Boehringer Ingelheim | Université franco-allemande Deutsch-Französische Hochschule | INSTITUT MERIEUX

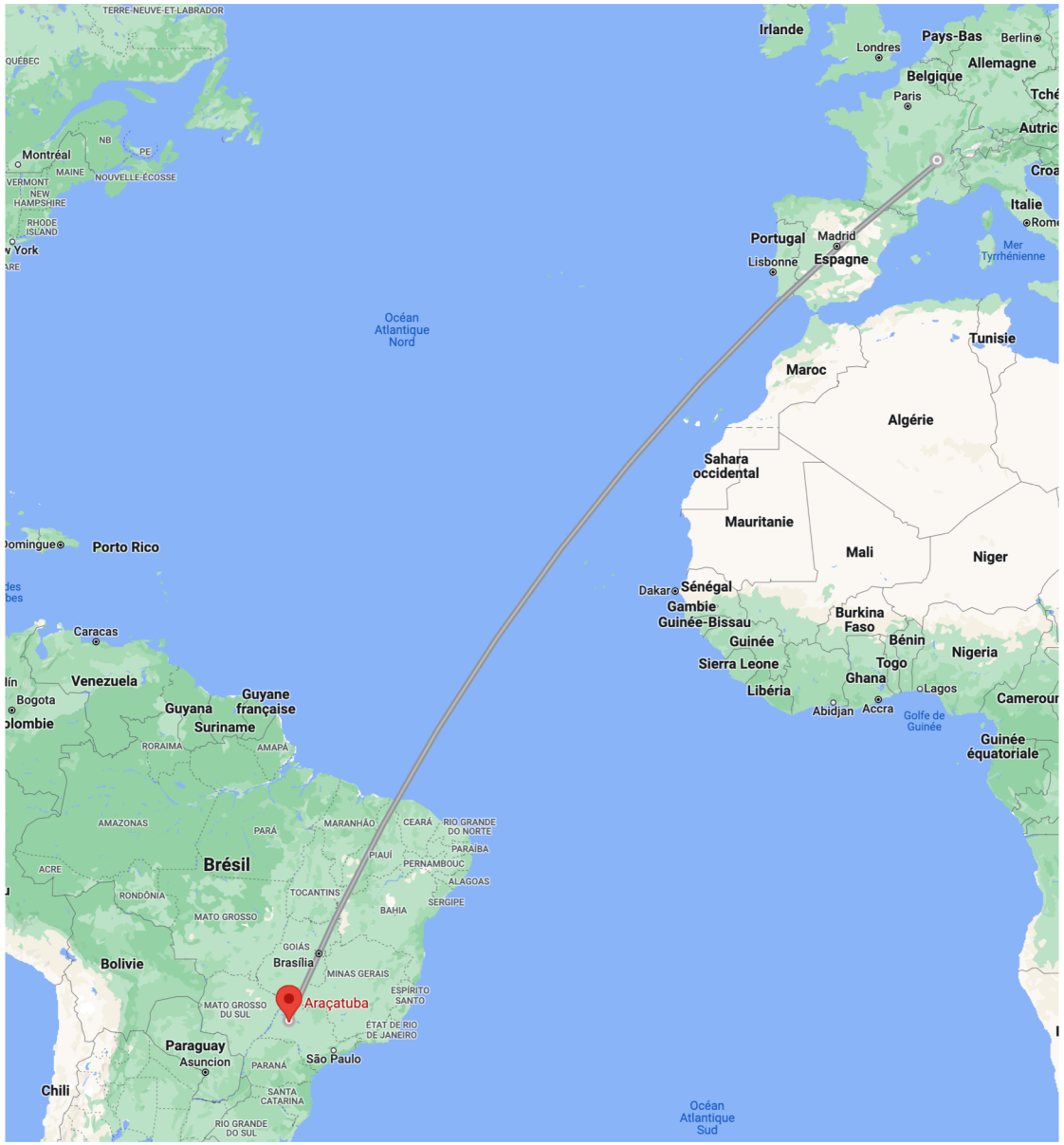
Lyon, 12/10/2022

# NEGLECTED AND EMERGING NEUROTROPIC INFECTIONS

**Guilherme Dias de Melo**
**Lyssavirus Epidemiology and Neuropathology Unit**
**Institut Pasteur**

INSTITUT PASTEUR

# BACKGROUND


Irlande
Londres
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Portugal
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# BACKGROUND

Prof Gisele F. Machado
& team

Prof Christiane Herden
& team

Dr Thierry Lang
& team

Dr Paola Minoprio
& team

Prof Hervé Bourhy
& team

- Comparative pathology
- Zoonosis
- Neglected diseases
- Public health

- Host-pathogen interaction
- Neurotropism
- (Neuro)infectious diseases
- (Neuro)behavior

# RABIES

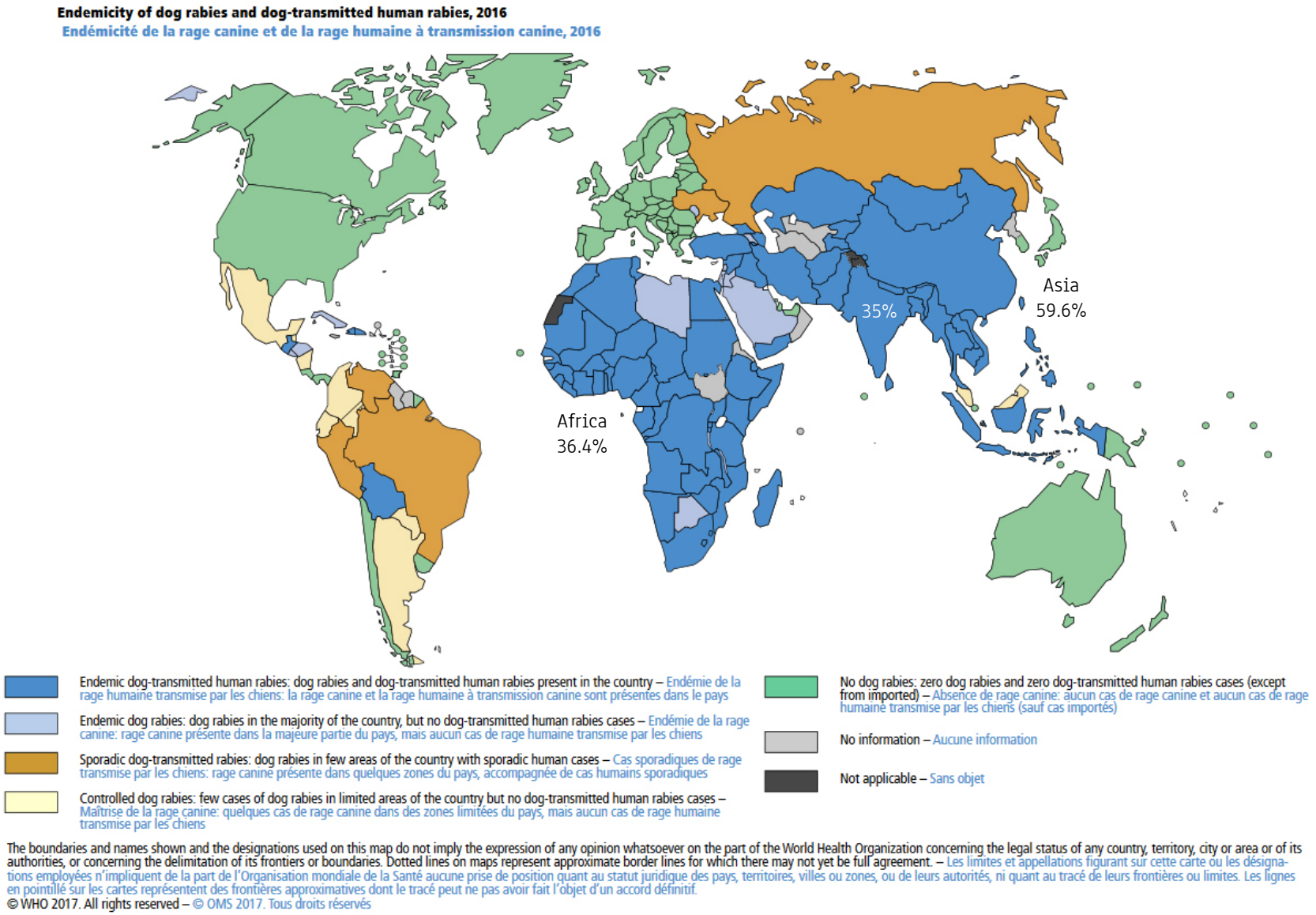
the most neglected disease

# RABIES | the most neglected disease


## KEY FACTS

- Vaccine-preventable disease (first human vaccination in 1885)
- 29 million people worldwide receive a post-exposure prophylaxis each year
- 40% of people bitten by suspect rabid animals are children under 15 years of age
- 59 000 human deaths annually in over 150 countries
- No treatment for symptomatic rabies

# RABIES | the most neglected disease



# RABIES | the most neglected disease

SACHSEN-ANHALT

#moderndenken

Alle Ministerien

Suche search

Landesamt für Verbraucherschutz

Wir über uns & Service | Hygiene | Lebensmittelsicherheit | Veterinärmedizin | Arbeitsschutz

Startseite > Wir über uns & Service > Die Pressestelle > **Tollwut bei einem illegal eingeführten Welpen – Gefahr für Mensch und Tier**

## Tollwut bei einem illegal eingeführten Welpen – Gefahr für Mensch und Tier

Landesamt für Verbraucherschutz - Presseinformation Nr. 35/2021
Halle, 28. September 2021

Selbst der süßeste Welpe kann eine potentiell tödliche Gefahr darstellen und die Bemühungen um die Tollwutfreiheit in Deutschland gefährden. Achten Sie auf die Tollwutimpfungen Ihrer Haustiere.

**Der Tollwut-Fall**

Am 15.09.2021 diagnostizierte das Lebensmittel- und Veterinärinstitut Braunschweig/Hannover (LAVES) die Infektion mit dem Tollwutvirus bei einem verstorbenen Welpen. Das acht Wochen alte Tier wurde Anfang September illegal von seinen Besitzern aus einem Türkei-Urlaub mitgebracht, ohne die geltenden Bestimmungen für die Einfuhr von Haustieren in die Europäische Union (EU) zu beachten. Der erkrankte Welpe wurde kurz darauf zunächst in einer Tierarztpraxis vorgestellt, dann in einer Tierklinik stationär aufgenommen, wo er am darauffolgenden Tag verstarb.

Le Monde

SANTÉ

# L'enfant revenu en France avec la rage est mort

**Le jeune garçon, qui avait été infecté par la maladie du Sri Lanka à la mi-août, avait été hospitalisé le 4 octobre après avoir présenté les premiers signes cliniques.**

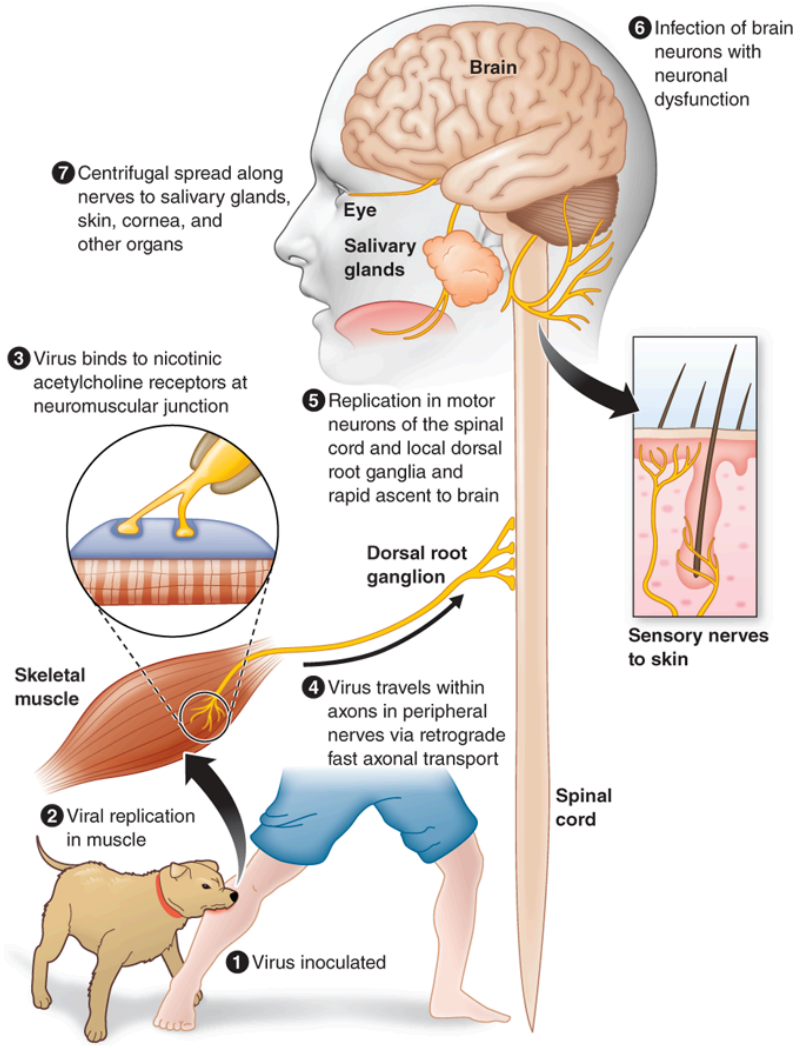
Le Monde avec AFP

Publié le 18 octobre 2017 à 20h41 • Mis à jour le 19 octobre 2017 à 06h36 • Lecture 1 min.

Le petit garçon de dix ans souffrant de la rage après avoir été mordu par un chiot au Sri Lanka est mort mardi soir à Lyon, a appris l'Agence France-Presse (AFP), mercredi 18 octobre.

Hors cas exceptionnels, la rage est toujours mortelle une fois que les signes cliniques sont apparus : l'enfant avait présenté les premiers signes neurologiques le 1er octobre.

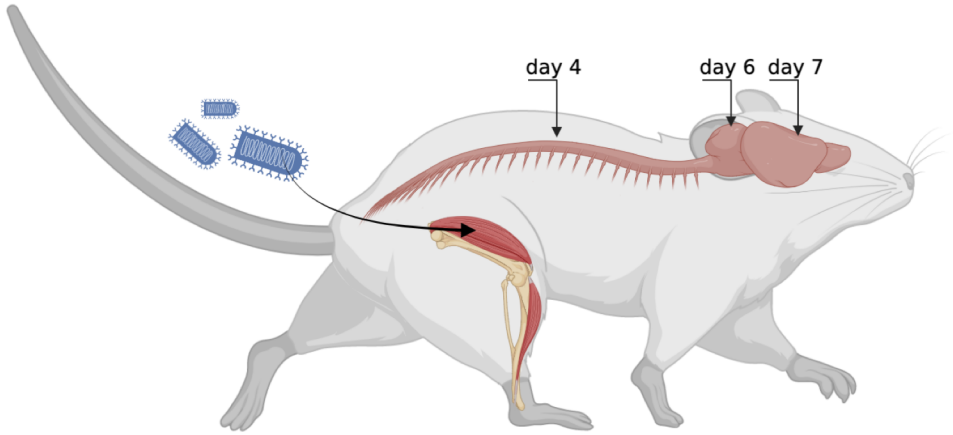
# RABIES | the most neglected disease

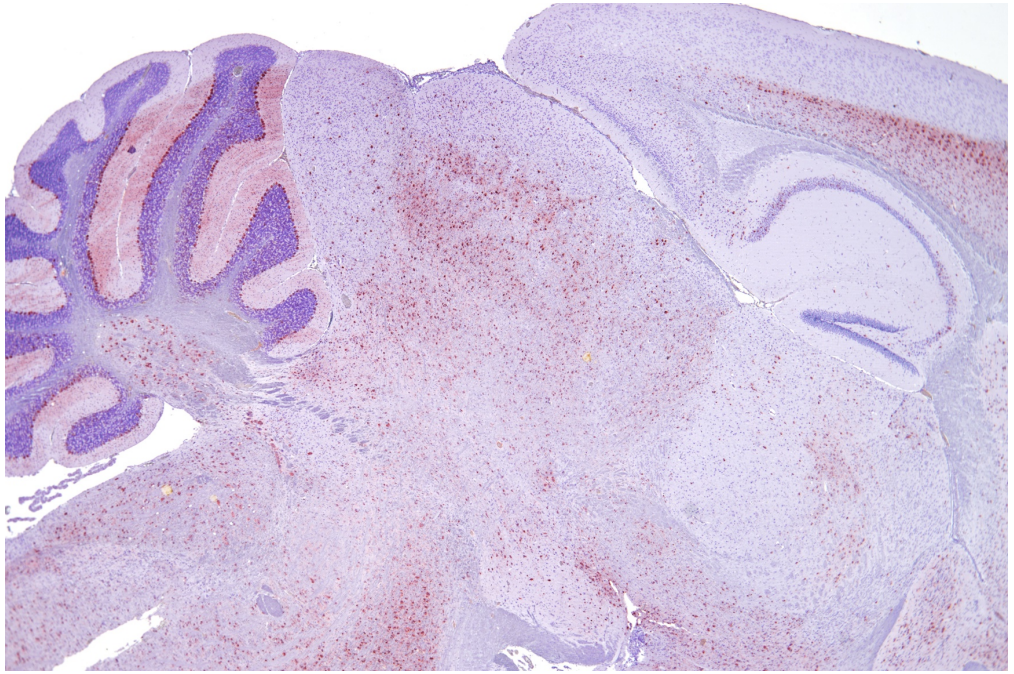





- incubation period : 2-3 months (range from 1 week to 1 year)

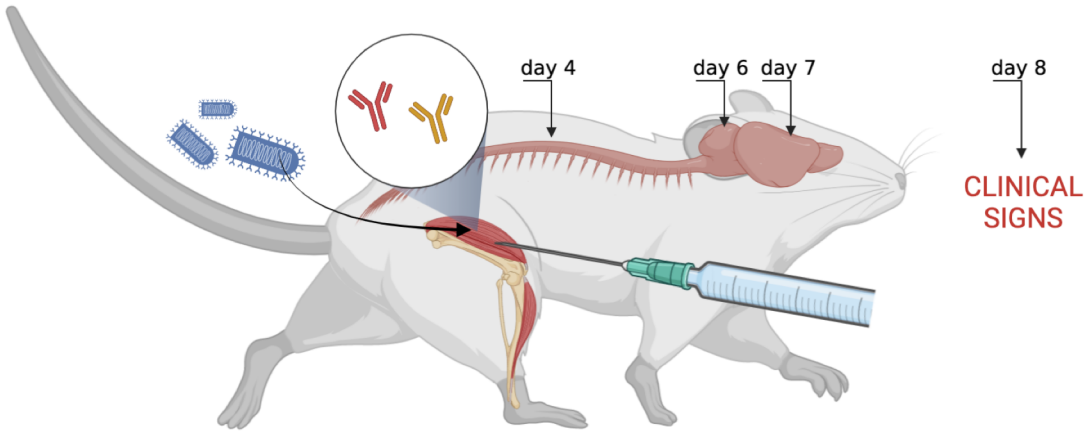
# RABIES | the most neglected disease

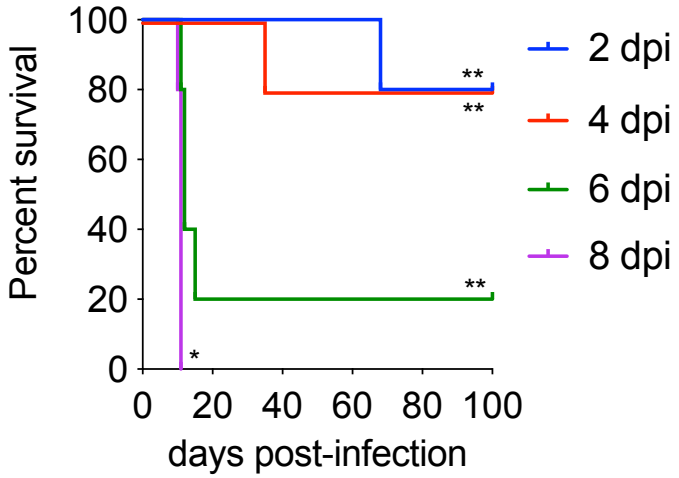


# RABIES | towards an efficienty therapy for symptomatic rabies

Intramuscular injection of
therapeutic monoclonal antibodies

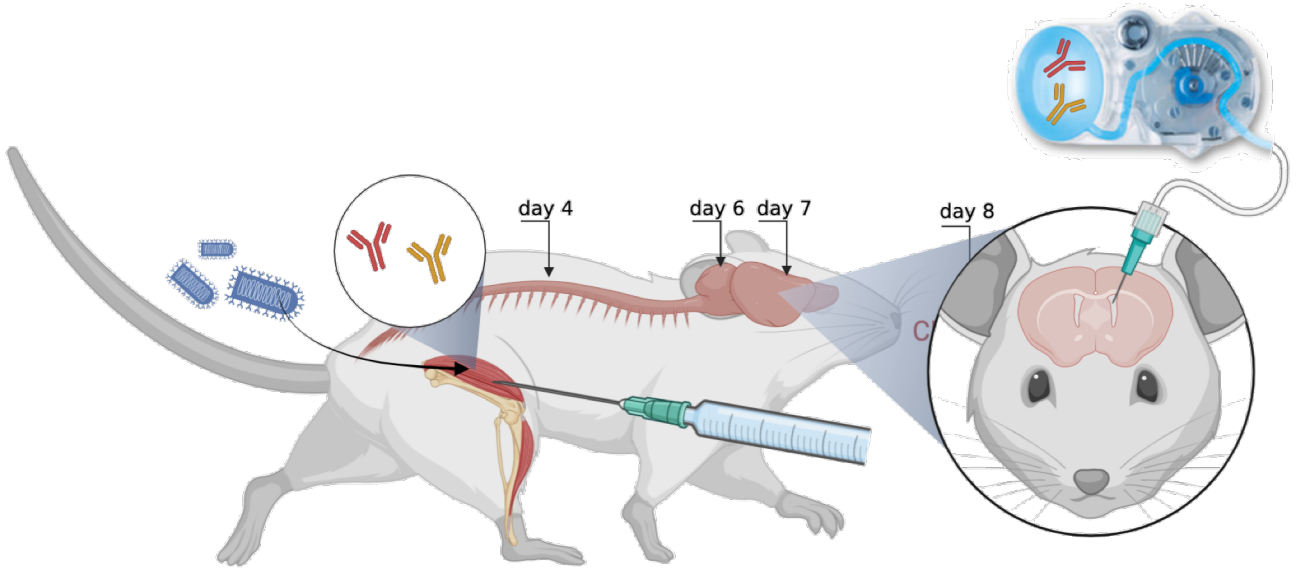


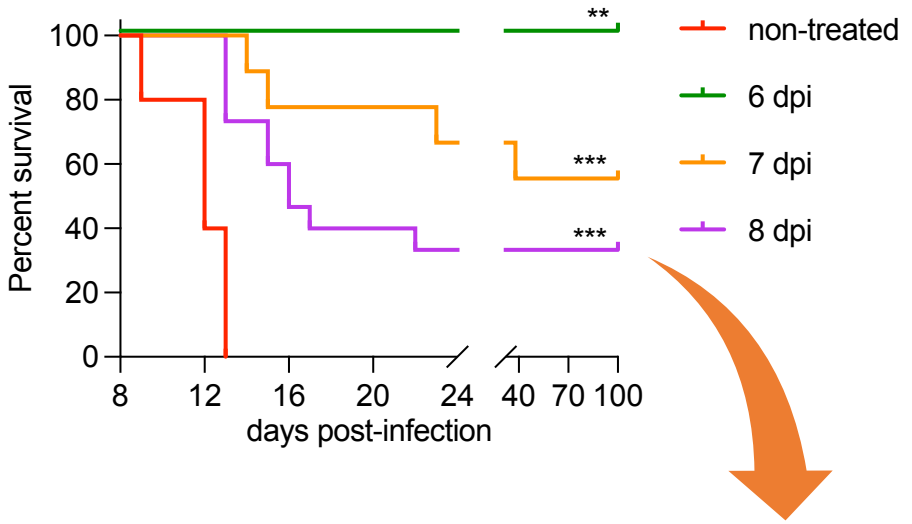




de Melo et al. *EMBO Mol Med* (2020)

# RABIES | towards an efficienty therapy for symptomatic rabies

Combined intramuscular injection and continuous intra-cerebro-ventricular infusion of therapeutic monoclonal antibodies

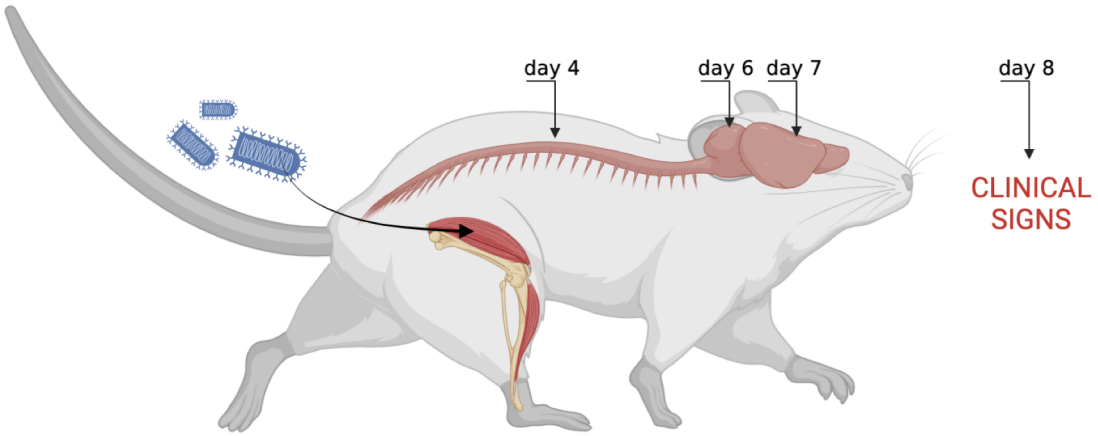



- complete viral clearance
- animals clinically healthy

de Melo et al. *EMBO Mol Med* (2020)

# RABIES | towards an efficienty therapy for symptomatic rabies




## CURRENT CHALLENGES

early diagnosis
- biomarkers
- behavioral changes

brain drug delivery
- less invasive techniques
- antibody engineering

# SARS-CoV-2

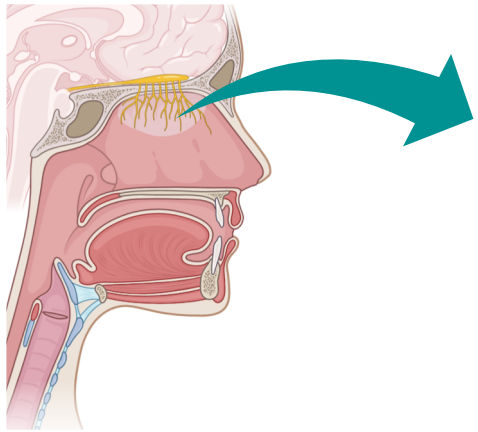
## a neurotropic pathogen?

# SARS-CoV-2 | a neurotropic pathogen?


## KEY FACTS

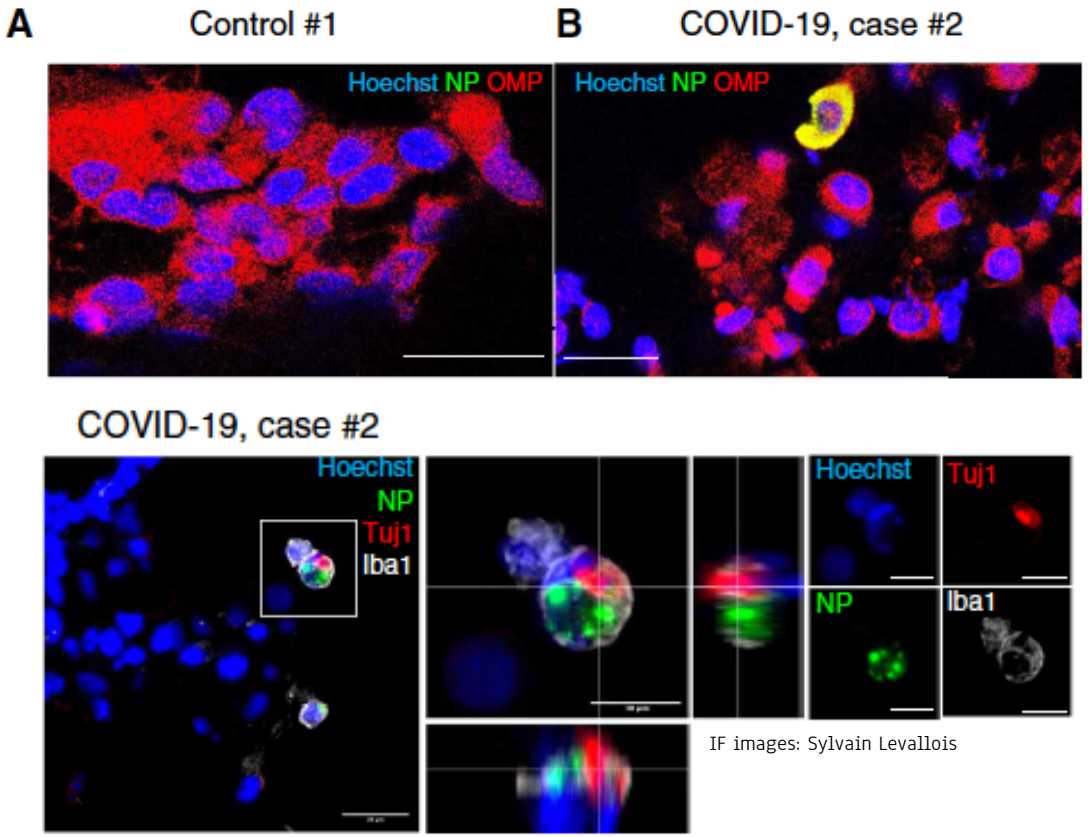
- More than 600 million cases
- More than 6,5 million deaths
- More than 12 million vaccine doses administred
- Respiratory and extra-respiratory symptoms
- Long-term neurologic sequelae

# SARS-CoV-2 | a neurotropic pathogen?



Anosmia

- hallmark of COVID-19 (SARS-CoV-2/Wuhan)

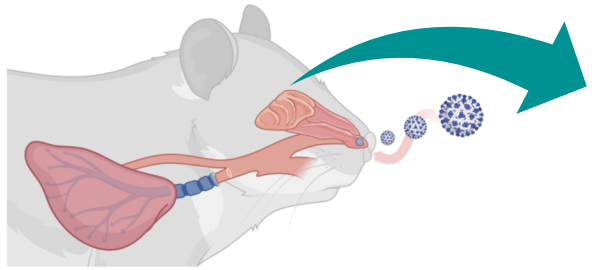


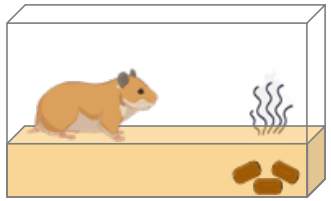

IF images: Sylvain Levallois

- Human anosmic patients: France, May-October 2020

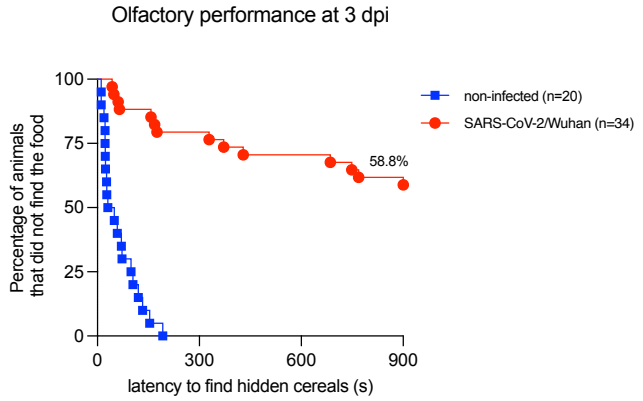
de Melo et al., *Sci Transl Med* (2021)

# SARS-CoV-2 | a neurotropic pathogen?



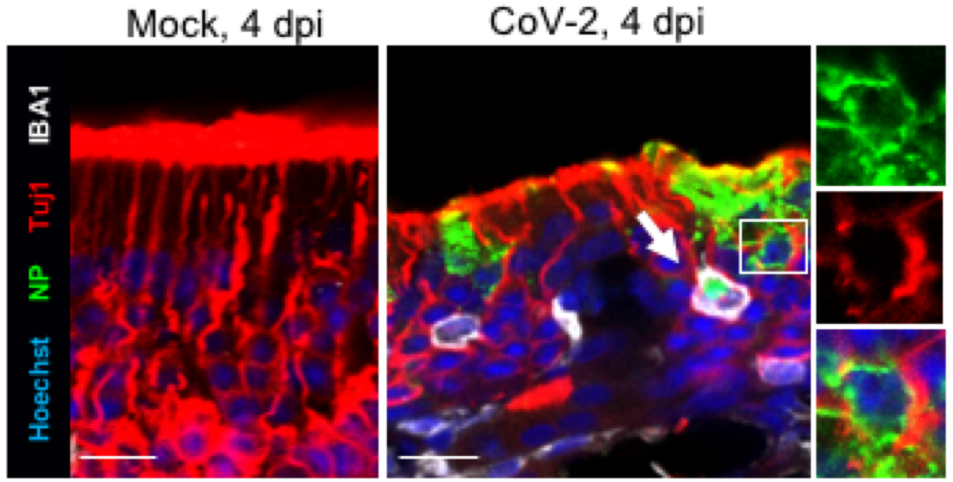


buried food finding test




Anosmia

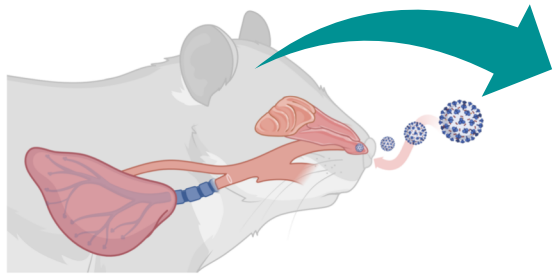
- hallmark of COVID-19 (SARS-CoV-2/Wuhan)



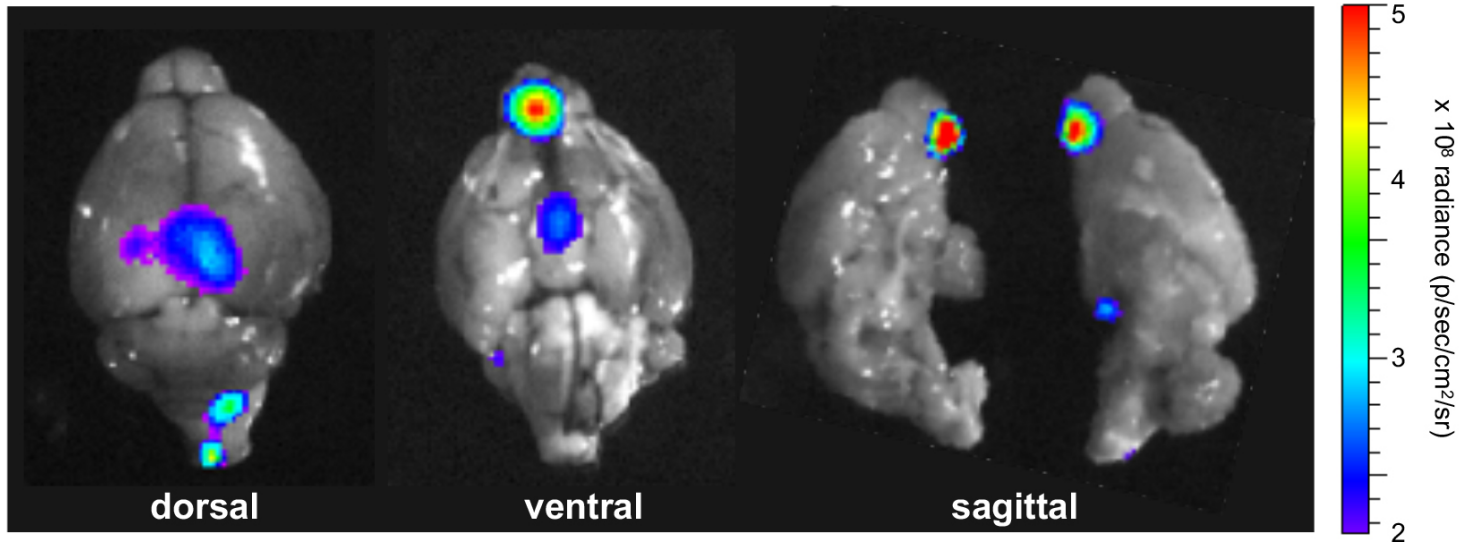

IF images: Sylvain Levallois

de Melo et al., *Sci Transl Med* (2021)

# SARS-CoV-2 | a neurotropic pathogen?

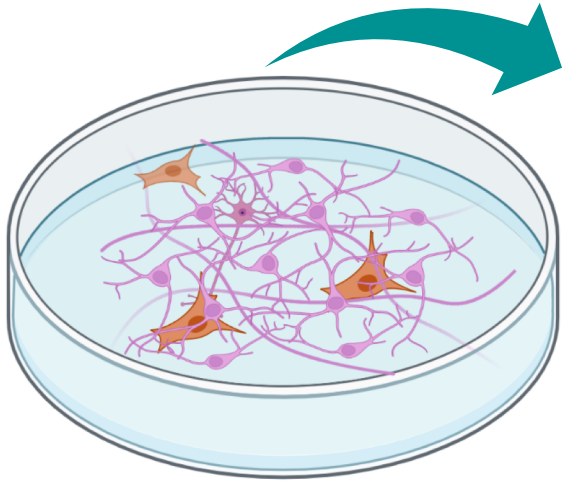


SARS-CoV-2/nLuc infecting the olfactory bulbs *in vivo*

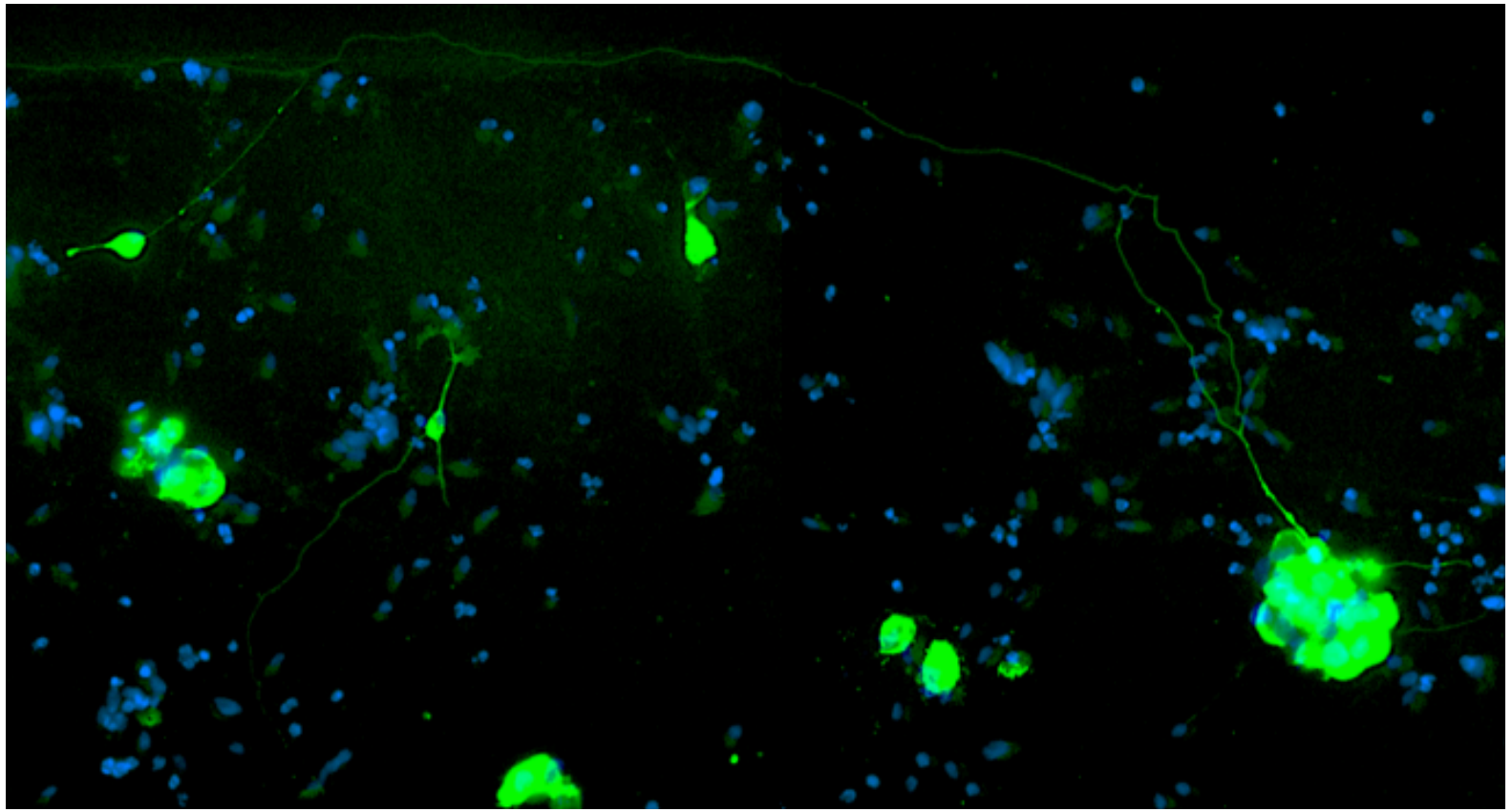



de Melo et al., submitted/*BioRxiv* (2022)

# SARS-CoV-2 | a neurotropic pathogen?



SARS-CoV-2 infecting human neurons *in vitro*



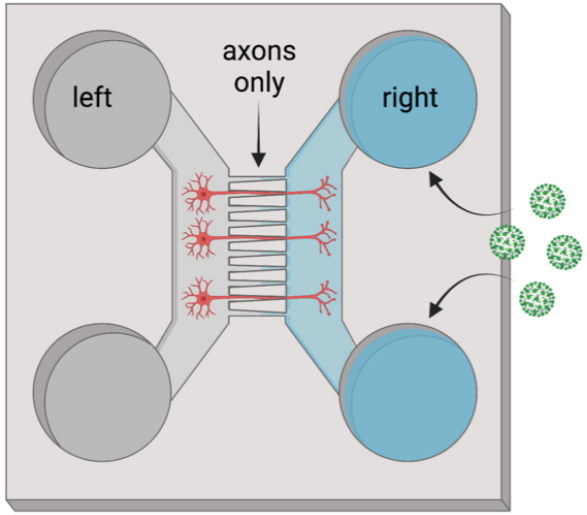
human stem cell-derived neurons

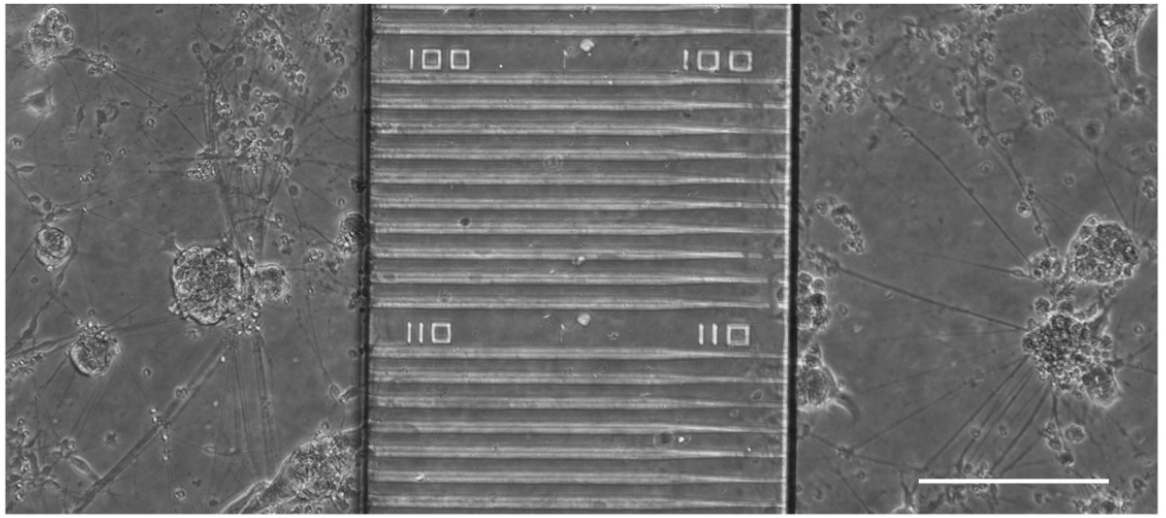
de Melo et al., submitted/*BioRxiv* (2022)

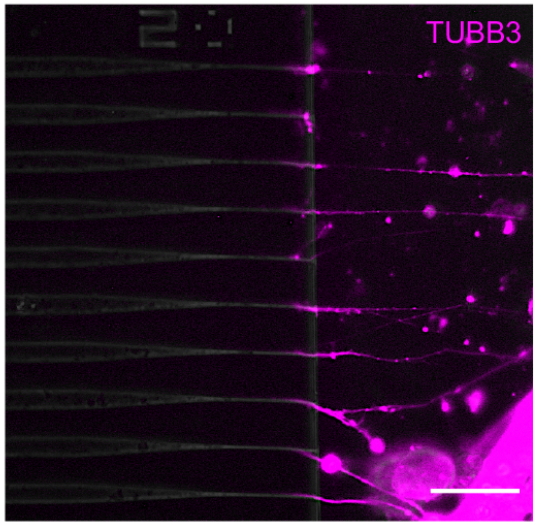
# SARS-CoV-2 | a neurotropic pathogen?

Brain on a chip

- SARS-CoV-2 transport along axons in neuron-epithelial networks



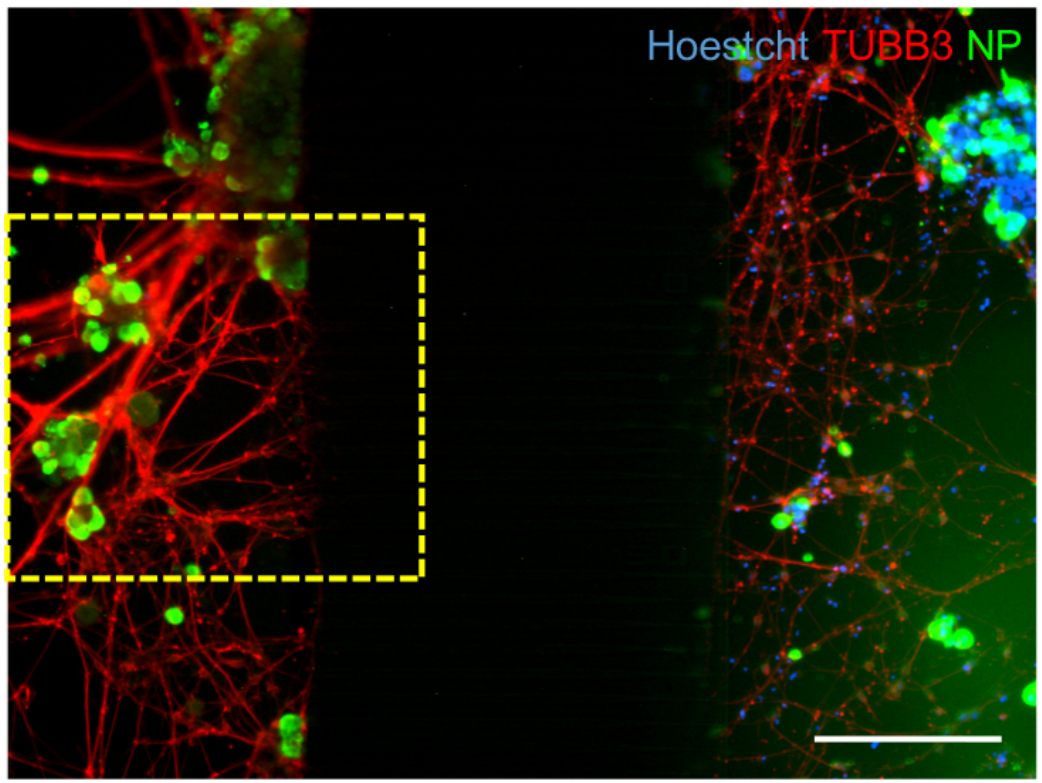



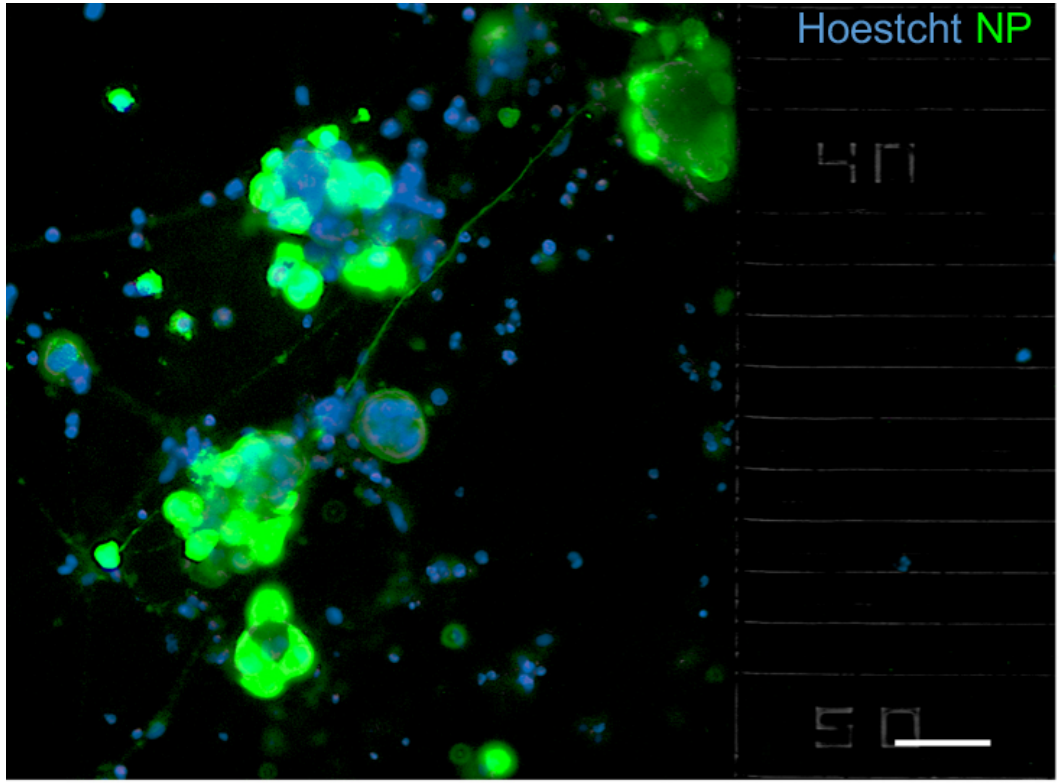

MicroBrain BT

# SARS-CoV-2 | a neurotropic pathogen?

Brain on a chip

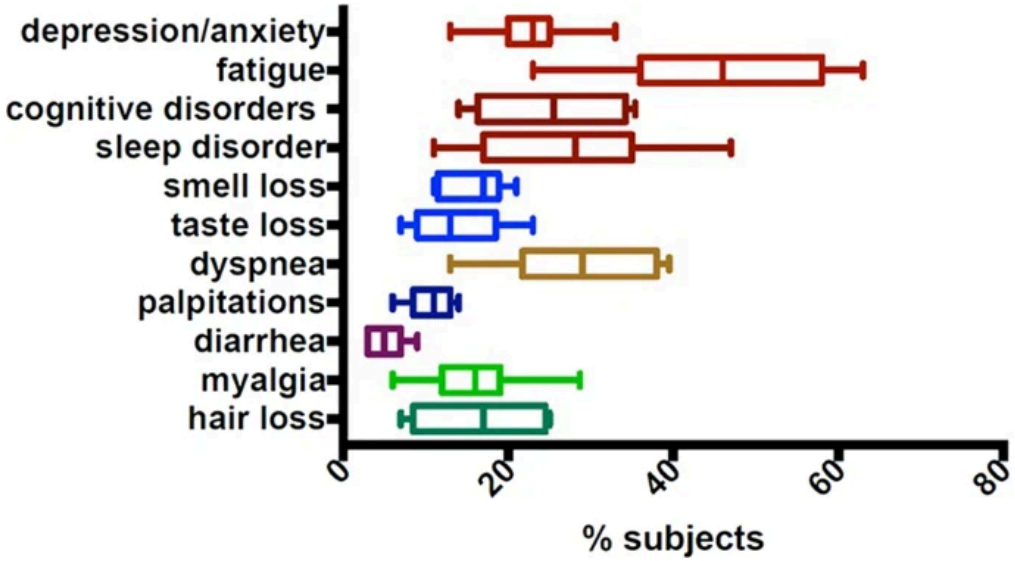
- SARS-CoV-2 transport along axons in neuron-epithelial networks



# LongCOVID | brain invasion and neuroinflammation

**Fig. 1: The frequency of the most common symptoms four week or more after the acute Covid-19 infection.**




Mantovani et al., *Cell Death & Diff* (2022)

## CURRENT CHALLENGES

late behavioral changes

- anxio-depressive symptoms
- memory/cognition troubles

persistent stimuli

- (neuro)inflammation
- virus

## Final remarks

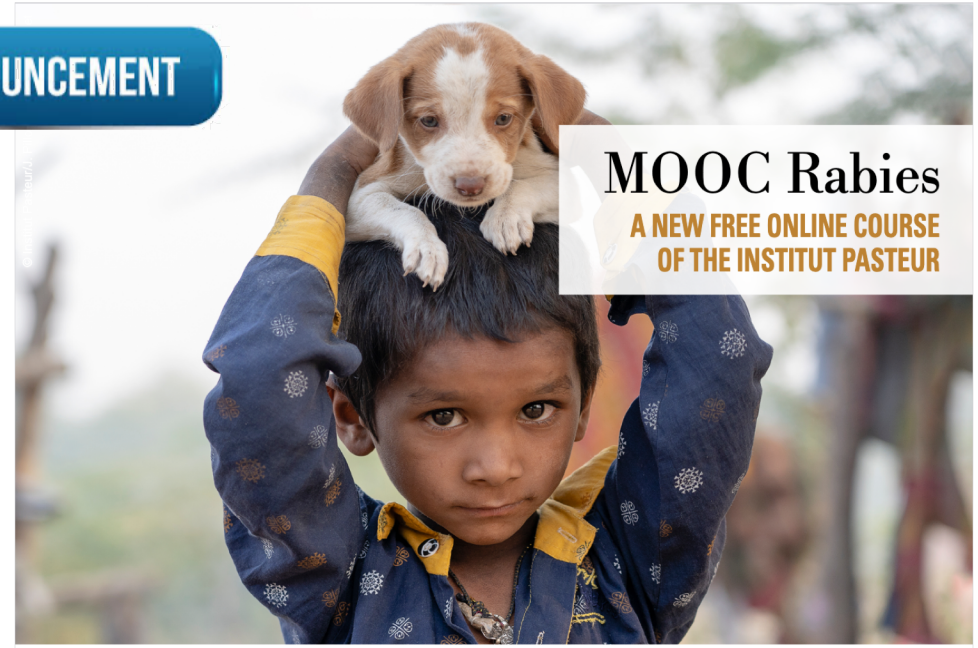
# RABIES

Towards an effective therapy for symptomatic cases

# SARS-CoV-2

An emerging virus that can infect (and persist ?) the brain

# ANNOUNCEMENT



# MOOC Rabies

## A NEW FREE ONLINE COURSE OF THE INSTITUT PASTEUR

Rabies is a fatal encephalitis caused by a Lyssavirus primarily transmitted by the bite or scratch of infected animals. Despite efforts in recent years, an estimated 60,000 human deaths from rabies still occur each year worldwide, primarily in Asia and Africa. The objective of this MOOC is to share the experiences and knowledge of international experts in animal and human public health on rabies. The course emphasizes the need for a multidisciplinary approach and «One Health» intersectoral cooperation for effective rabies control and elimination. This course explains the pathophysiology, epidemiology, vaccines and elimination strategies of the rabies virus.

### AT THE END OF THIS COURSE, YOU WILL BE ABLE TO:

- Explain the transmission, symptoms and clinical management of rabies
- Specify the importance of different animal reservoirs in the spread of the virus
- Describe human and animal vaccination strategies to combat rabies virus
- Identify the role of international organizations in rabies elimination
- Discuss rabies control strategies in different regions of the world

- Starts on Nov. 8, 2022
- Free registration
- Certificate available: 150€
- Total estimated time: 18 h
- Webinar with experts
- English with French subtitles

### REGISTER ON:

https://www.fun-mooc.fr/en/courses/rabies/

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because knowledge belongs to humanity"

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Thank you