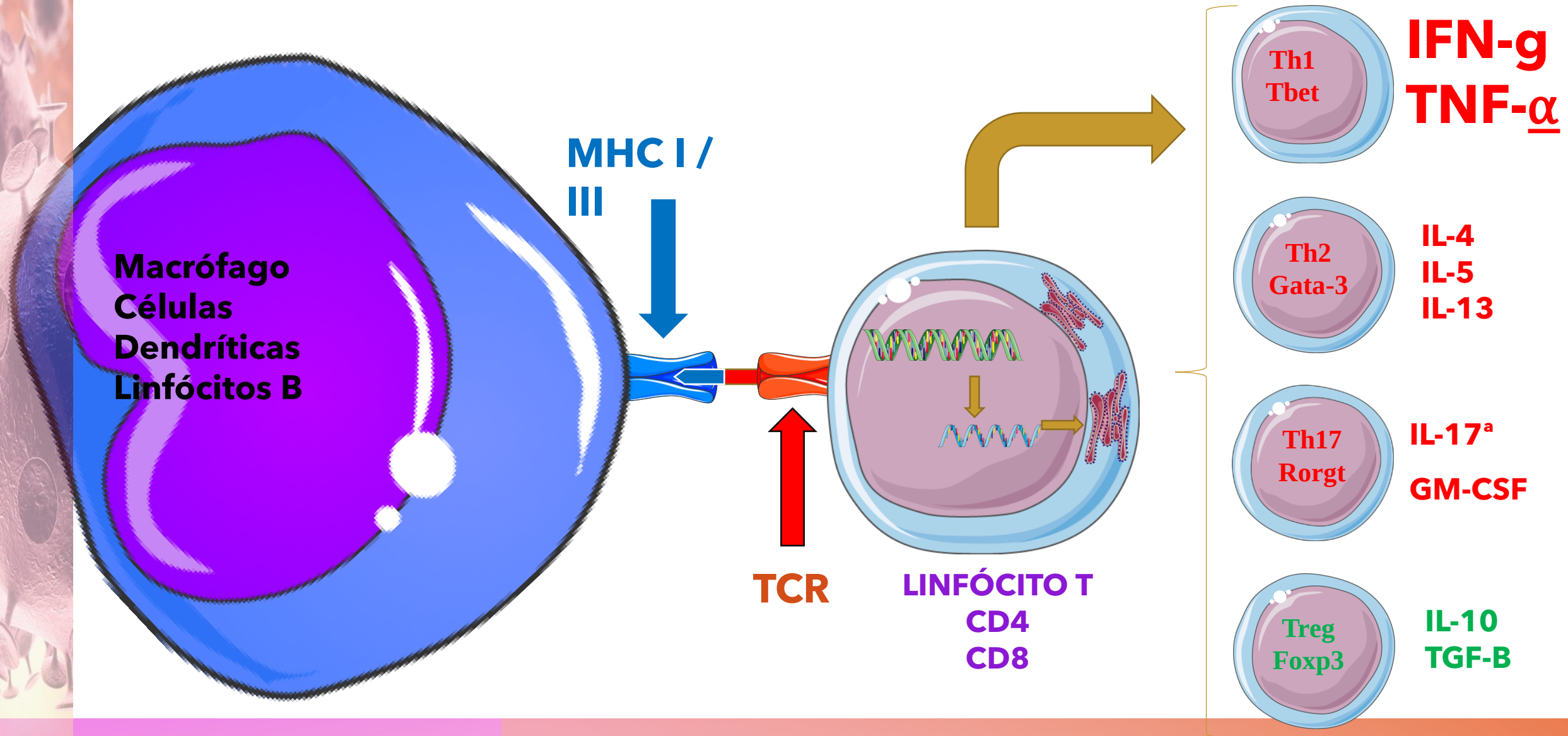
RECONHECIMENTO DE ANTÍGENOS

ATIVAÇÃO DE NF-KB – NF-AT



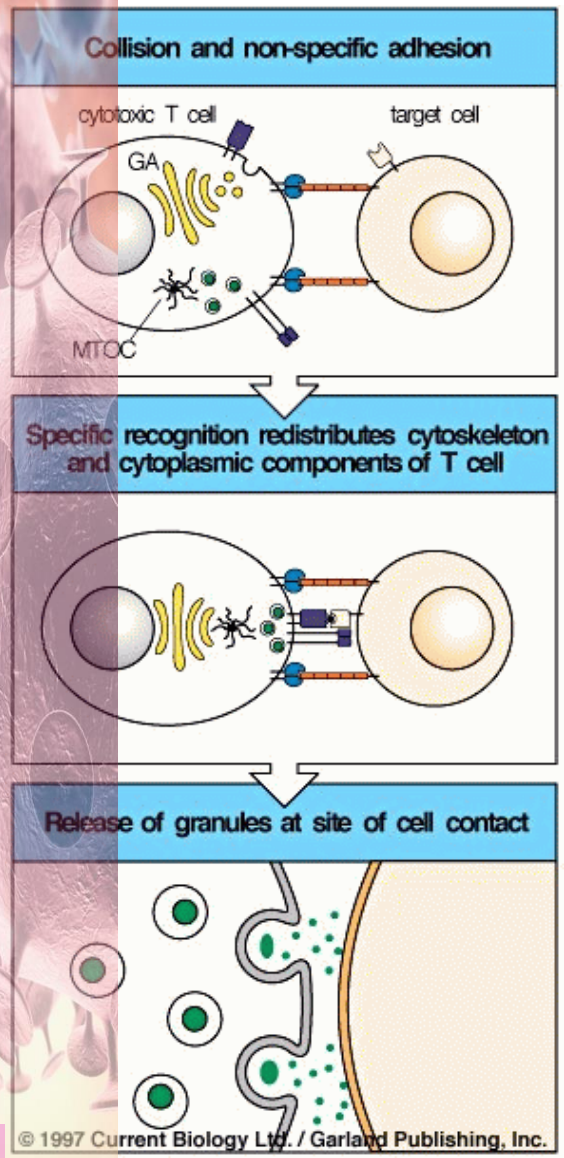
Imunobiologia de Janeway. 8ª Ed.
Abbas A:Imunologia celular e molecular. 8ª Ed.

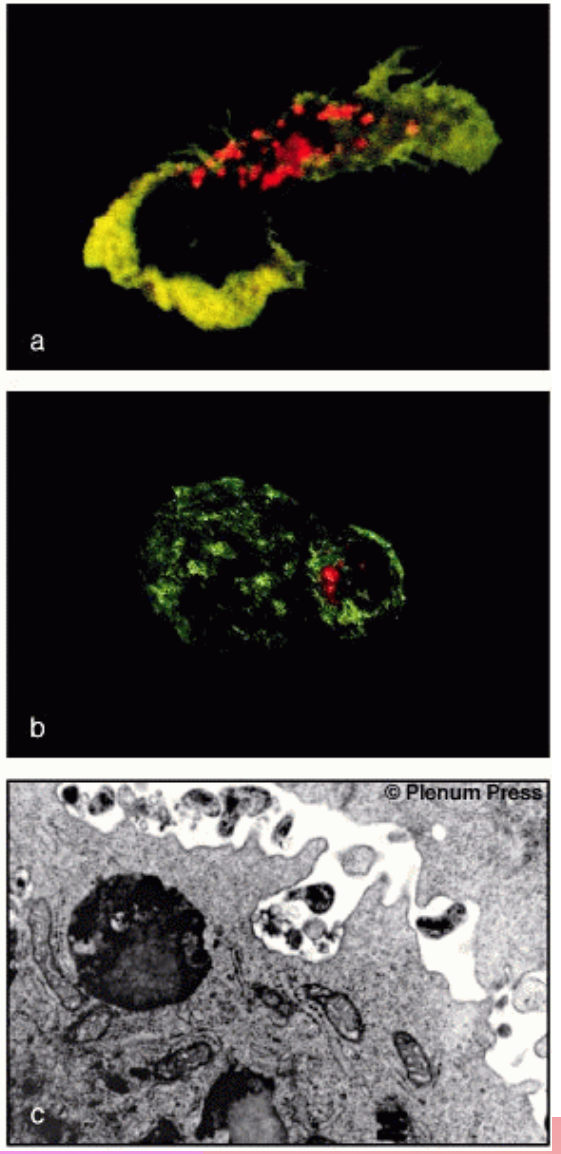
DIFERENCIAÇÃO FUNCIONAL DE LINFÓCITOS T



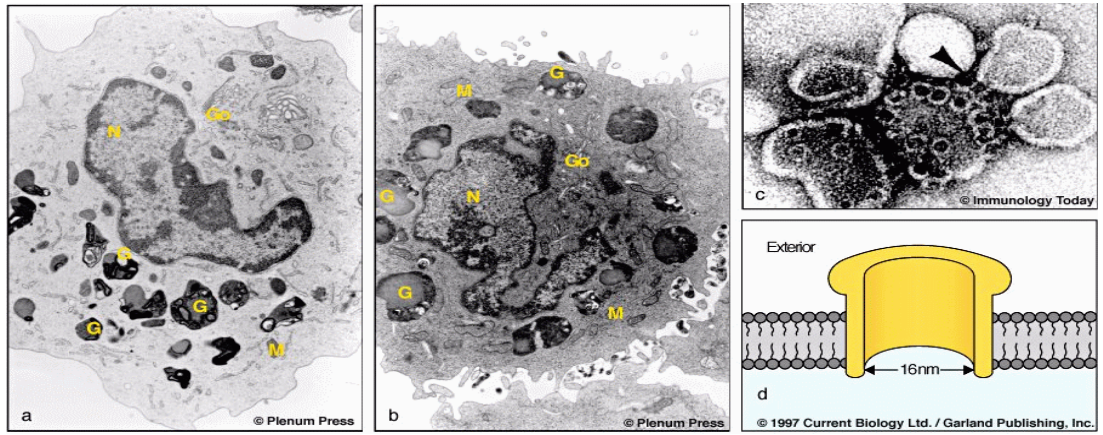
Imunobiologia de Janeway. 8ª Ed.
Abbas A:Imunologia celular e molecular. 8ª Ed.

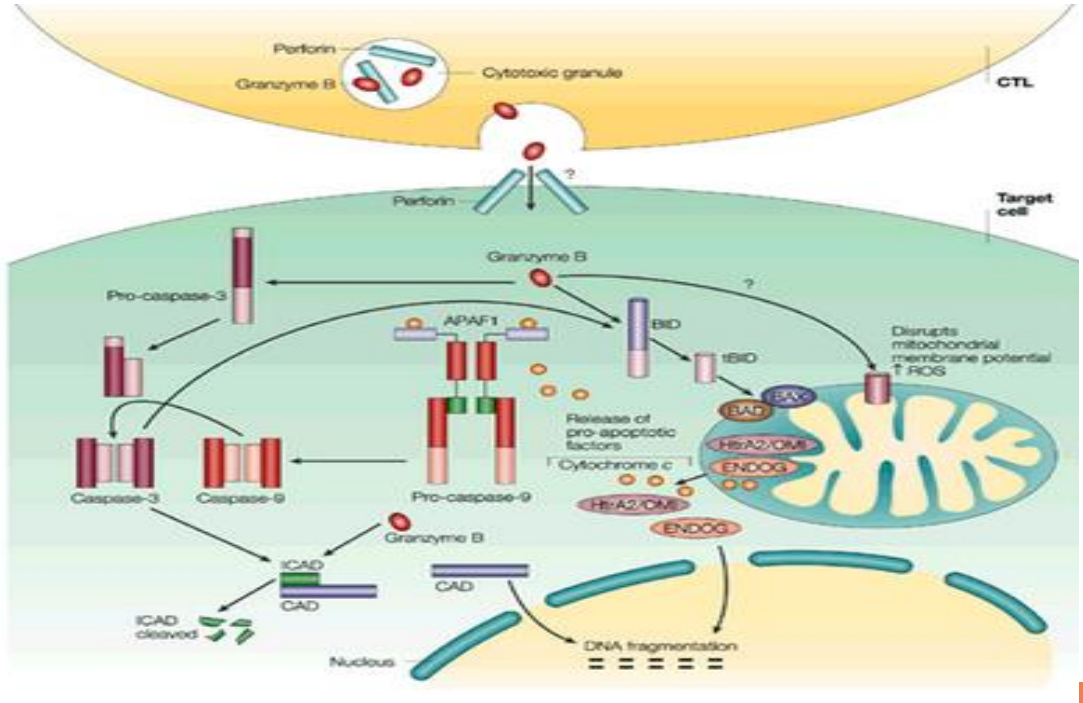
Linfócitos T CD8 - Citotóxicos

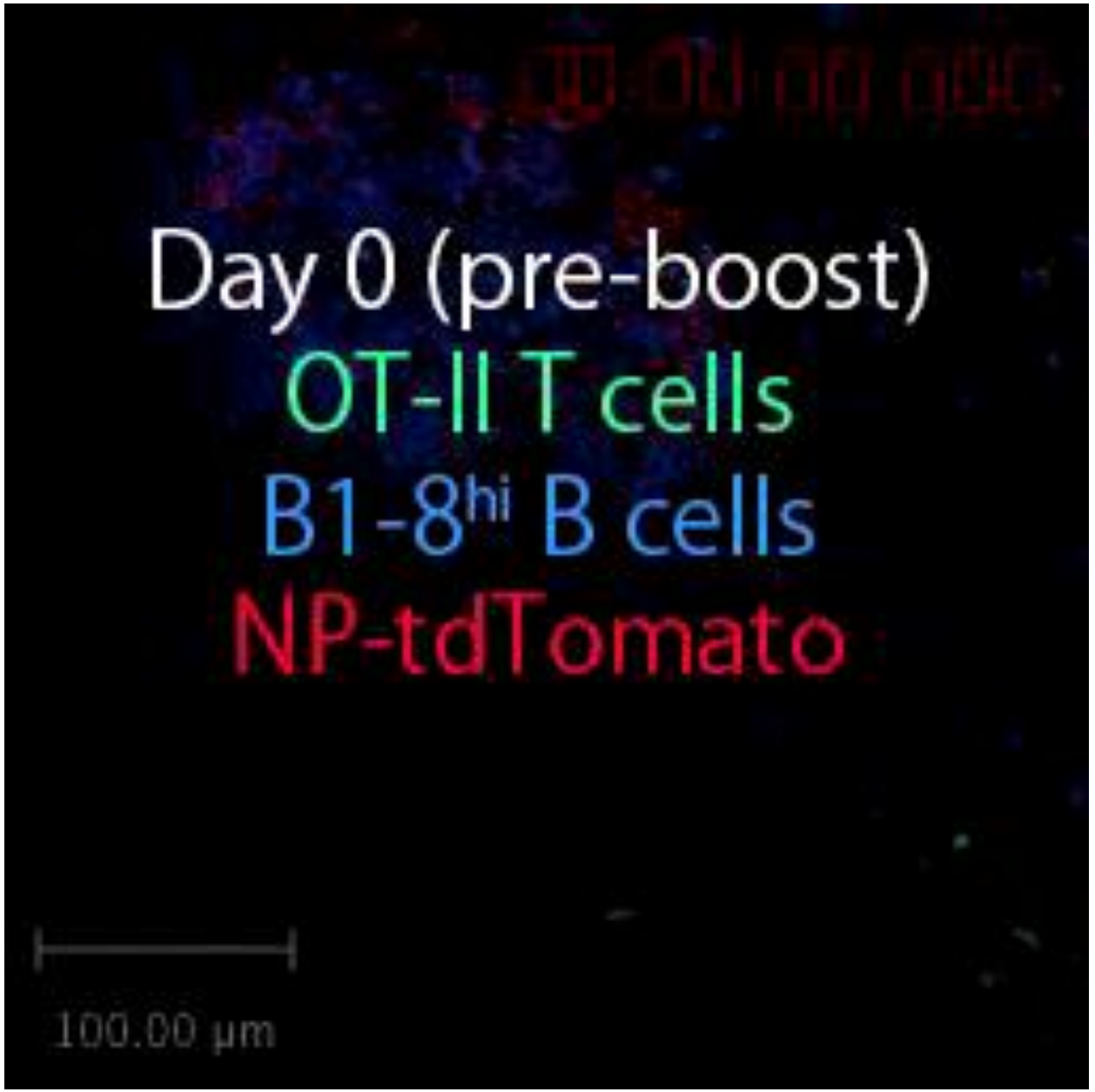




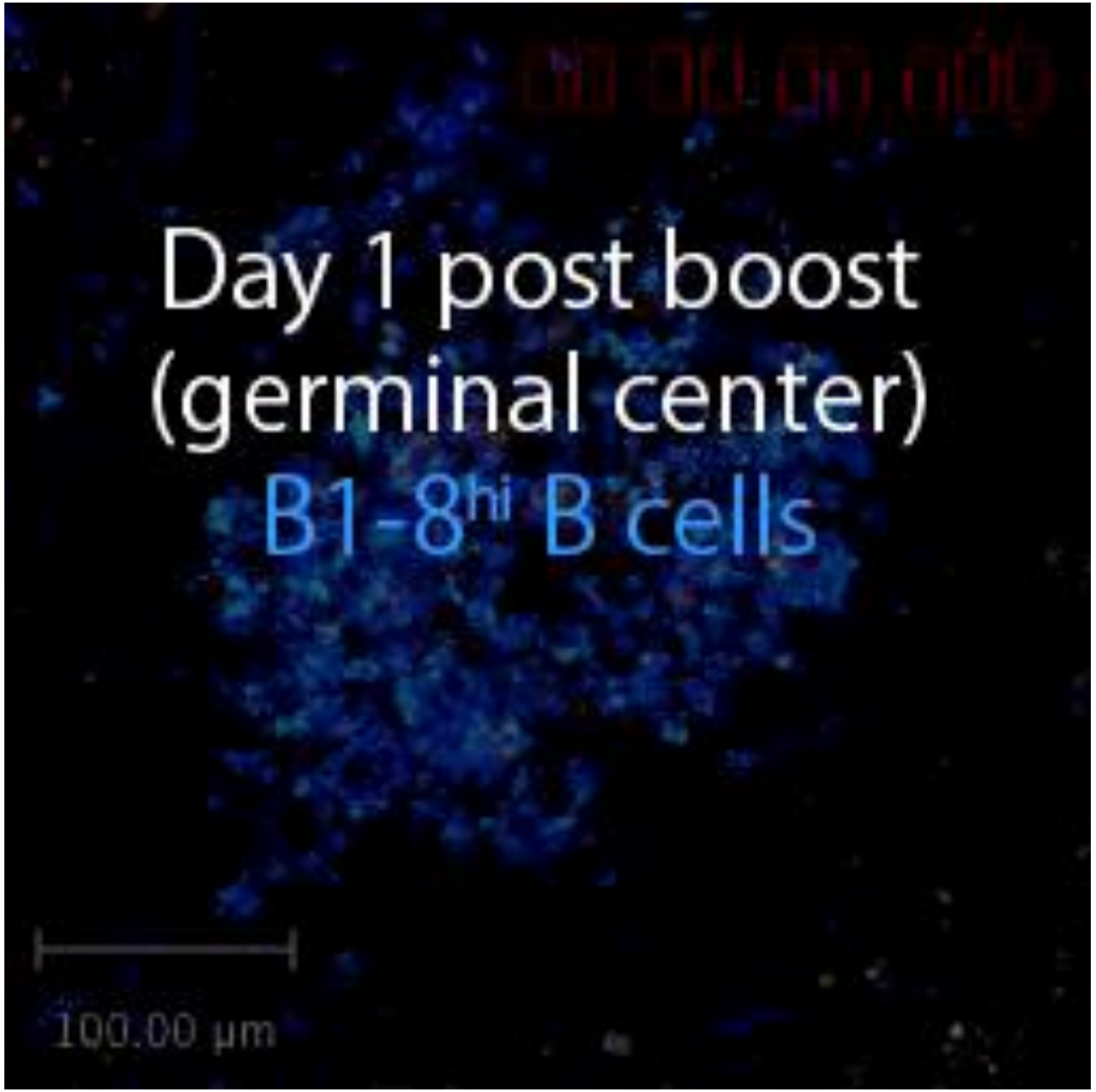
Granzimas e Perforinas



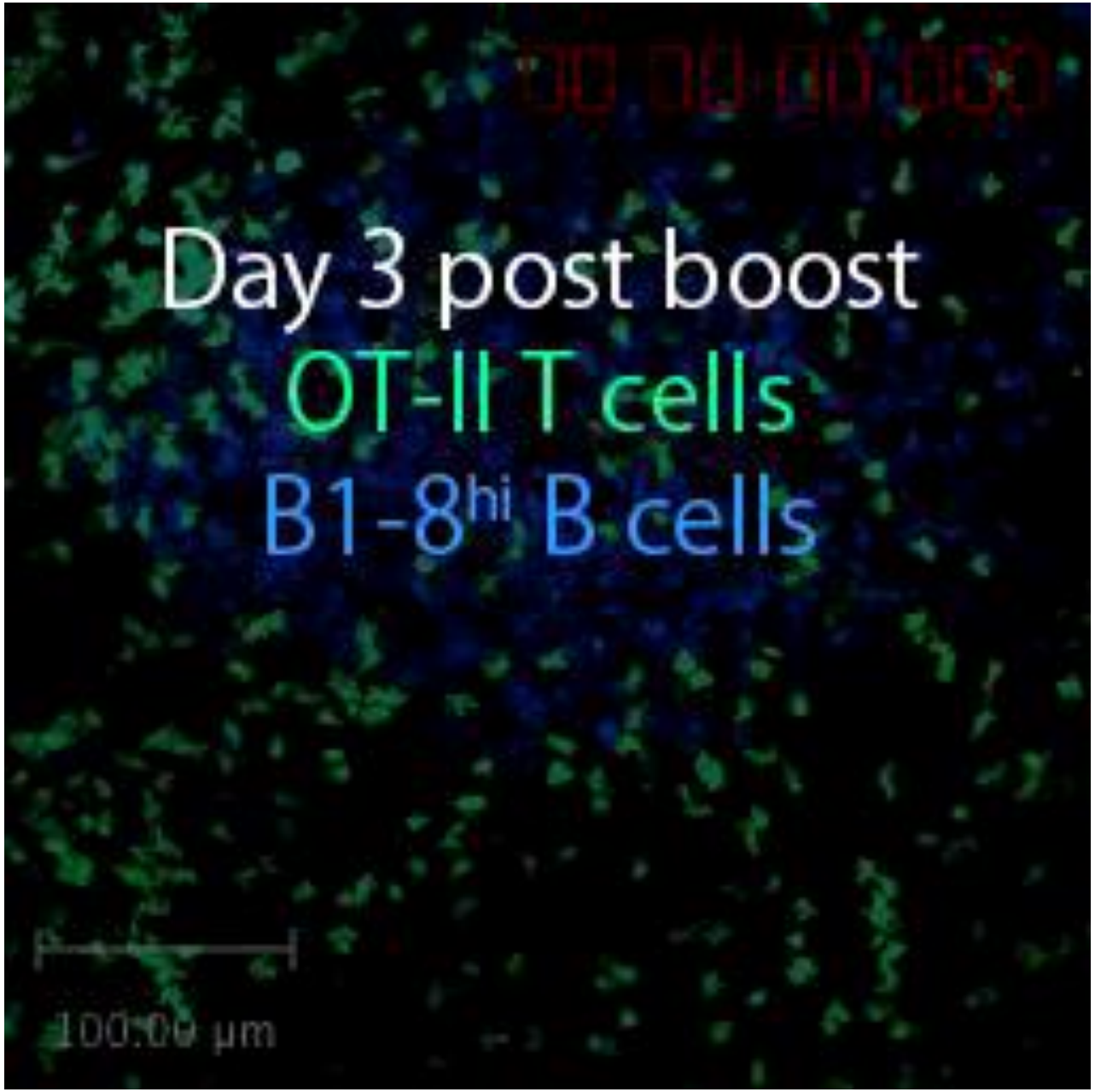




T follicular helper cell dynamics in germinal centers. Shulman Z et al. Science. 2013 Aug 9;341(6146):673-7.

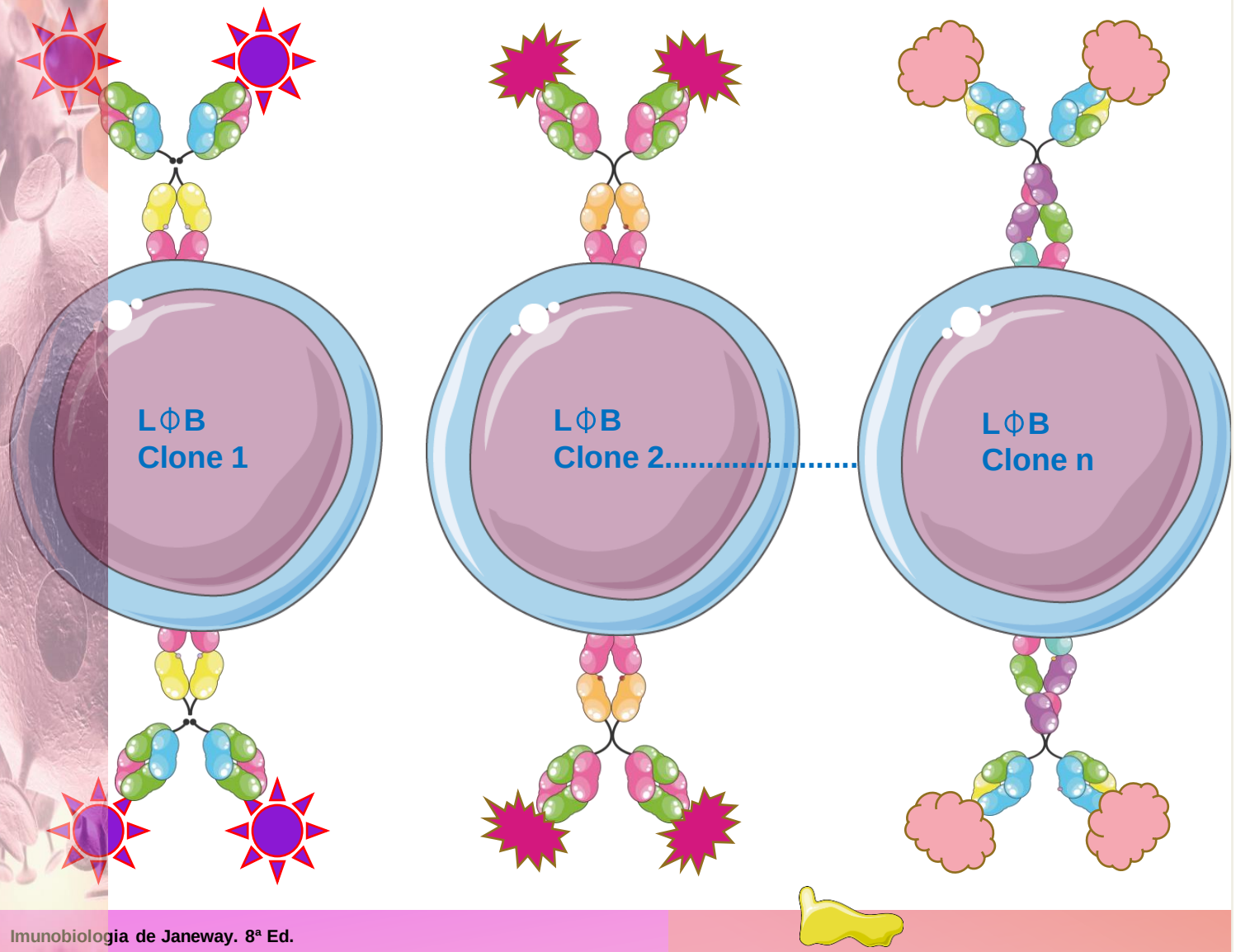


T follicular helper cell dynamics in germinal centers. Shulman Z et al. Science. 2013 Aug 9;341(6146):673-7.



T follicular helper cell dynamics in germinal centers. Shulman Z et al. Science. 2013 Aug 9;341(6146):673-7.

ATIVAÇÃO IMUNIDADE ADAPTATIVA LINFÓCITOS B – ANTÍGENOS SOLÚVEIS DE QUALQUER NATUREZA

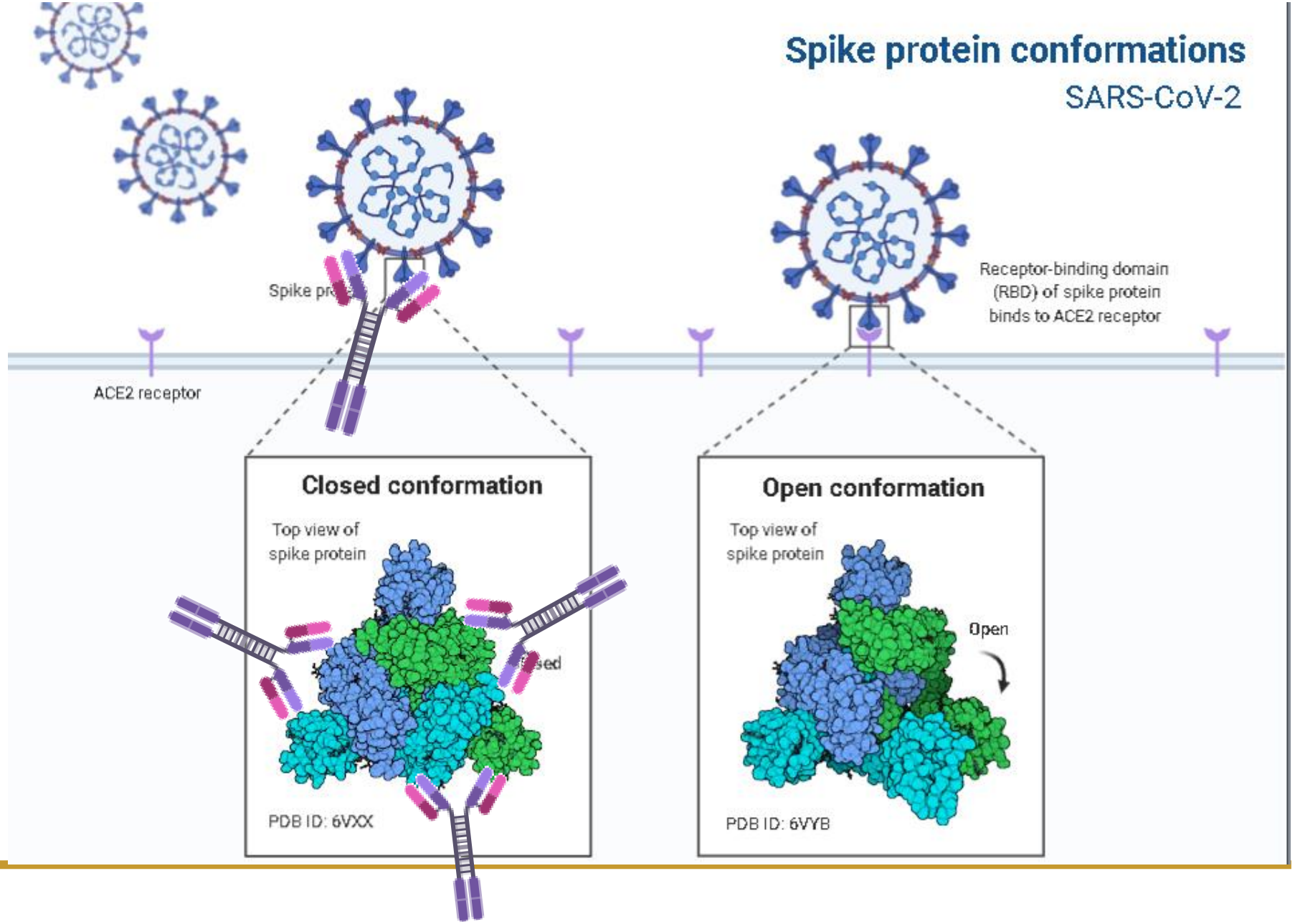


Imunobiologia de Janeway. 8ª Ed.
Abbas A:Imunologia celular e molecular. 8ª Ed.

ANTICORPOS NEUTRALIZANTES

Anti-SPIKE

Evitar a ADESÃO à Superfície da Célula e Invasão Viral



Então...como seria um **resumo** de tudo isso no **PULMÃO**?

Ambiente Pulmonar – Alvéolos

PNEUMÓCITOS E MACRÓFAGOS EXPRESSAM

ACE-2 / TMPRSS2

TLRs
NLRs
MAVS

aço Alveolar
Ar

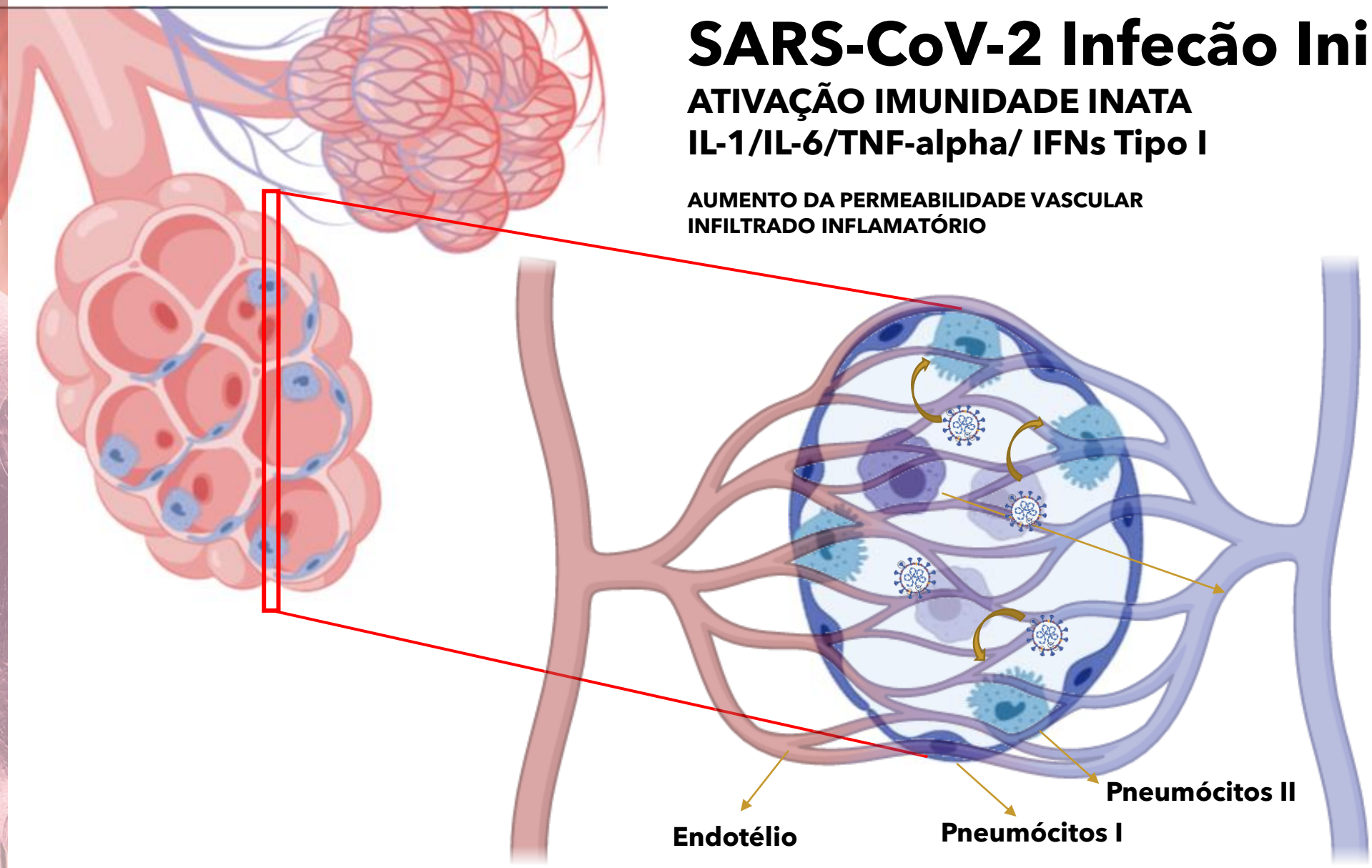
Moléculas
Surfactante
Proteínas

Células
Macrófagos
mócitos I e II
s Endoteliais

SARS-CoV-2 Infecão Inicial

ATIVAÇÃO IMUNIDADE INATA
IL-1/IL-6/TNF-alpha/ IFNs Tipo I

AUMENTO DA PERMEABILIDADE VASCULAR
INFILTRADO INFLAMATÓRIO

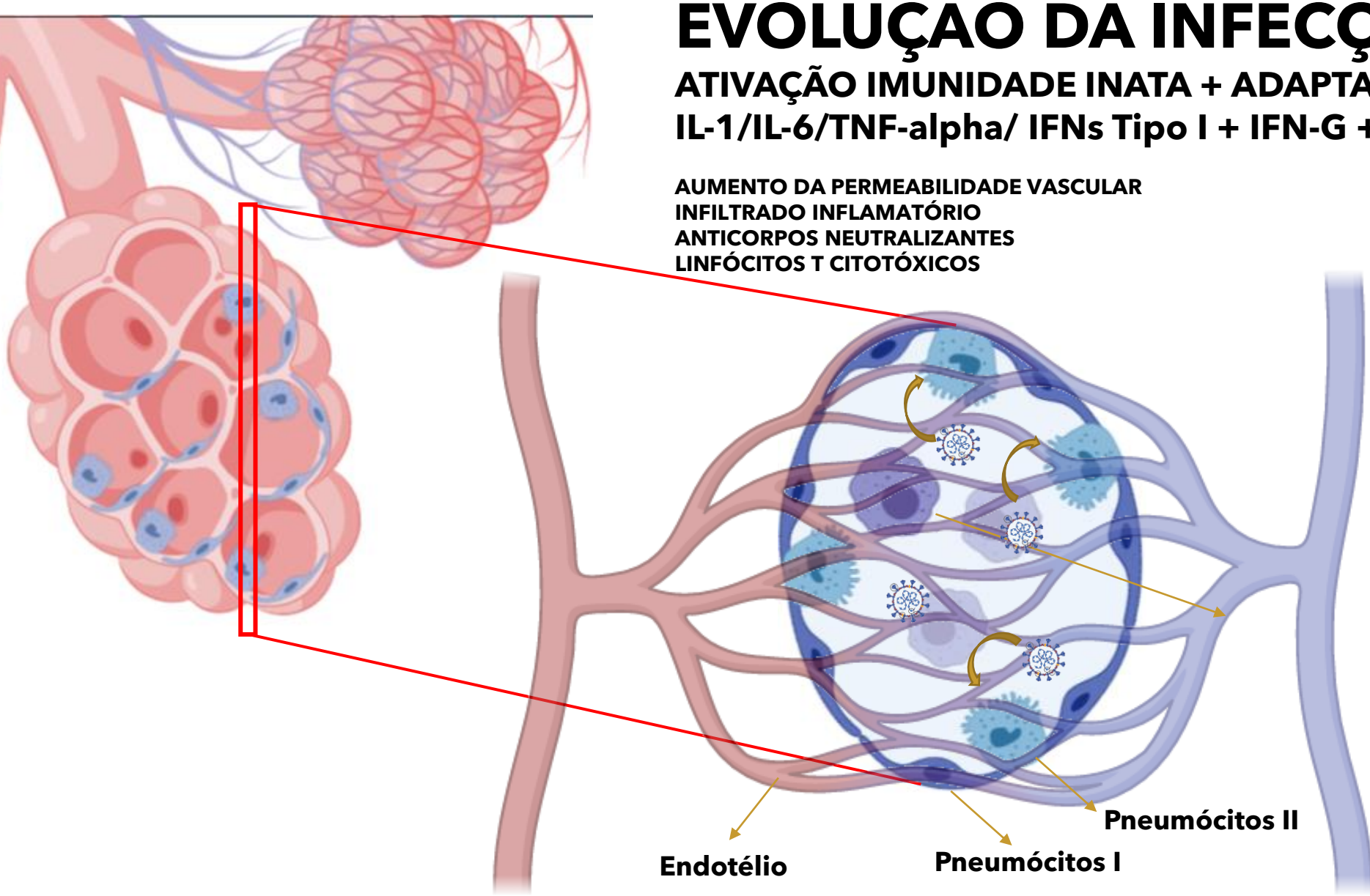


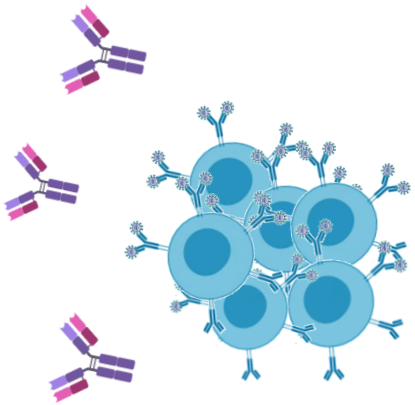
EVOLUÇÃO DA INFECÇÃO

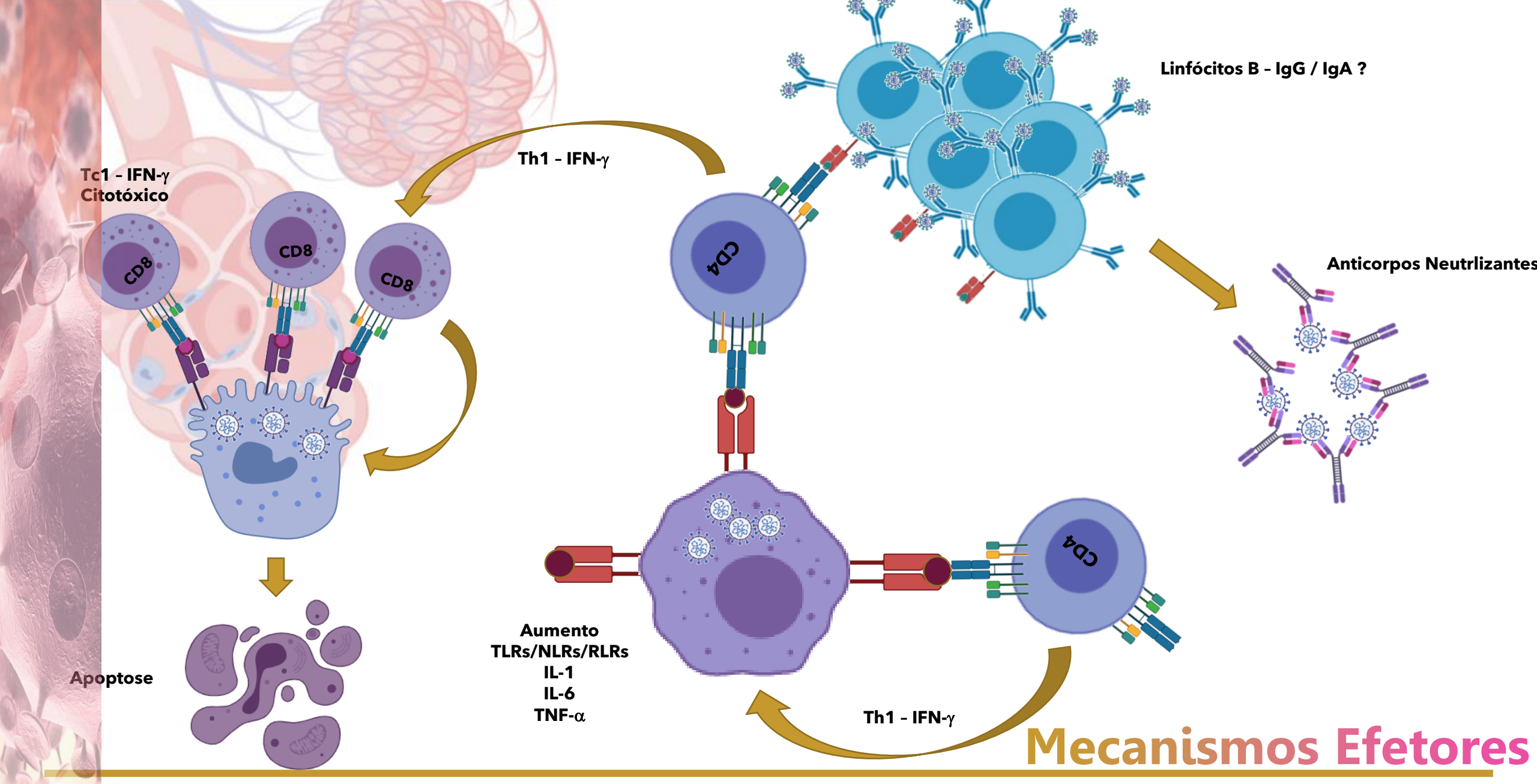
ATIVAÇÃO IMUNIDADE INATA + ADAPTATIVA

IL-1/IL-6/TNF-alpha/ IFNs Tipo I + IFN-G + ANTICORPOS

AUMENTO DA PERMEABILIDADE VASCULAR
INFILTRADO INFLAMATÓRIO
ANTICORPOS NEUTRALIZANTES
LINFÓCITOS T CITOTÓXICOS



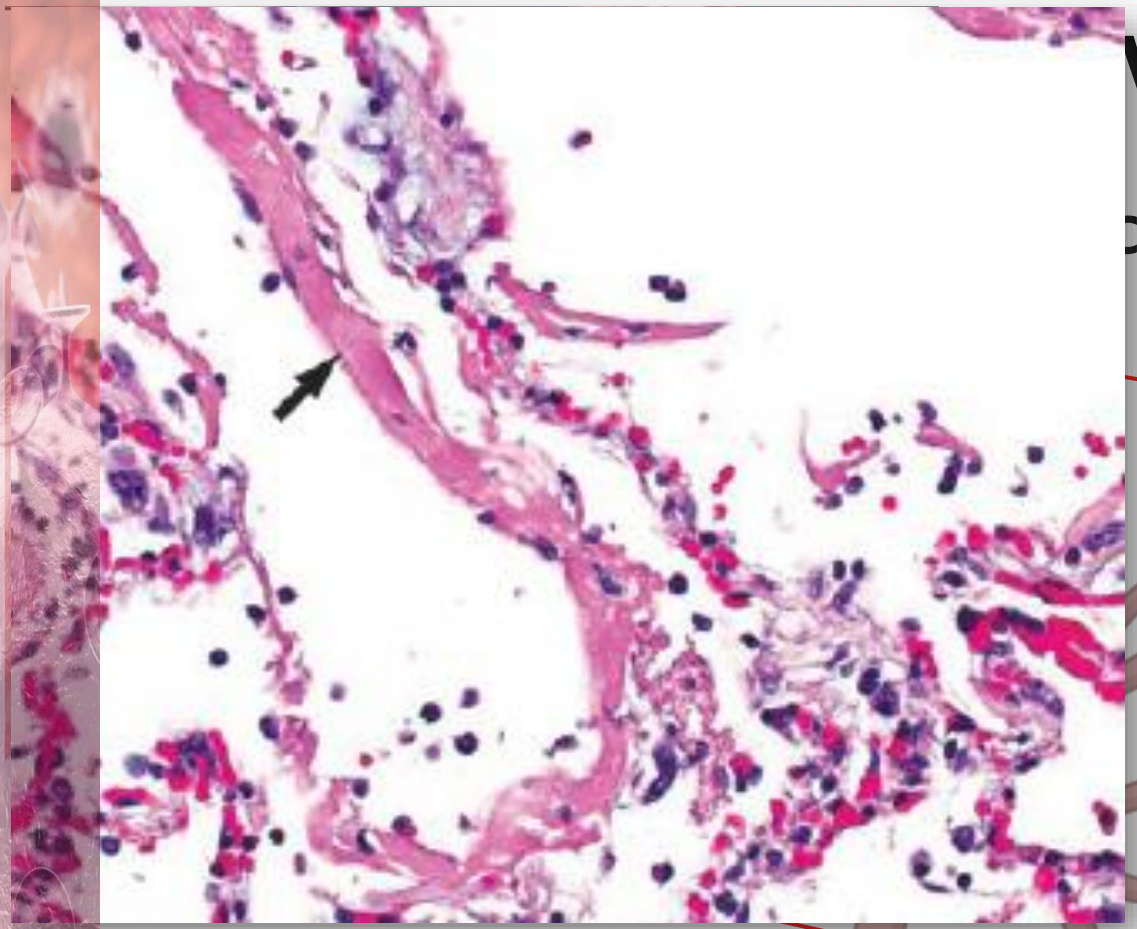


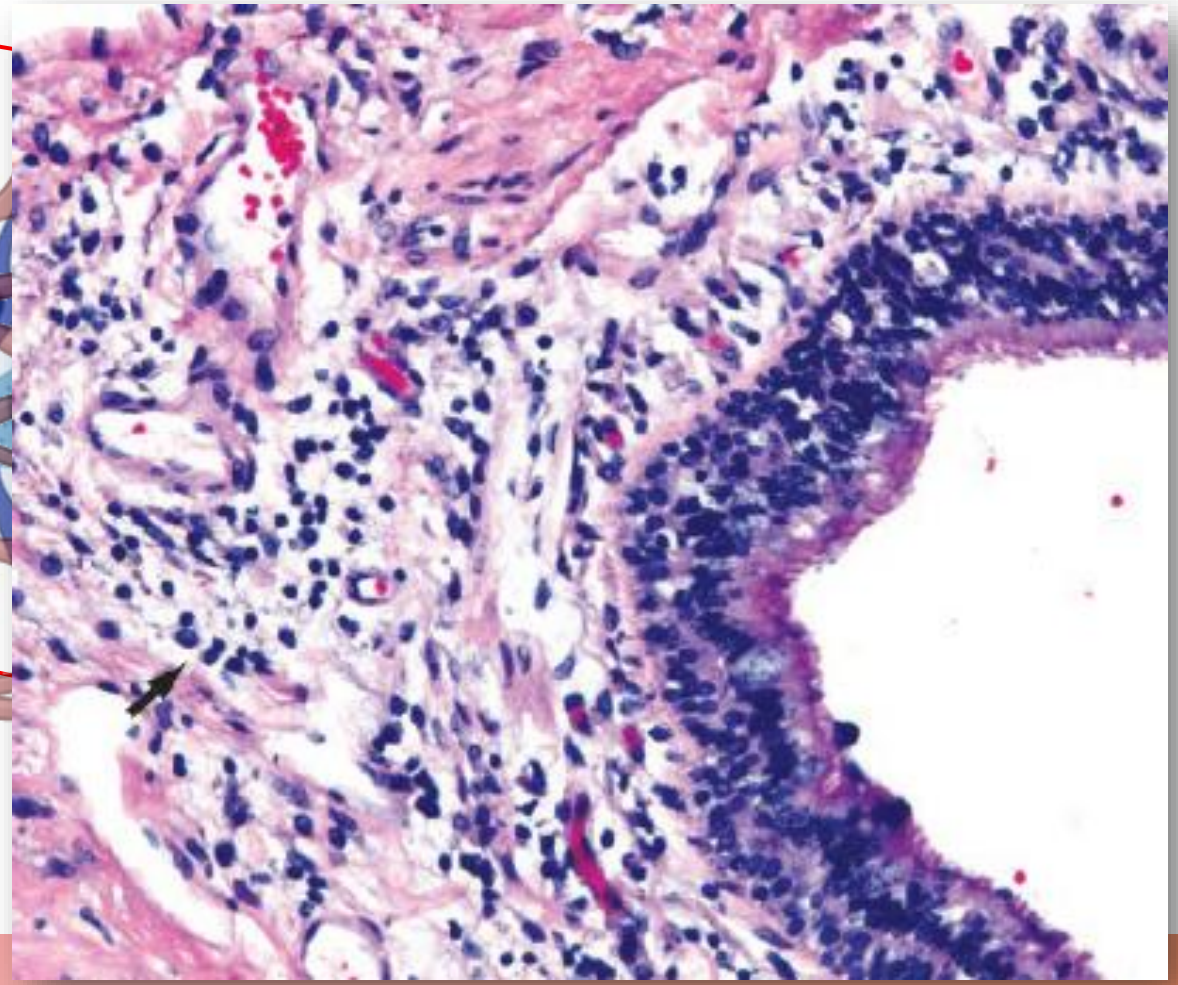


Mecanismos Efetores

VID-19 GRAVE

CERBAÇÃO DA RESPOSTA IMUNE





Endotélio

COVID-19 Autopsies, Oklahoma, USA

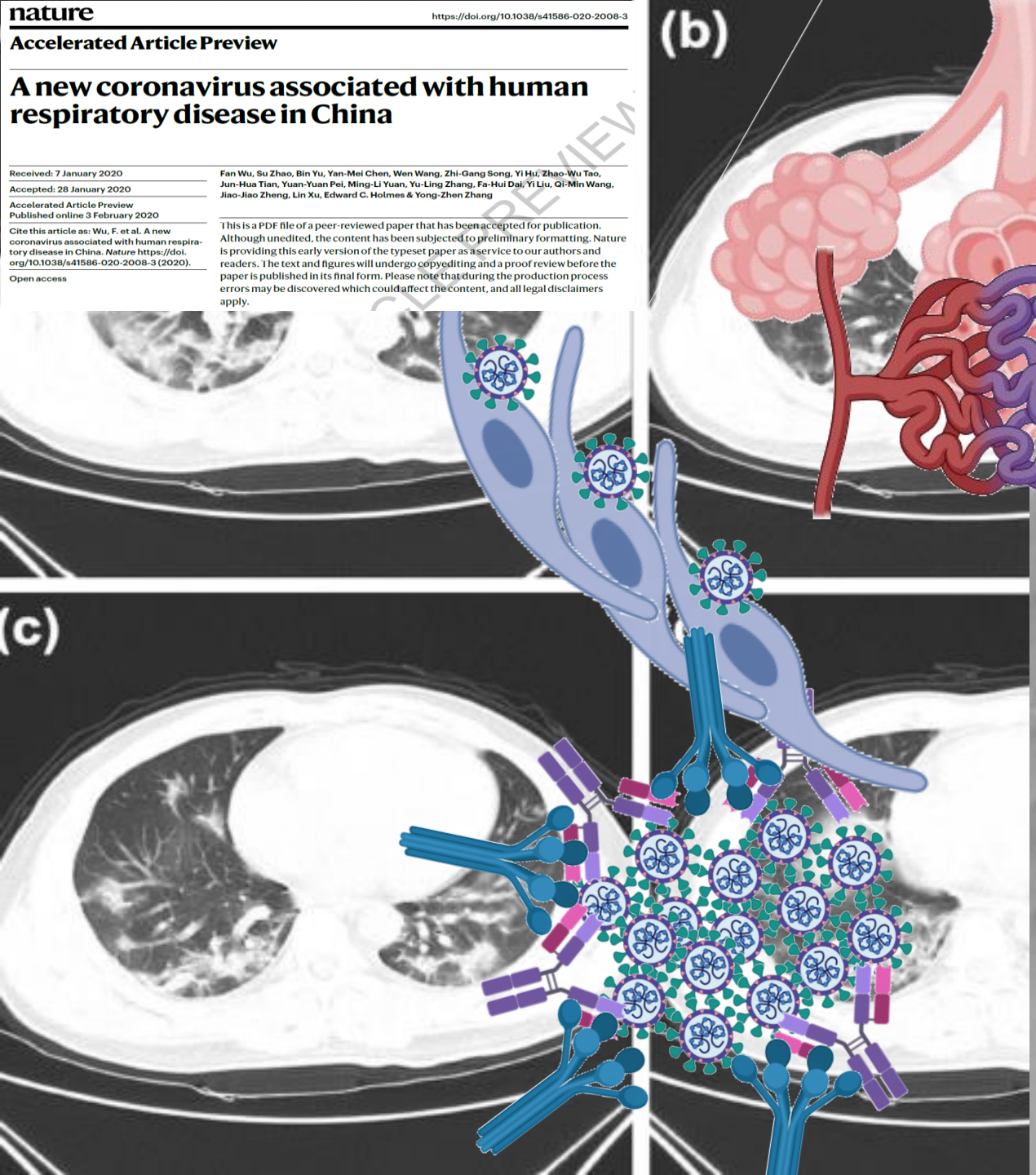
Lisa M. Barton, MD, PhD,[1] Eric J. Duval, DO,[1] Edana Stroberg, DO,[1] Subha Ghosh, MD,[2] and Sanjay Mukhopadhyay, MD[2,]*

nature
https://doi.org/10.1038/s41586-020-2008-3
Accelerated Article Preview

A new coronavirus associated with human respiratory disease in China

Received: 7 January 2020
Accepted: 28 January 2020
Accelerated Article Preview
Published online 3 February 2020
Cite this article as: Wu, F. et al. A new coronavirus associated with human respiratory disease in China. *Nature* https://doi.org/10.1038/s41586-020-2008-3 (2020).
Open access

Fan Wu, Su Zhao, Bin Yu, Yan-Mei Chen, Wen Wang, Zhi-Gang Song, Yi Hu, Zhao-Wu Tao, Jun-Hua Tian, Yuan-Yuan Pei, Ming-Li Yuan, Yu-Ling Zhang, Fa-Hui Dai, Yi Liu, Qi-Min Wang, Jiao-Jiao Zheng, Lin Xu, Edward C. Holmes & Yong-Zhen Zhang

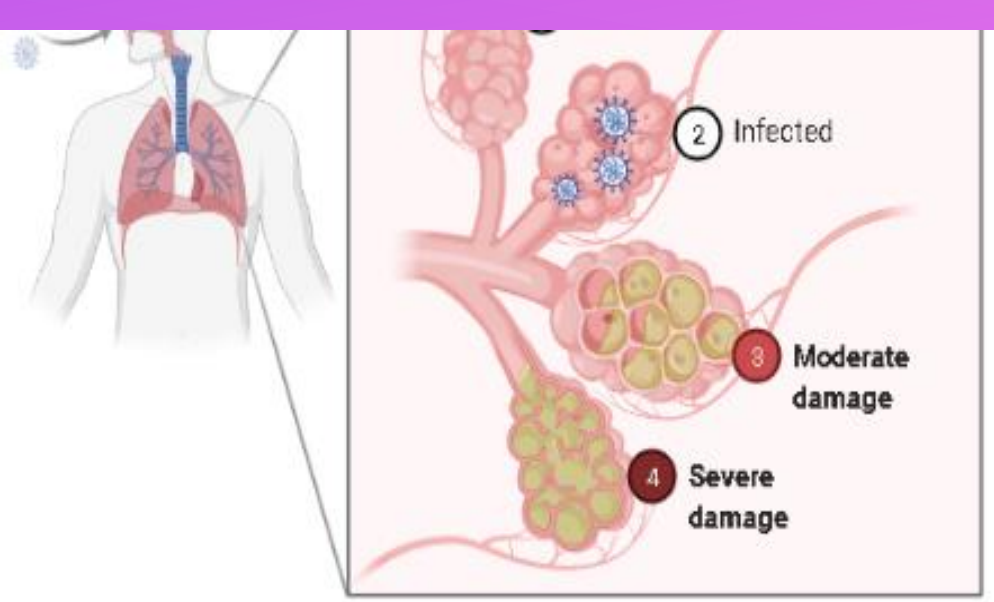


Cytokine Storm
IL-1
IL-6
TNF-a

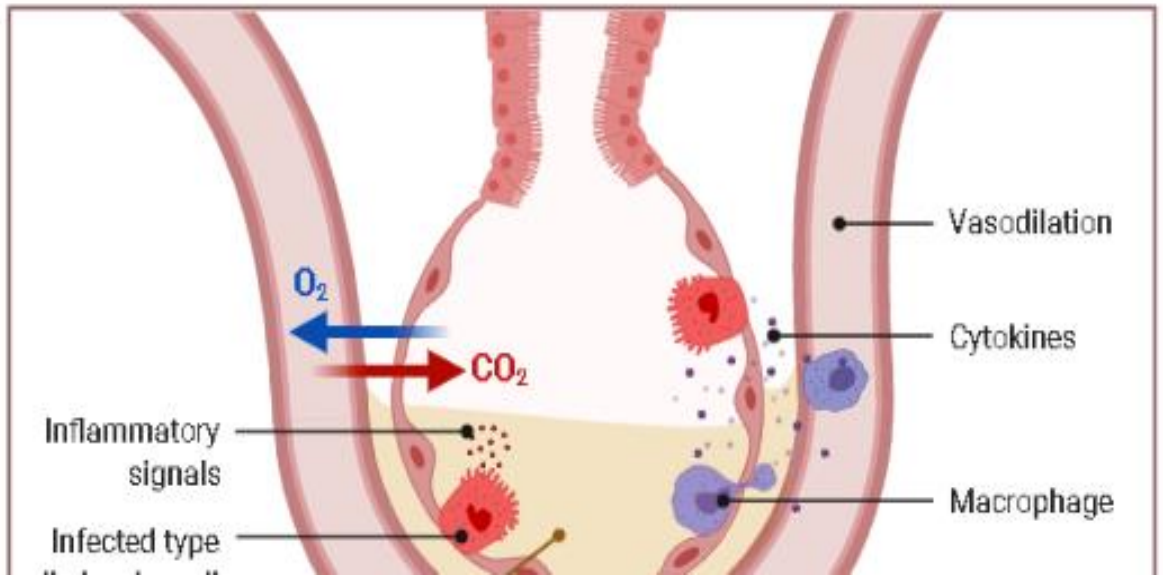
Imunocomplexo?
Complemento

Microtrombos

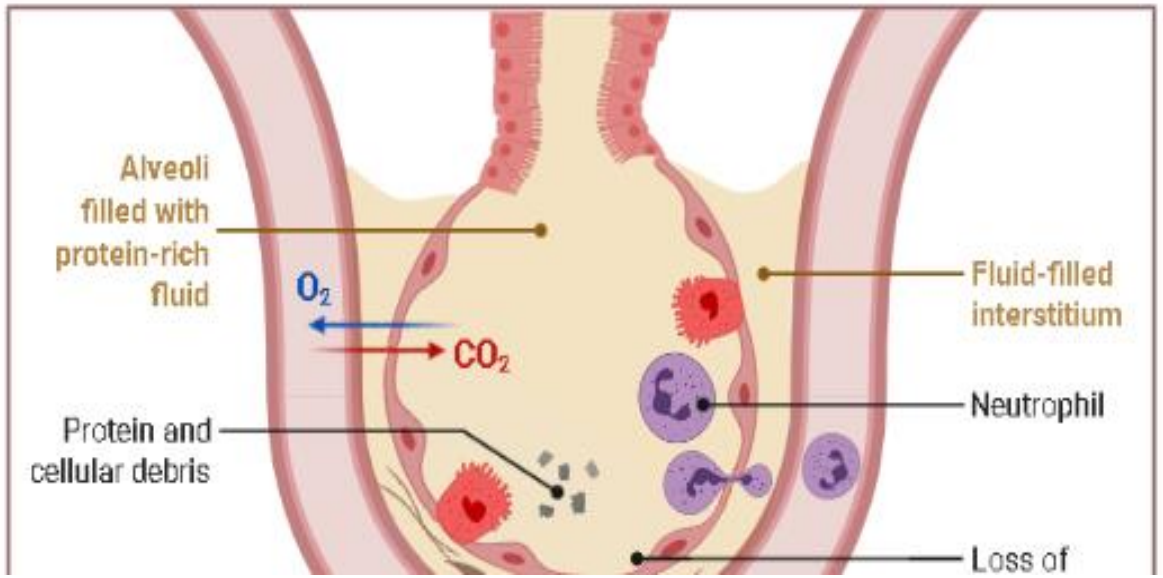
Effects of SARS-CoV-2 on respiration



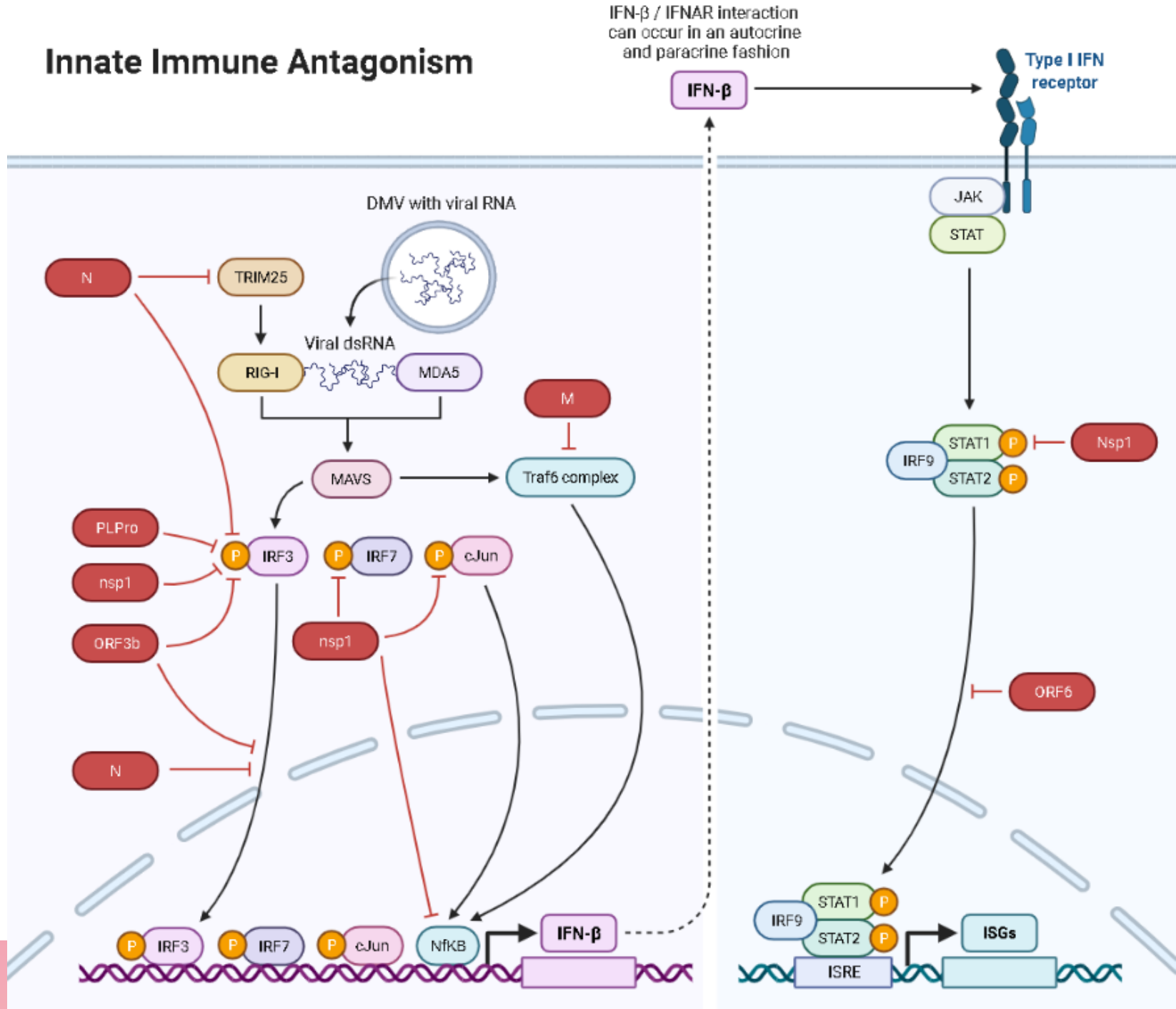
3 Moderate damage: Accumulating fluid, reduced gas exchange



4 Severe damage: Build up of protein-rich fluid, very limited gas exchang



Como o SARS-CoV2 Escapa Do Sistema Imune ?



De onde ele tirou ISSO ?

ARTIGOS INTERESSANTES

nature medicine

BRIEF COMMUNICATION

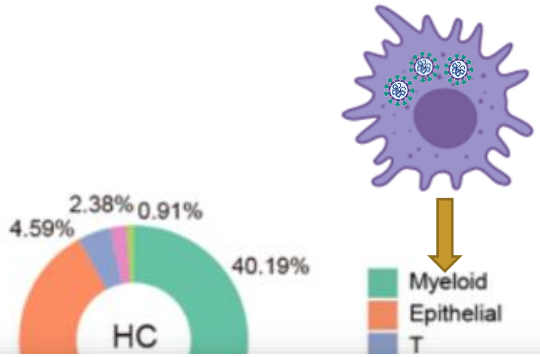
https://doi.org/10.1038/s41591-020-0901-9

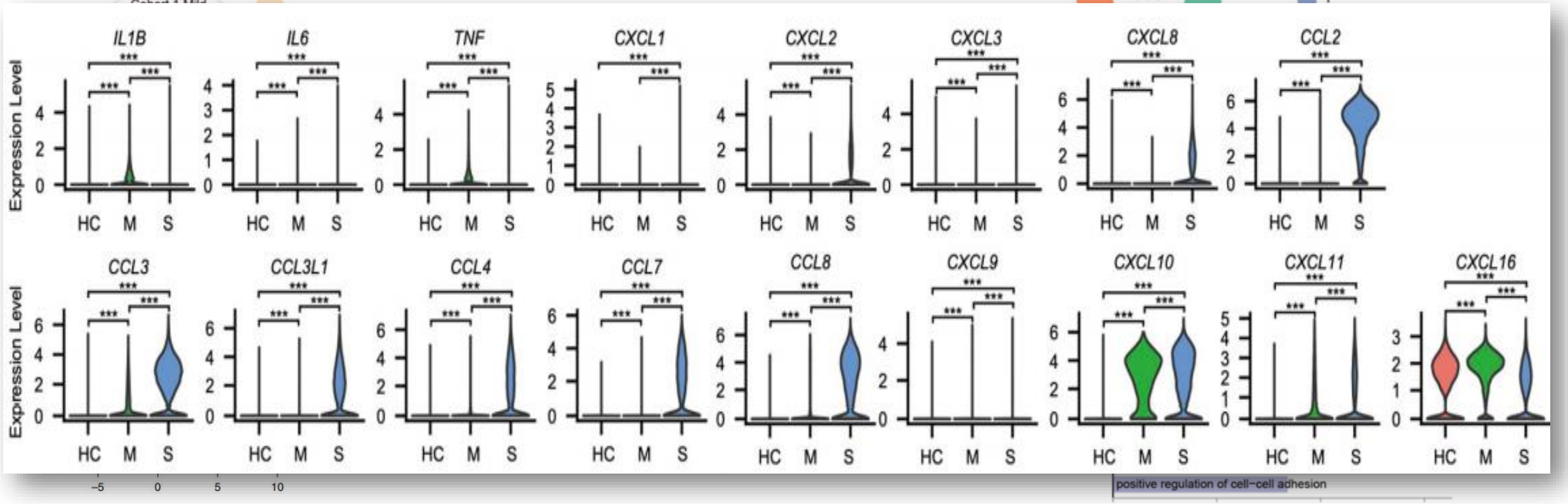
Check for updates

Single-cell landscape of bronchoalveolar immune cells in patients with COVID-19

Mingfeng Liao[1,6], Yang Liu[1,6], Jing Yuan[2,6], Yanling Wen[1], Gang Xu[1], Juanjuan Zhao[1], Lin Cheng[1], Jinxiu Li[2], Xin Wang[1], Fuxiang Wang[2], Lei Liu[1,3]✉, Ido Amit[4]✉, Shuye Zhang[5]✉ and Zheng Zhang[1,3]✉

3 Clusters de Macrófagos



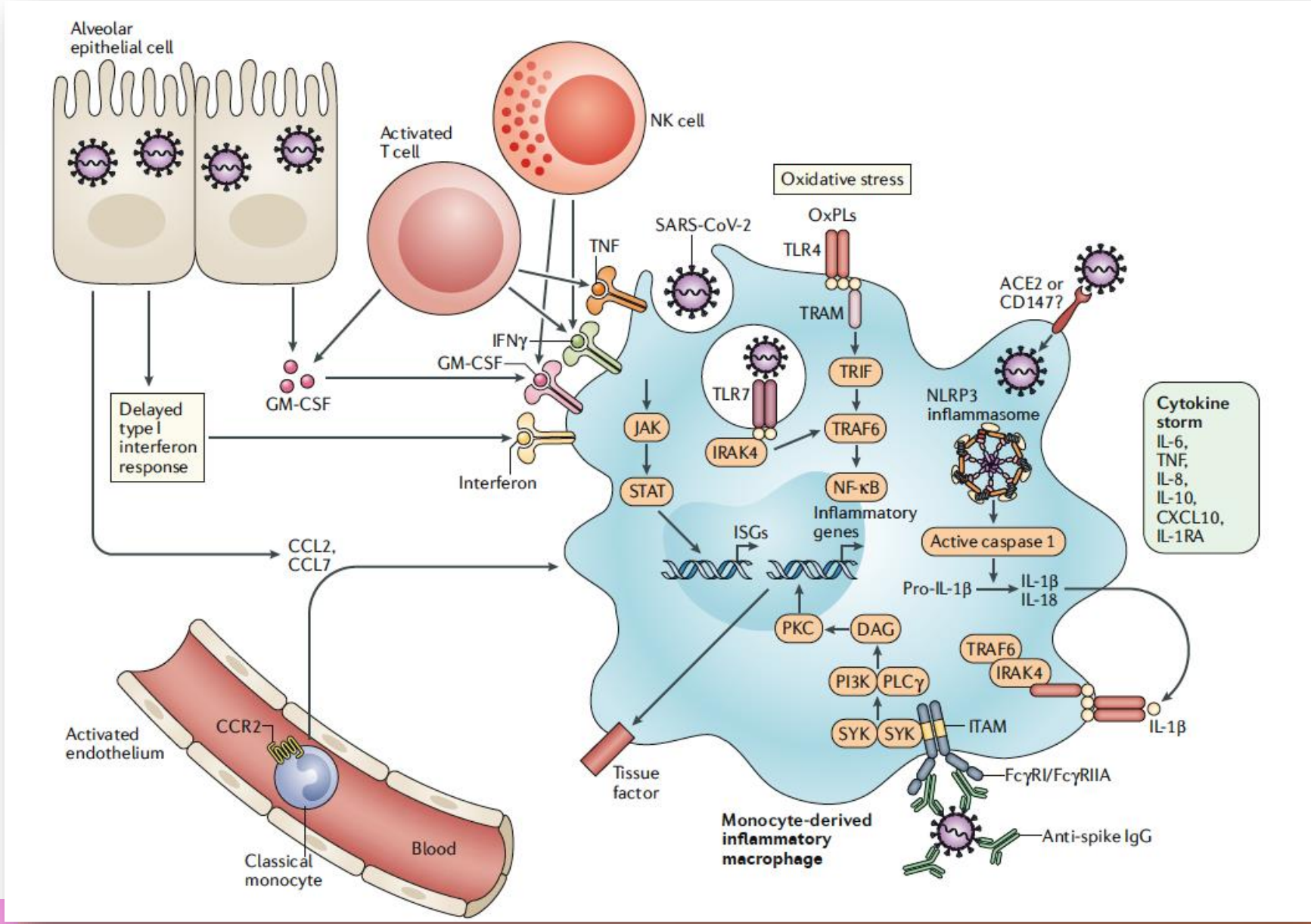


Resposta Imune Efetora
Proteção - Cura

Resposta Imune Exacerbada ou Deficiente
Imunopatologia

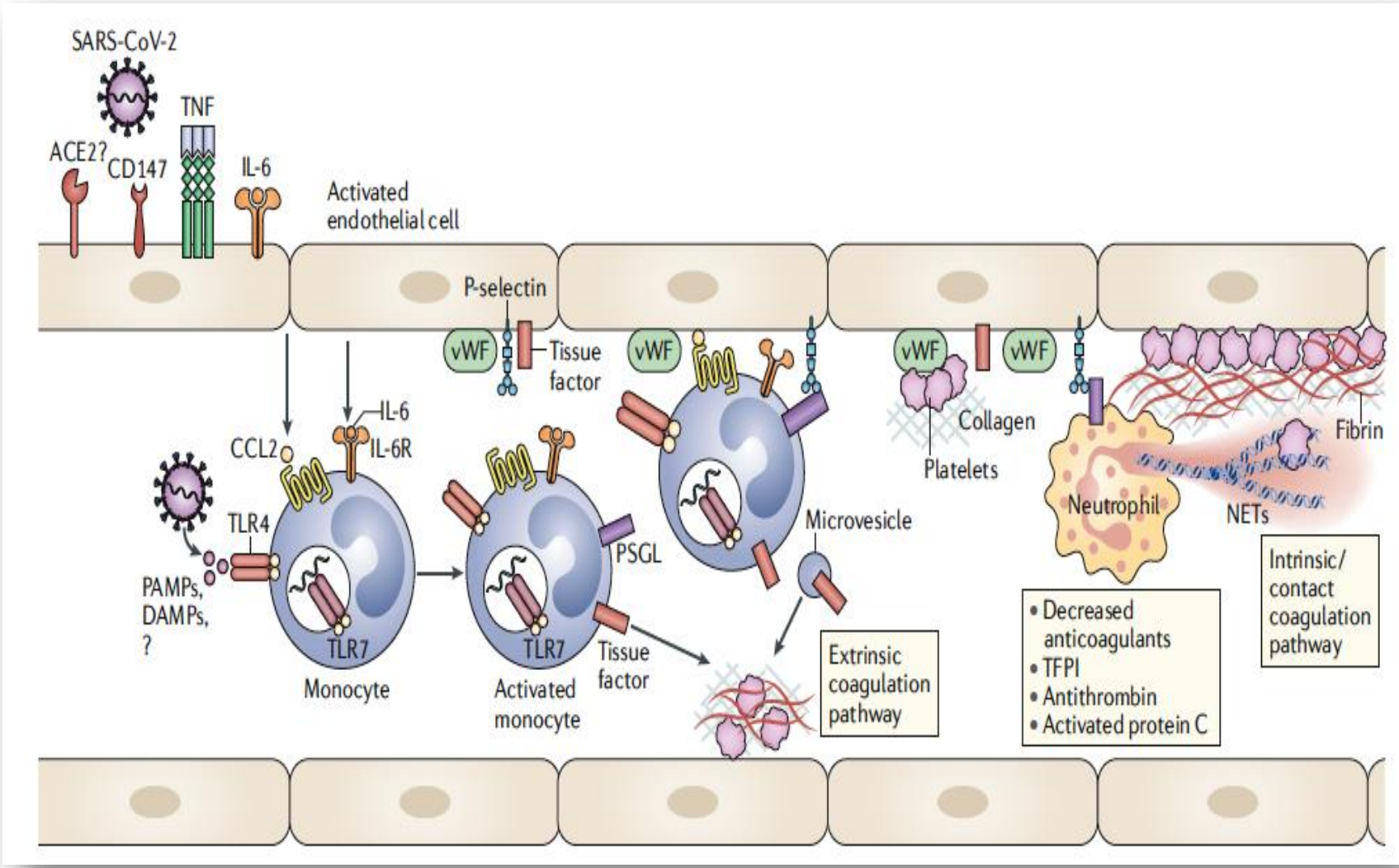
Pathological inflammation in patients with COVID-19: a key role for monocytes and macrophages

Miriam Merad and Jerome C. Martin



Pathological inflammation in patients with COVID-19: a key role for monocytes and macrophages

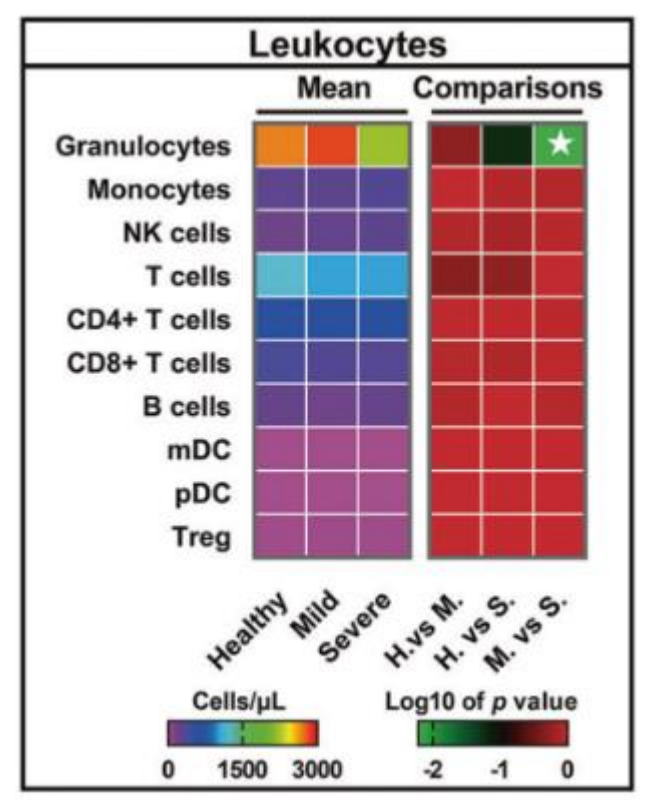
Miriam Merad and Jerome C. Martin



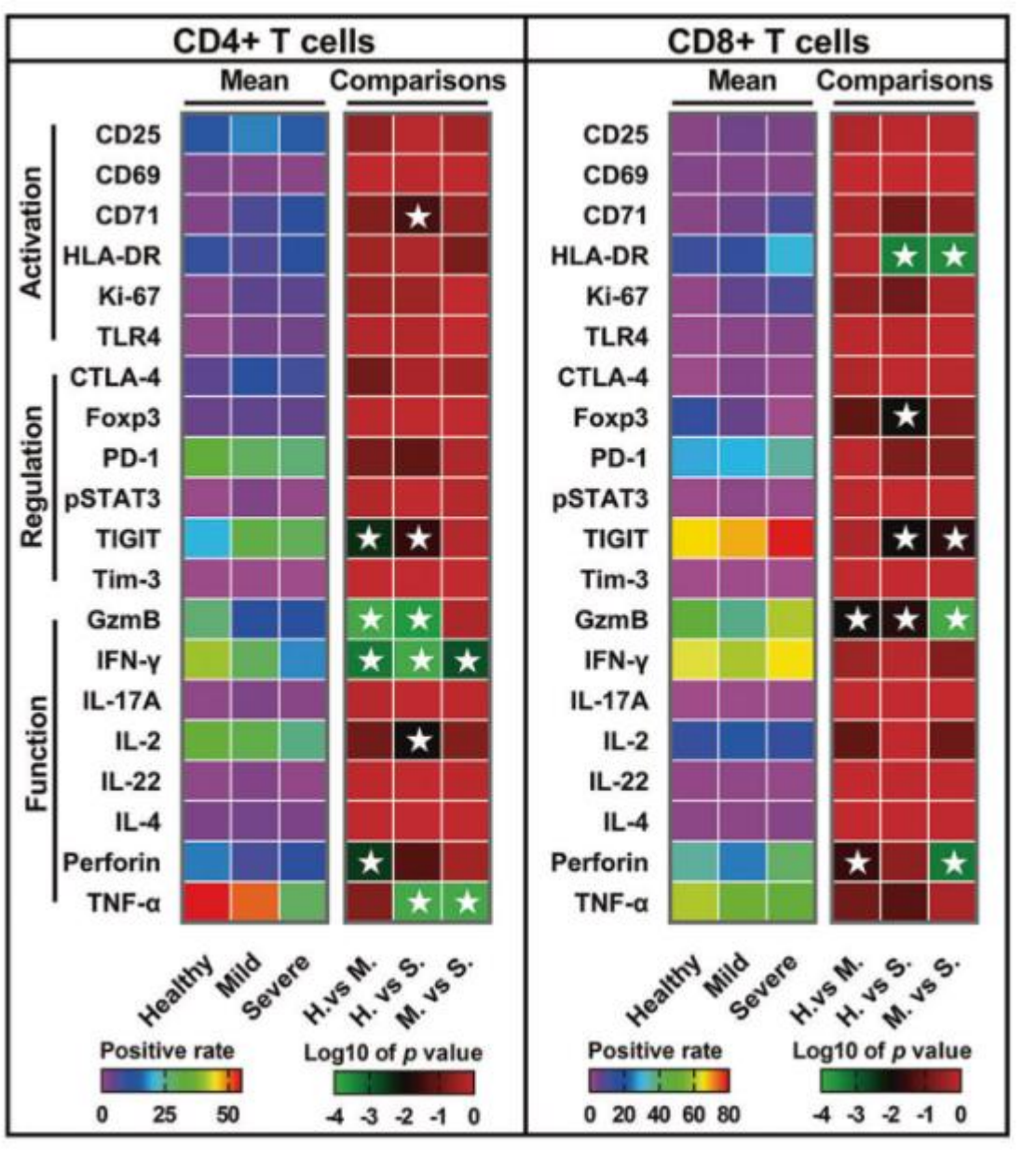
CORRESPONDENCE

Elevated exhaustion levels and reduced functional diversity of T cells in peripheral blood may predict severe progression in COVID-19 patients

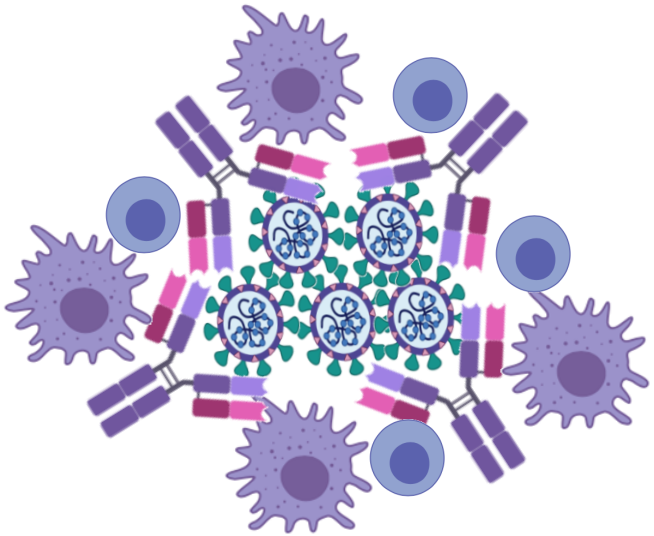
Hong-Yi Zheng[1], Mi Zhang[2], Cui-Xian Yang[2], Nian Zhang[2], Xi-Cheng Wang[2], Xin-Ping Yang[2], Xing-Qi Dong[2] and Yong-Tang Zheng[1]

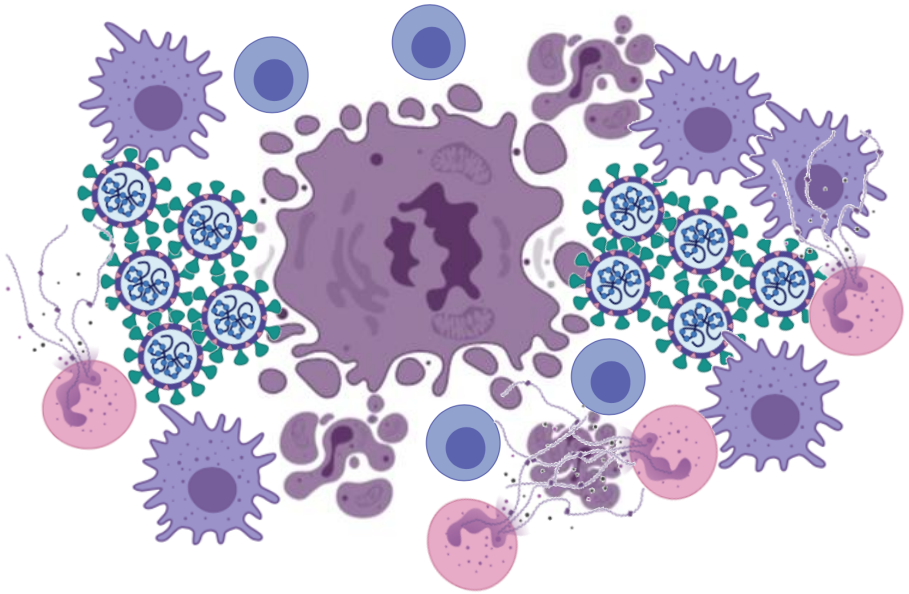


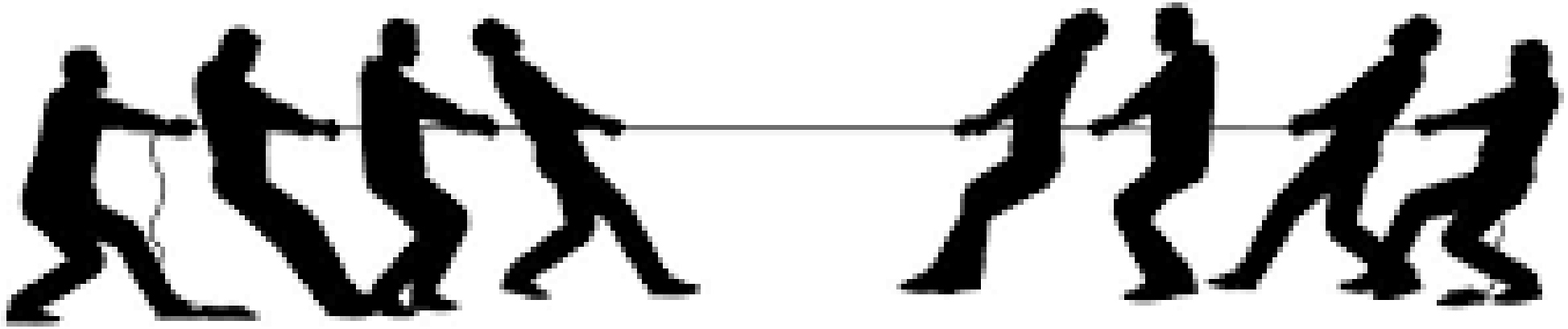
Restrição de Repertório ???



Aumento de Populações - Redução da diversidade funcional







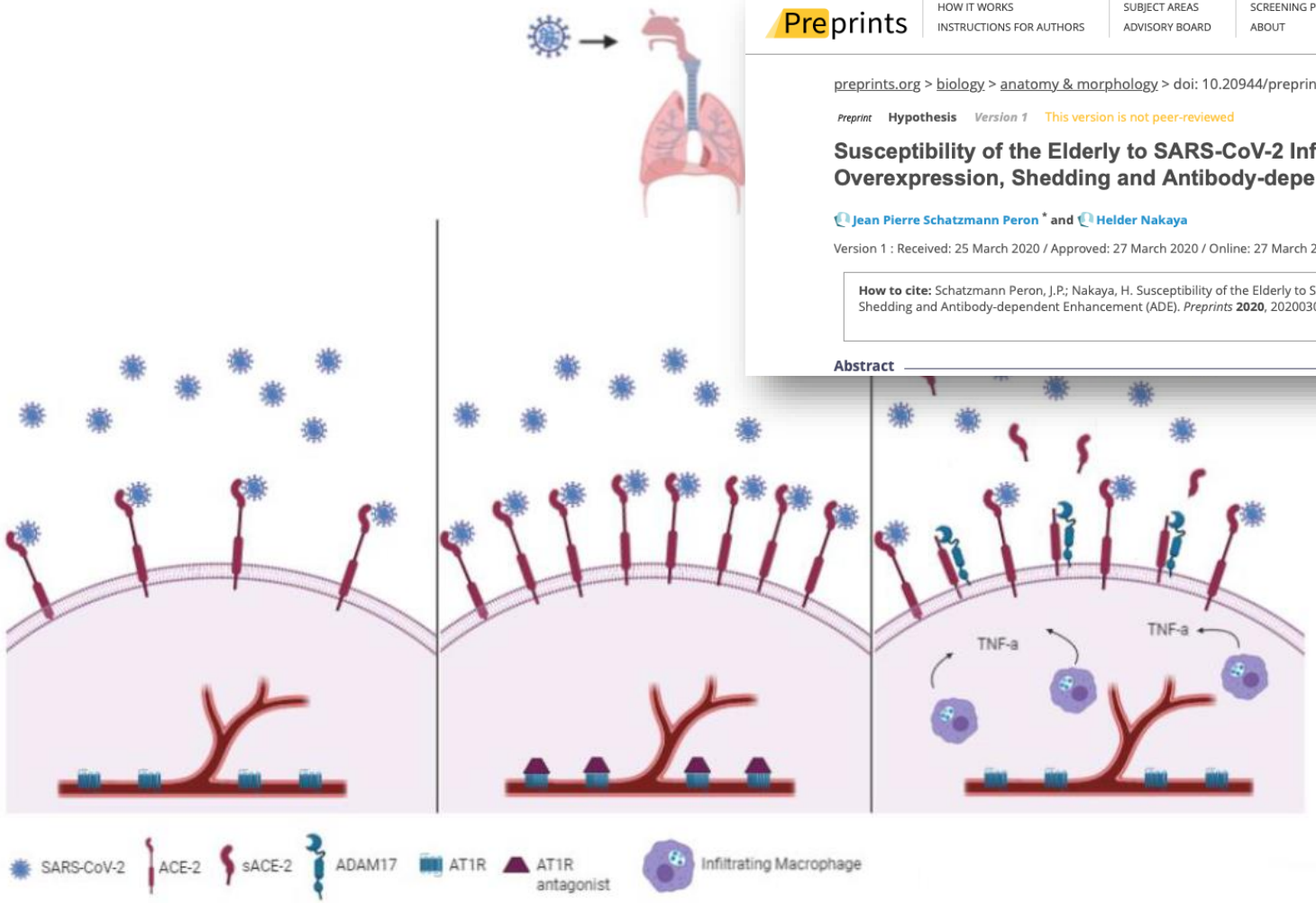
Resposta Imune Efetora
Proteção - Cura

Resposta Imune Exacerbada ou Deficiente
Imunopatologia

SARS-COV-2 – ACE-2

AUMENTO ACE-2 EM COMORBIDADES

ADE – IGG E FCGR



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Posted March 27, 2020.

Bruna GG Pinto, Antonio ER Oliveira, Youvika Singh, Leandro Jimenez, Andre NA Goncalves, Rodrigo LT Ogava, Rachel Creighton, Jean PS Peron, Helder I Nakaya

doi: https://doi.org/10.1101/2020.03.21.20040261

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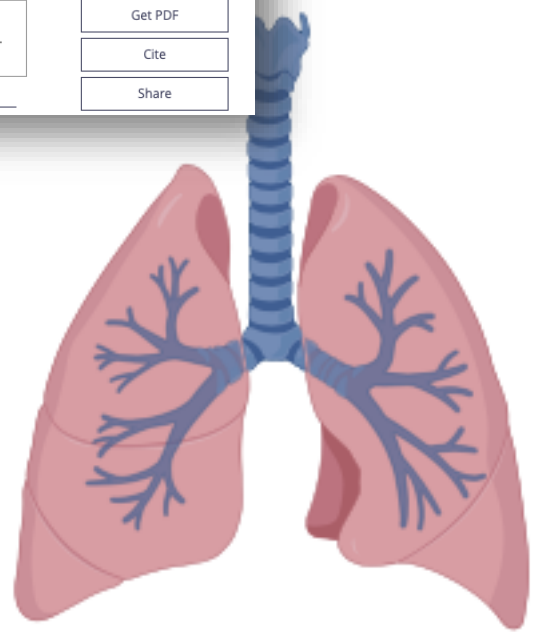
Abstract



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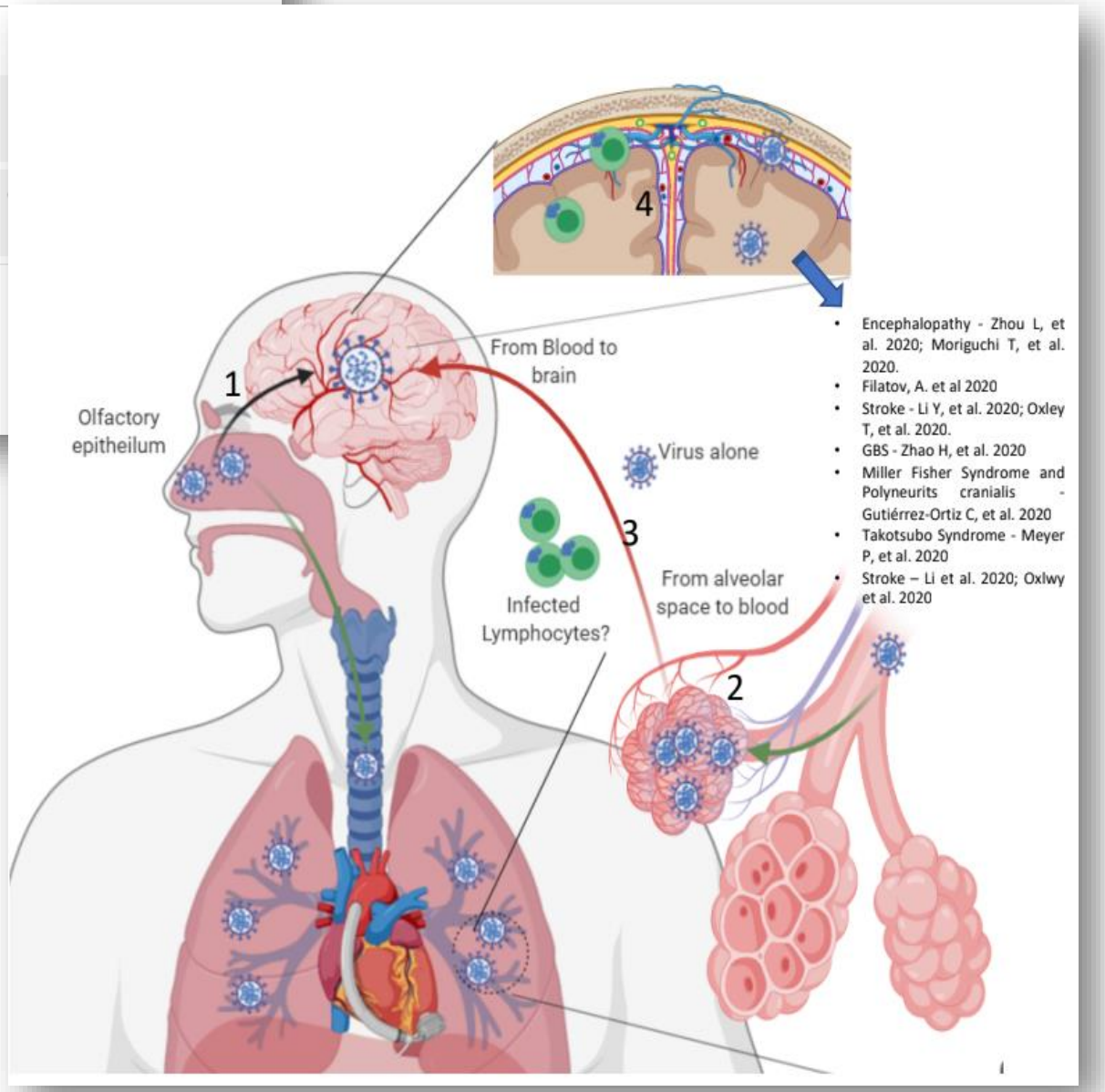
Isabelle Pastor Bandeira *, Marco Antônio Machado Schlindwein, Leticia Caroline Breis, Jean Pierre Schatzmann Peron, Marcus Vinicius Magno Gonçalves

Version 1 : Received: 17 April 2020 / Approved: 17 April 2020 / Online: 17 April 2020 (15:27:14 CEST)

How to cite: Pastor Bandeira, I.; Machado Schlindwein, M.A.; Breis, L.C.; Schatzmann Peron, J.P.; Magno Gonçalves, M.V. Neurological Complications of Pandemic COVID-19: What Have We Got So Far?. *Preprints* **2020**, 2020040304 (doi: 10.20944/preprints202004.0304.v1). Copy



SNC

Encefalite
Leptomeningite
ADEM
AVC
Vírus no líquor

SNP

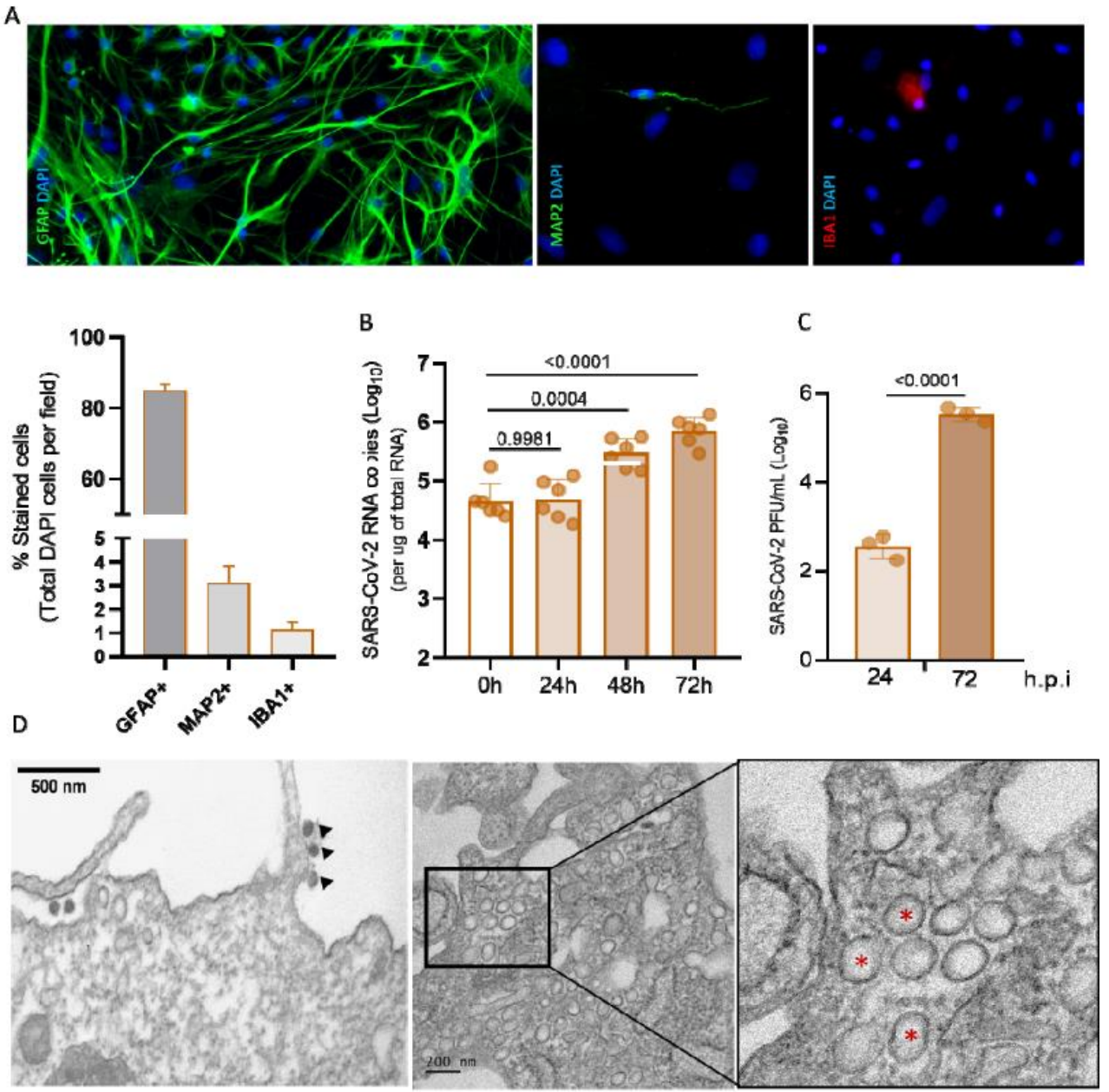
Guillain-Barré
Síndrome Takotsubo
Miller Fisher

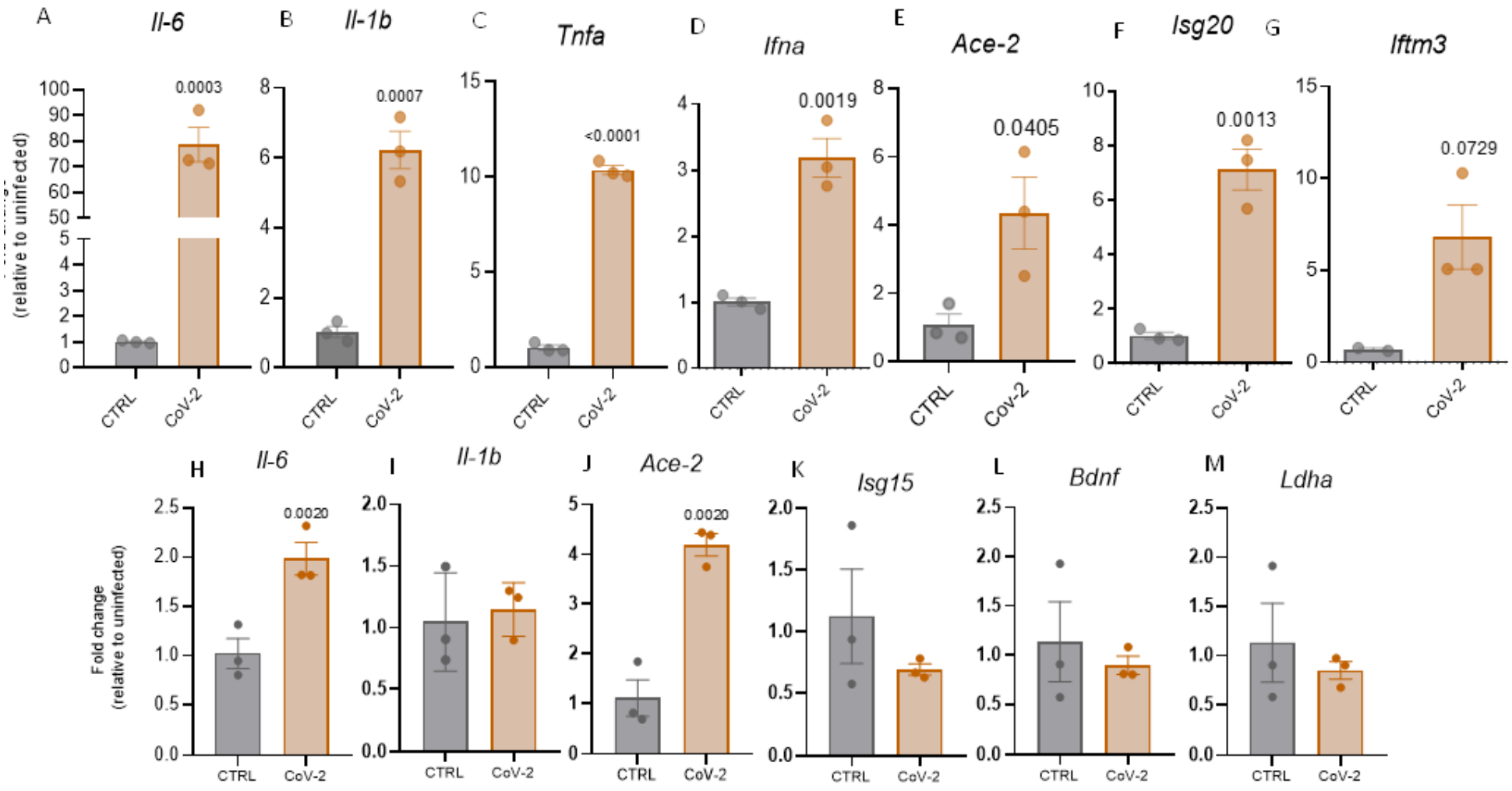
New Results

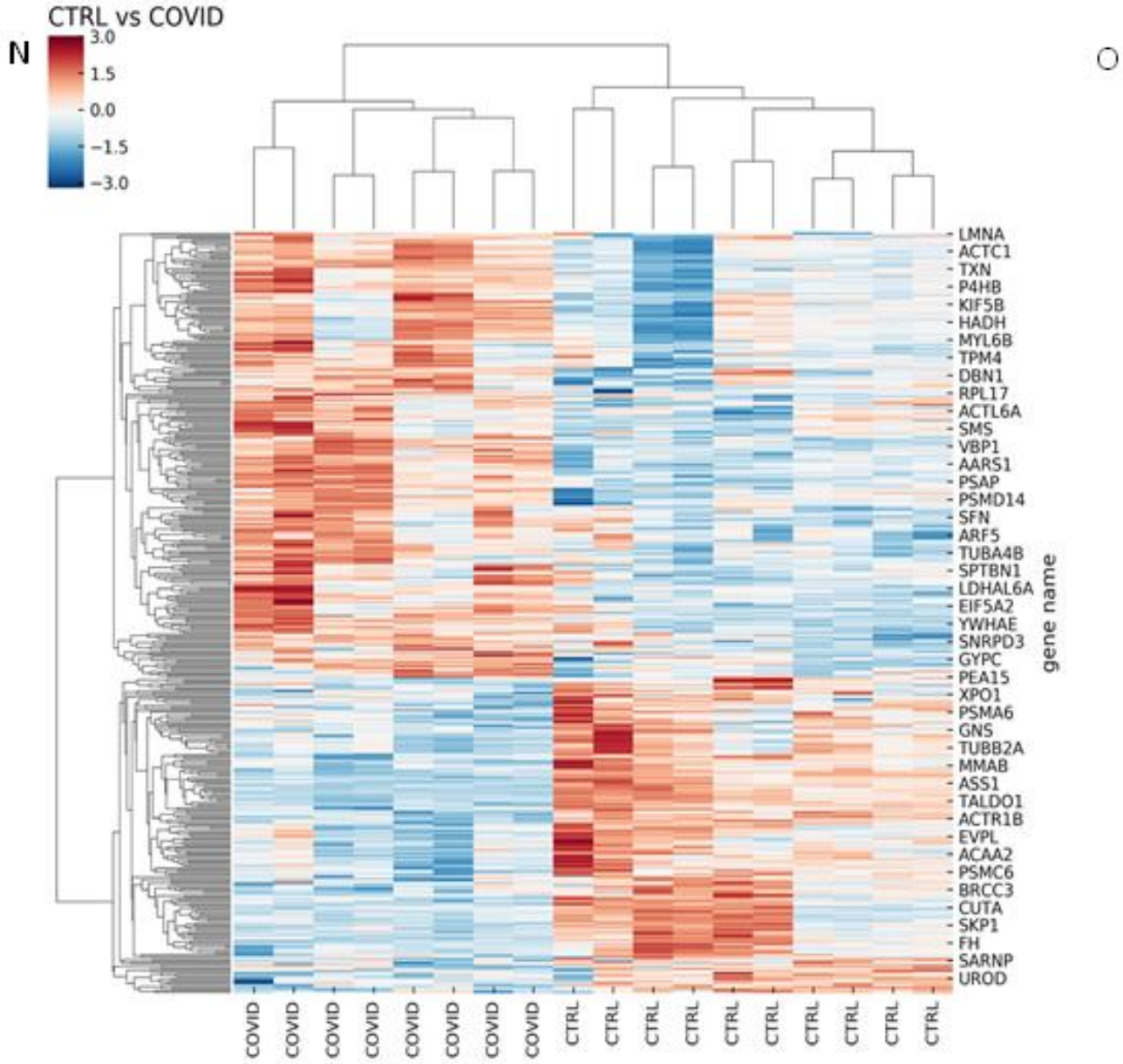
SARS-CoV-2 Infection Impacts Carbon Metabolism and Depends on Glutamine for Replication in Syrian Hamster Astrocytes

Lilian Gomes Oliveira, Yan de Souza Angelo, Pedro Yamamoto, Victor Corasolla Carregari, Fernanda Crunfli, Guilherme Reis-de-Oliveira, Licia Costa, Erica Almeida Duque, Nilton Barreto Santos, Glaucia Maria Almeida, Egidi Mayara Silva Firmino, Isadora Marques Paiva, Carolina M. Polonio, Nagela G. Zanluqui, Marilia Garcia Oliveira, Gustavo Gastao Davanzo, Marina Cacador Ayupe, Caio Loureiro Salgado, Angélica Cristine Almeida Campos, Luiz Gustavo Bentim Góes, Marielton Passos Cunha, Maria Regina Dimperio Lima, Denise Morais Fonseca, Ana Marcia Sa Guimaraes, Paola Marcela Minoprio, Carolina Demarchi Munhoz, Claudia Madalena Cabrera Mori, Pedro Manoel Moraes-Vieira, Thiago M. Cunha, Daniel Martins-de-Souza, Jean Pierre Schatzmann Peron

doi: https://doi.org/10.1101/2021.10.23.465567




A
Il-6
0.0003
B
Il-1b
0.0007
C
Tnfa
<0.0001
D
Ifna
0.0019
E
Ace-2
0.0405
F
Isg20
0.0013
G
Iftm3
0.0729
(relative to uninfected)
CTRL
CoV-2
H
Il-6
0.0020
I
Il-1b
J
Ace-2
0.0020
K
Isg15
L
Bdnf
M
Ldha
Fold change
(relative to uninfected)


N
CTRL vs COVID
3.0
1.5
0.0
−1.5
−3.0
LMNA
ACTC1
TXN
P4HB
KIF5B
HADH
MYL6B
TPM4
DBN1
RPL17
ACTL6A
SMS
VBP1
AARS1
PSAP
PSMD14
SFN
ARF5
TUBA4B
SPTBN1
LDHAL6A
EIF5A2
YWHAE
SNRPD3
GYPC
PEA15
XPO1
PSMA6
GNS
TUBB2A
MMAB
ASS1
TALDO1
ACTR1B
EVPL
ACAA2
PSMC6
BRCC3
CUTA
SKP1
FH
SARNP
UROD
gene name
COVID
COVID
COVID
COVID
COVID
COVID
COVID
COVID
CTRL
CTRL
CTRL
CTRL
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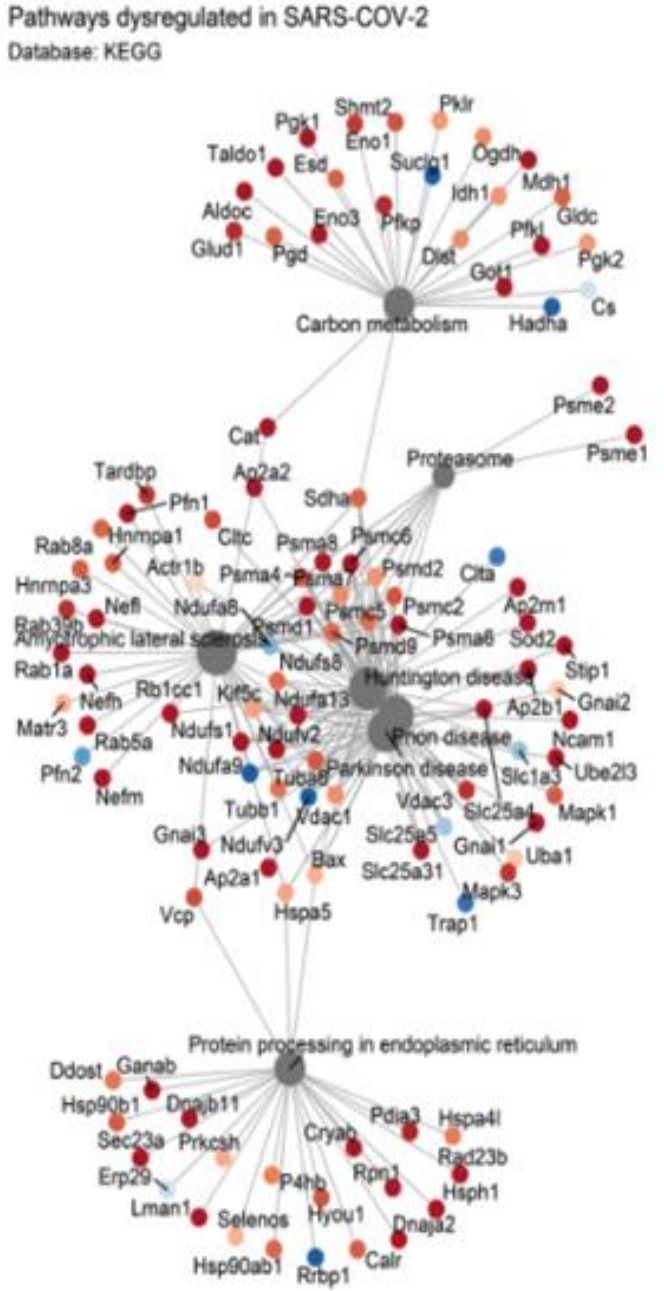
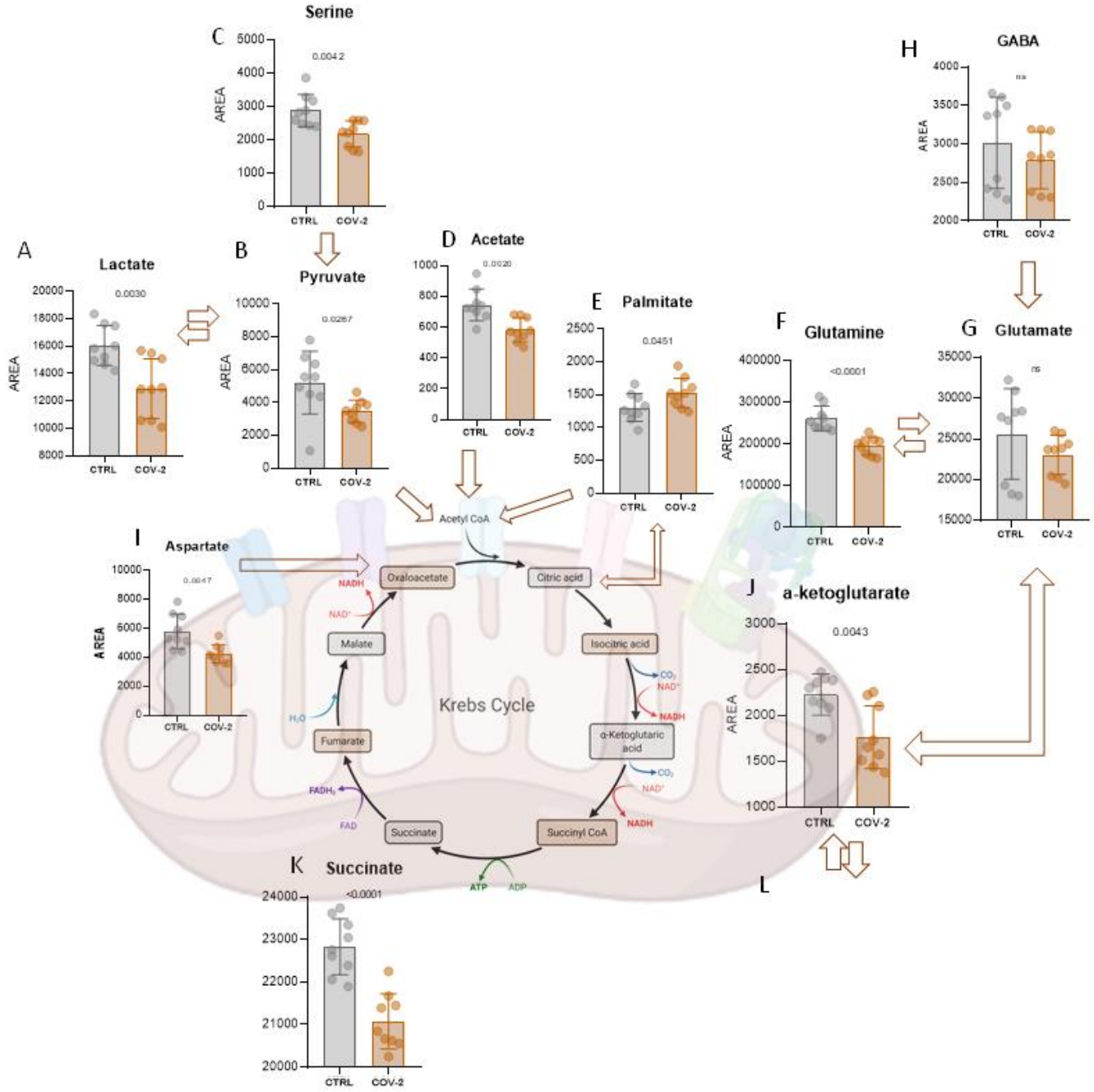
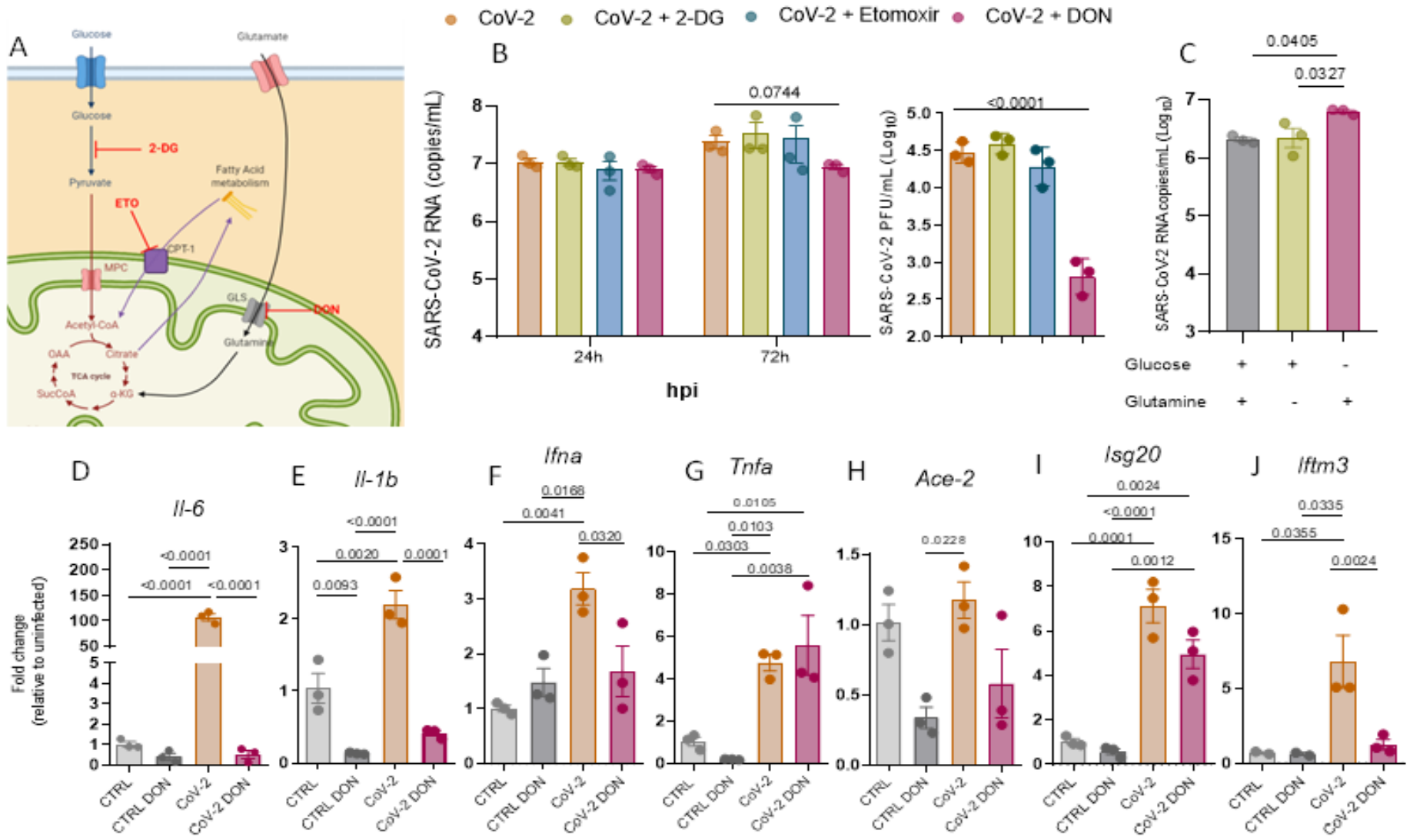
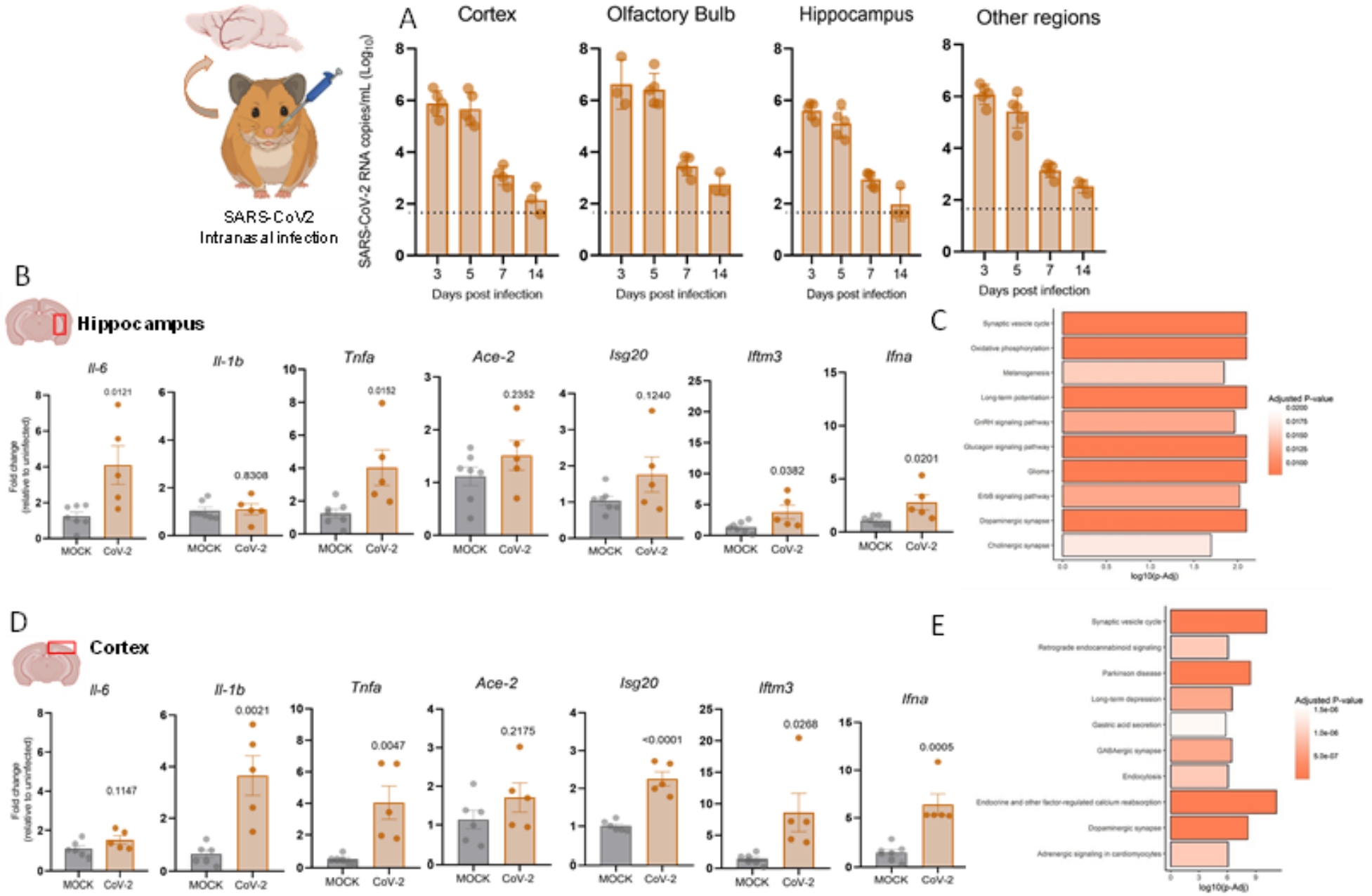
CTRL

O


Pathways dysregulated in SARS-COV-2
Database: KEGG
Carbon metabolism
Proteasome
Huntington disease
Prion disease
Parkinson disease
Protein processing in endoplasmic reticulum

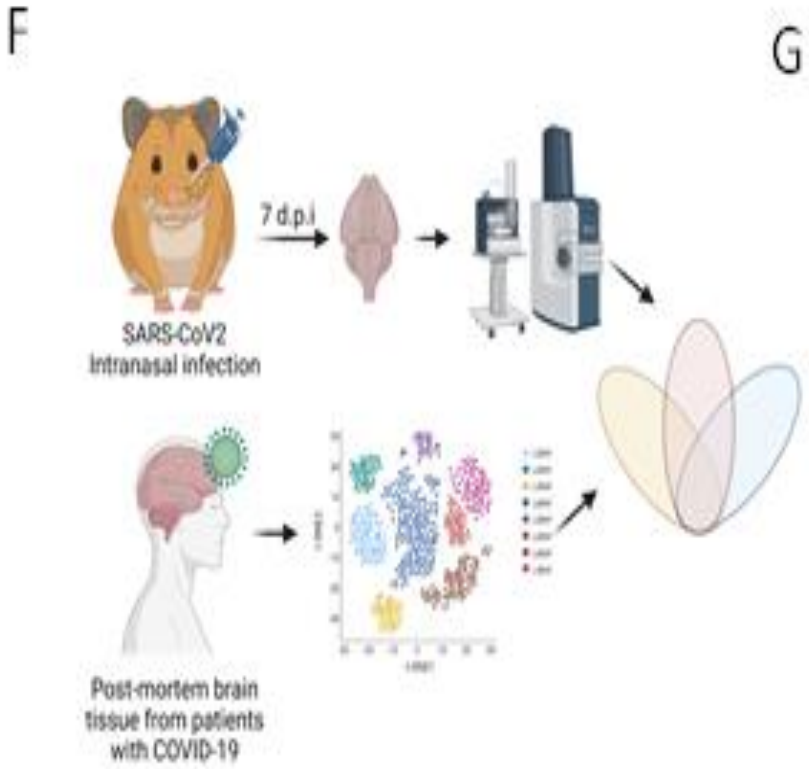

A
Lactate
0.0030
AREA
CTRL
COV-2
B
Pyruvate
0.0257
C
Serine
0.0042
D
Acetate
0.0020
E
Palmitate
0.0451
F
Glutamine
<0.0001
G
Glutamate
ns
H
GABA
ns
I
Aspartate
0.0047
J
a-ketoglutarate
0.0043
K
Succinate
<0.0001
L
Acetyl CoA
Oxaloacetate
Citric acid
Isocitric acid
α-Ketoglutaric acid
Succinyl CoA
Succinate
Fumarate
Malate
NADH
NAD+
FADH2
FAD
ATP
ADP
Krebs Cycle

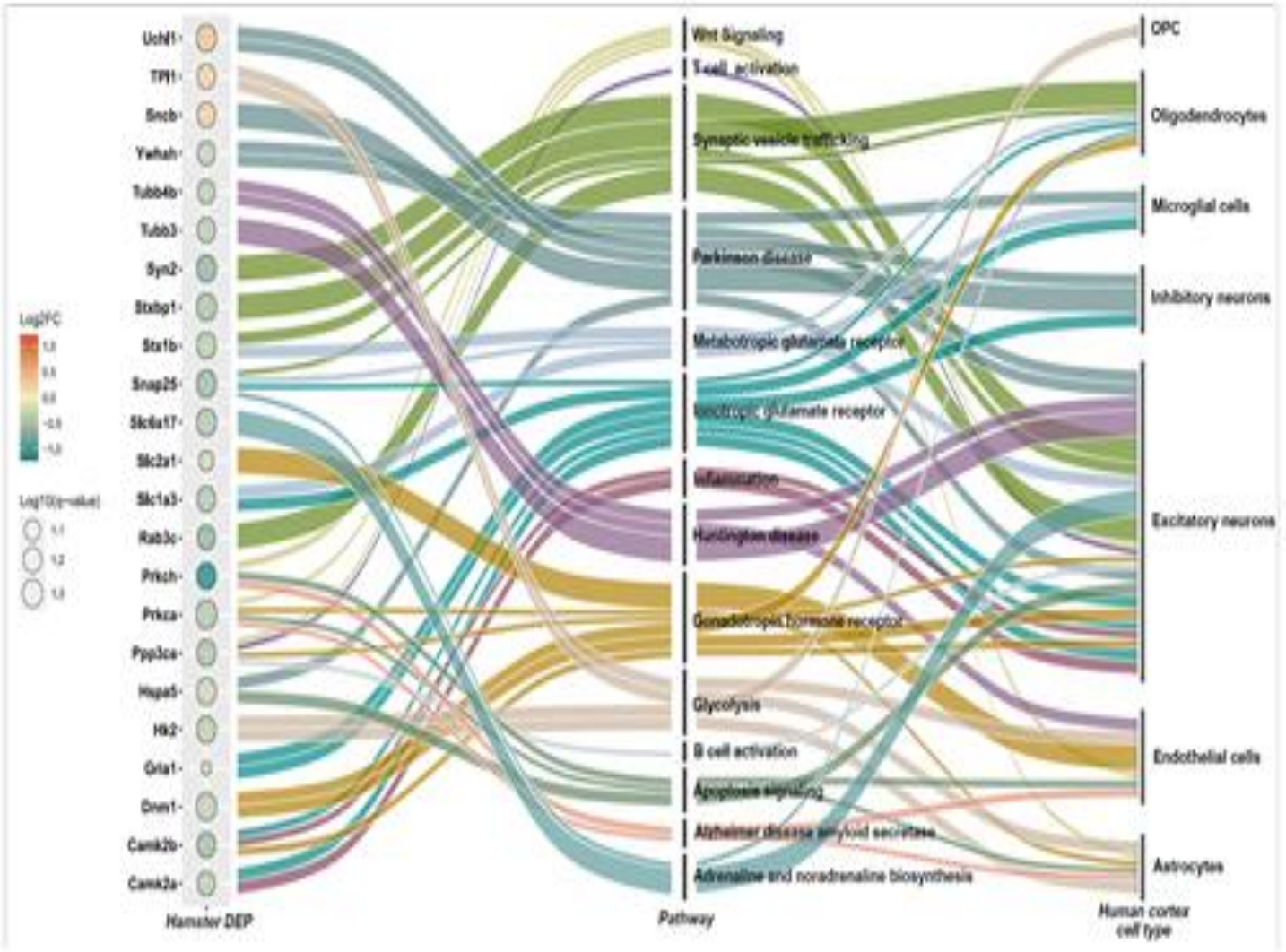

A
Glucose
Glutamate
Glucose
2-DG
Pyruvate
Fatty Acid metabolism
ETO
CPT-1
MPC
GLS
DON
Acetyl-CoA
Glutamine
OAA
Citrate
TCA cycle
SucCoA
α-KG
CoV-2
CoV-2 + 2-DG
CoV-2 + Etomoxir
CoV-2 + DON
B
SARS-CoV-2 RNA (copies/mL)
0.0744
24h
72h
hpi
SARS-CoV-2 PFU/mL (Log10)
<0.0001
C
0.0405
0.0327
SARS-CoV-2 RNA copies/mL (Log10)
Glucose + + -
Glutamine + - +
D
Il-6
Fold change (relative to uninfected)
<0.0001
<0.0001
<0.0001
E
Il-1b
<0.0001
0.0020
0.0001
0.0093
F
Ifna
0.0168
0.0041
0.0320
G
Tnfa
0.0105
0.0103
0.0303
0.0038
H
Ace-2
0.0228
I
Isg20
0.0024
<0.0001
0.0001
0.0012
J
Iftm3
0.0335
0.0355
0.0024
CTRL
CTRL DON
CoV-2
CoV-2 DON


SARS-CoV2
Intranasal infection
A
Cortex
Olfactory Bulb
Hippocampus
Other regions
SARS-CoV-2 RNA copies/mL (Log10)
Days post infection
B
Hippocampus
Il-6
Il-1b
Tnfa
Ace-2
Isg20
Iftm3
Ifna
Fold change (relative to uninfected)
MOCK
CoV-2
0.0121
0.8308
0.0152
0.2352
0.1240
0.0382
0.0201
C
Adjusted P-value
log10(p-Adj)
D
Cortex
0.1147
0.0021
0.0047
0.2175
<0.0001
0.0268
0.0005
E

Proteômica Hamster

Singel Cell RNAseq Humano





GRANDES MAZELAS DA HUMANIDADE - INFECÇÕES

EBOLA

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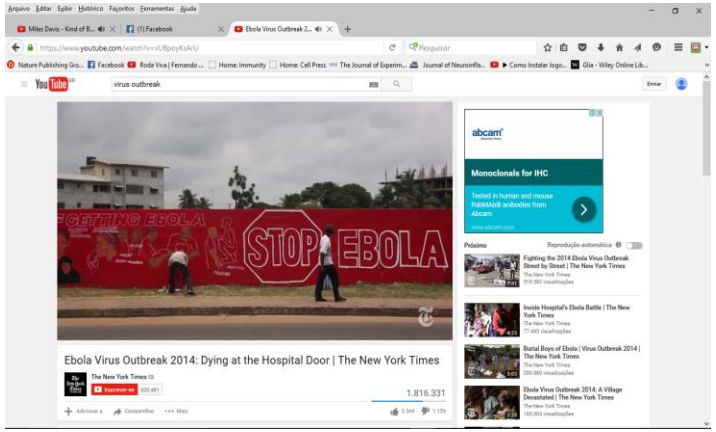

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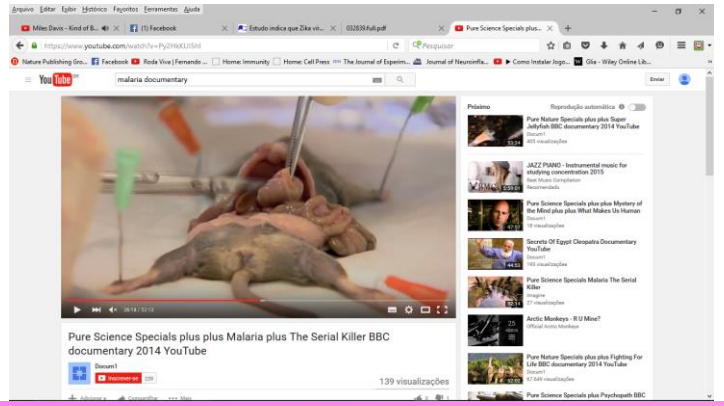
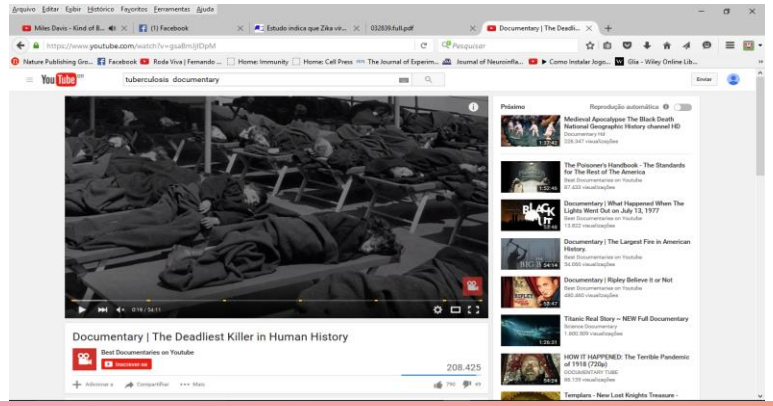


Malária

SARS

https://www.youtube.com/watch?v=JBagOaneLeo

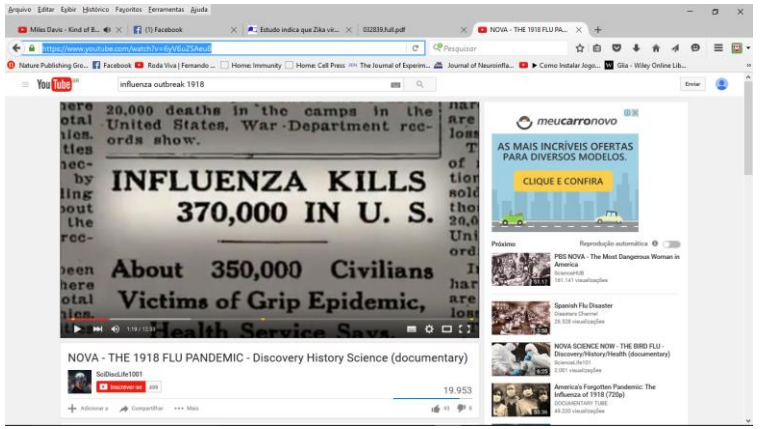
https://www.youtube.com/watch?v=gsaBmJjIDpM



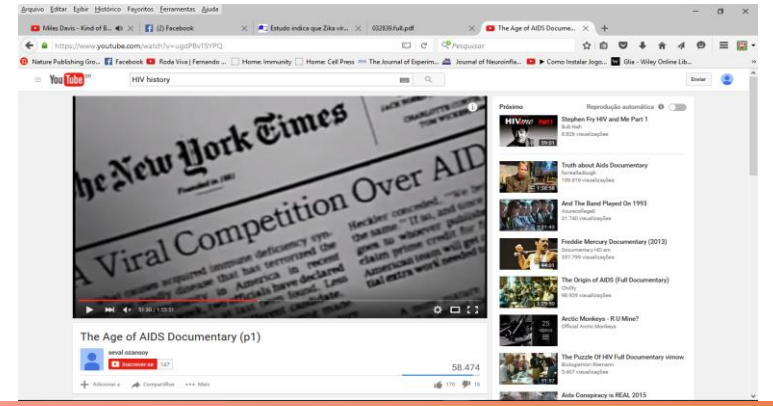
Tuberculose

Influenza

https://www.youtube.com/watch?v=6yV6uZSAeu8



https://www.youtube.com/watch?v=ugdPBvTSYPQ



HIV

Neuroimmune Interactions Lab

DEPARTAMENTO DE Imunologia
INSTITUTO DE CIÊNCIAS BIOMÉDICAS - USP

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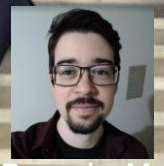

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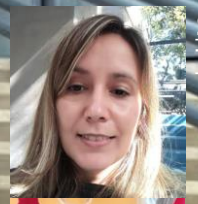
CAPES



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Claudia
Technician

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Lilian - PhD
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