Mechano-microbiology: how bacteria sense and respond to forces

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Global Health Institute and Institute for Bioengineering
School of Life Sciences

EPFL

Harnessing the power of data to tackle AMR - April 23, 2024

Will AI solve the AMR crisis?

Certainly not by itself.

We need new, high-quality data

Mechanics: a missing link in microbiology

The functions of many bacterial genes are unknown ⟶ New antibiotics 

Persat, Cell 2015
Dufrene, Nature Reviews Microbiology 2020

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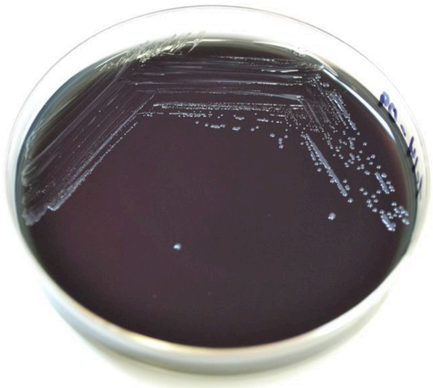

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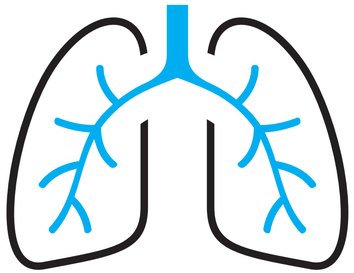

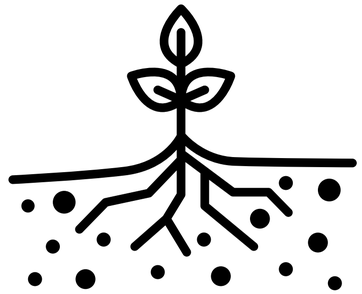

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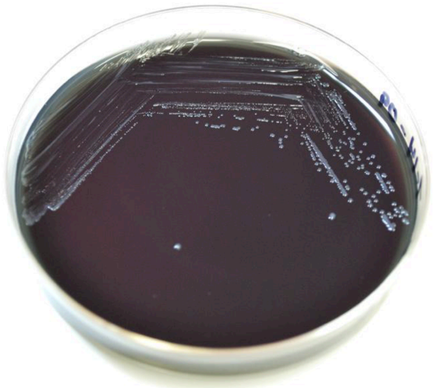

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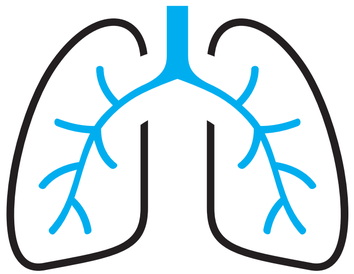

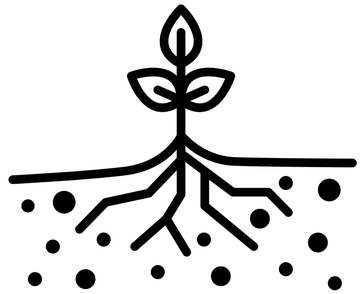

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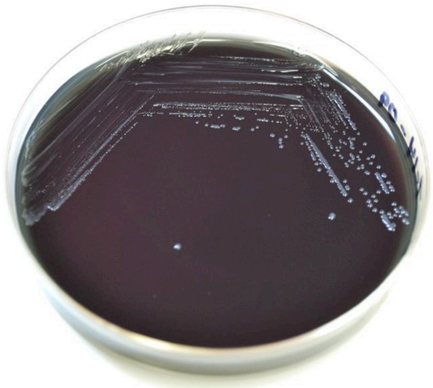

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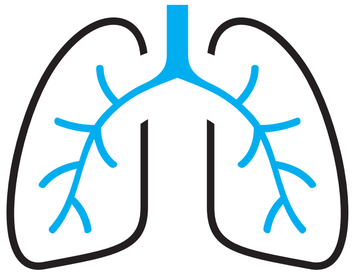

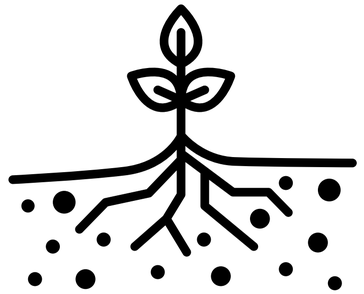

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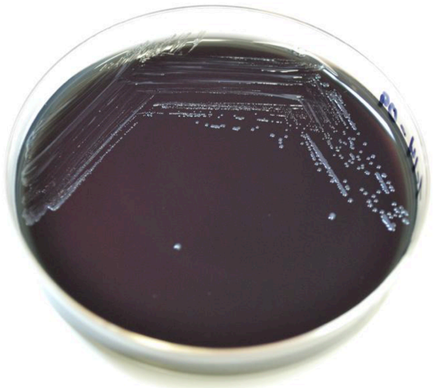

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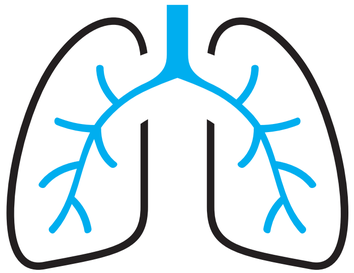

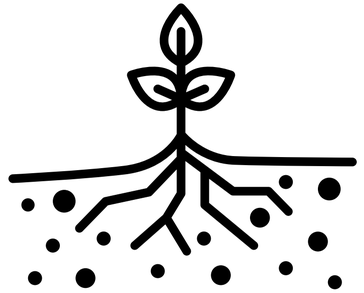

My lab's interdisciplinary approach:

Engineer mechanical microenvironments

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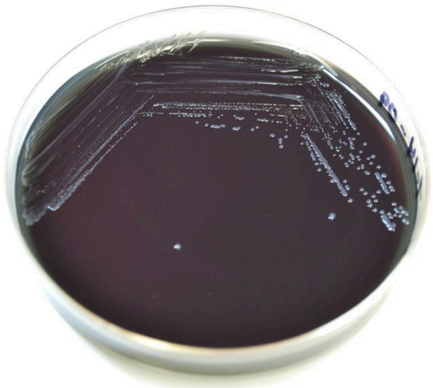

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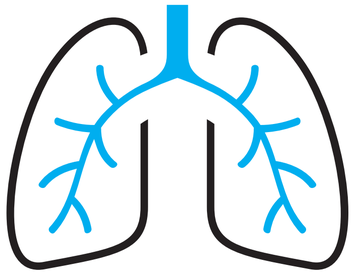

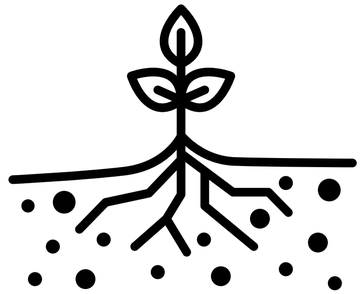

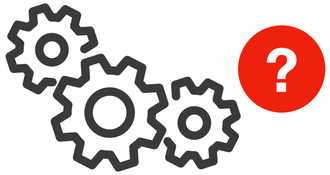

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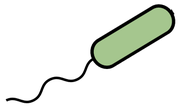
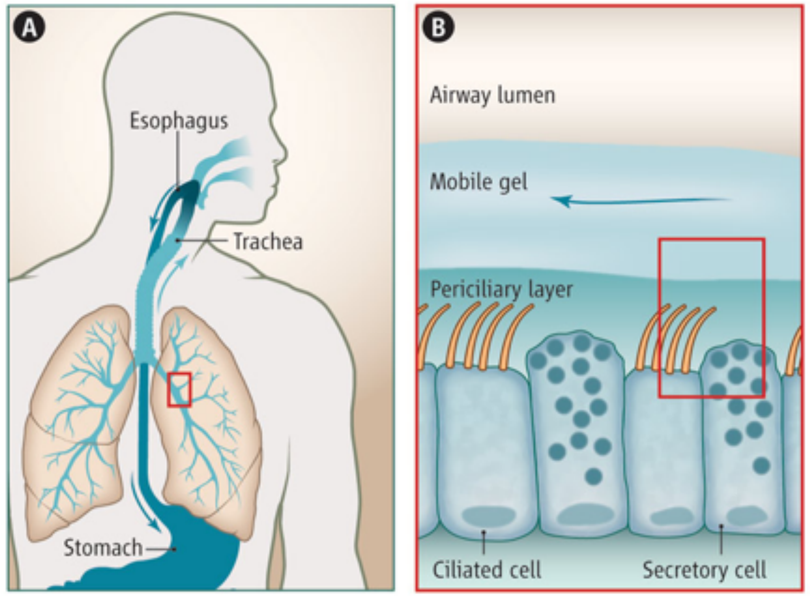


Investigate how forces regulate **bacterial physiology**

Persat, Cell 2015
Dufrene, Nature Reviews Microbiology 2020

The airway is a mechanically complex environment



Dickey, 2012, Science

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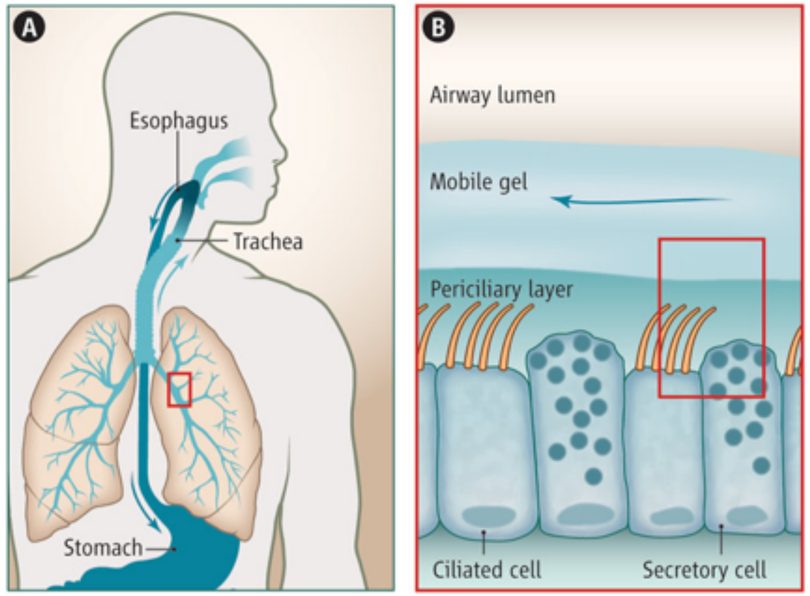

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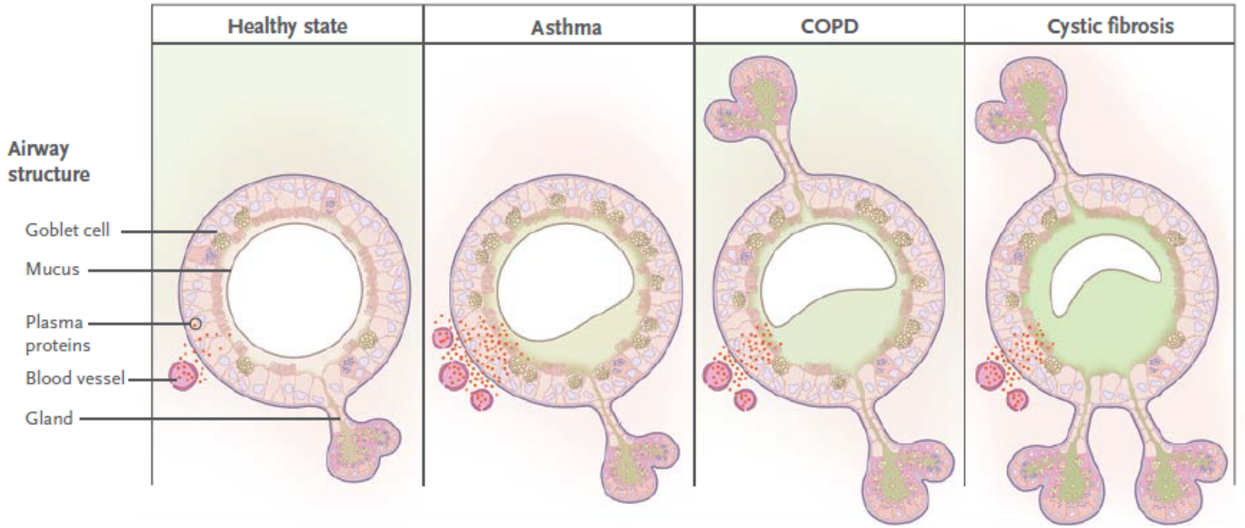

Fahy and Dickey, 2010, NEJM

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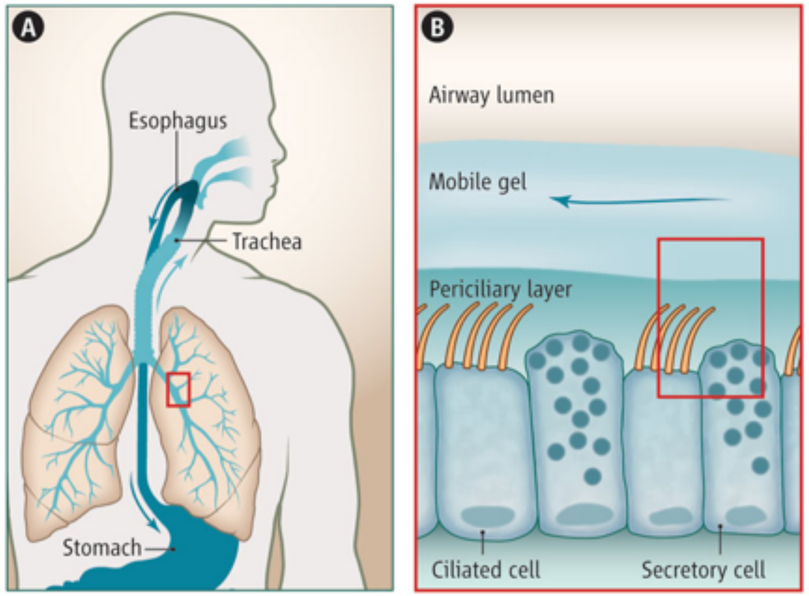

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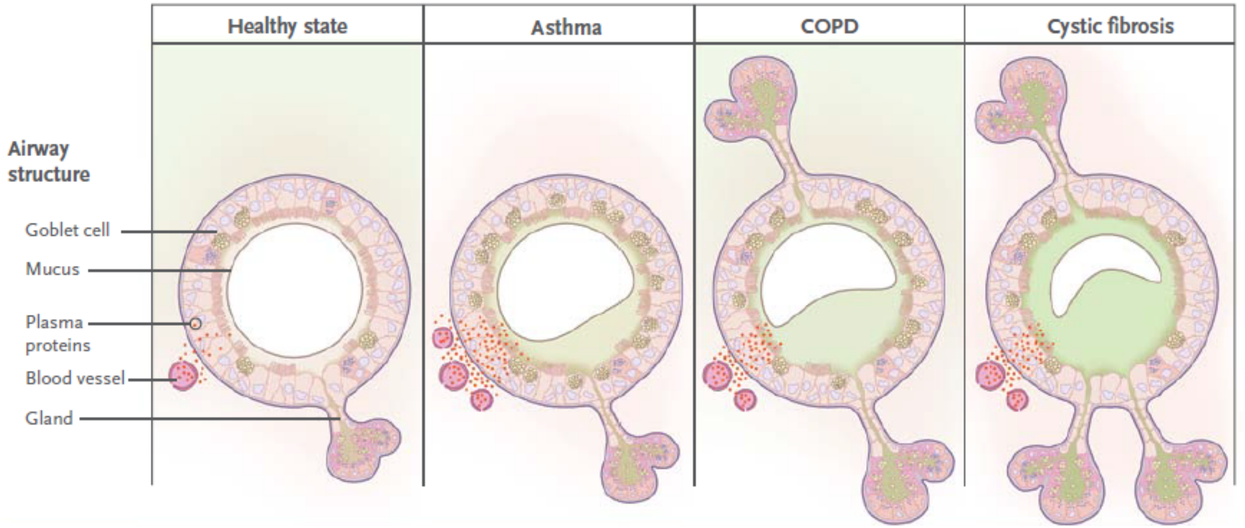
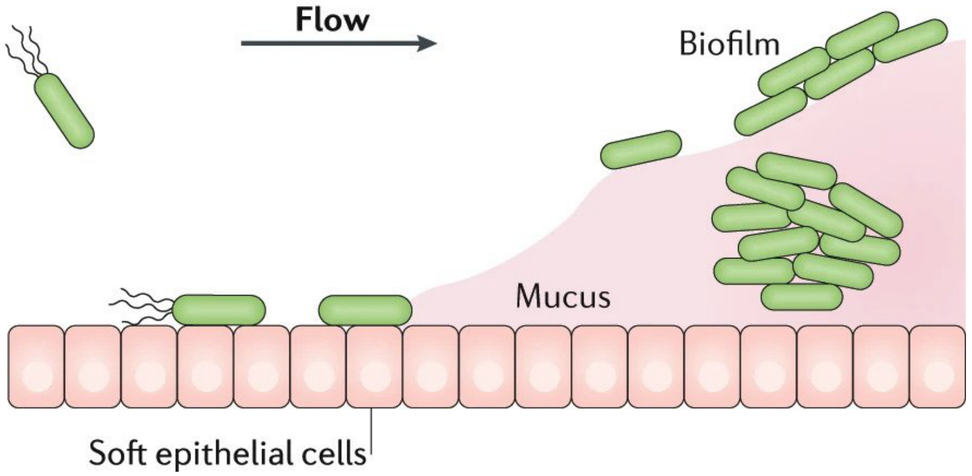


Fahy and Dickey, 2010, NEJM

Mucus is the most accessible material in the airway

Compromised mucus is associated with sensitivity to *P. aeruginosa* infections

Mechanobiology in the soft world



Dufrêne and Persat, *Nat. Rev. Micro.* 2020

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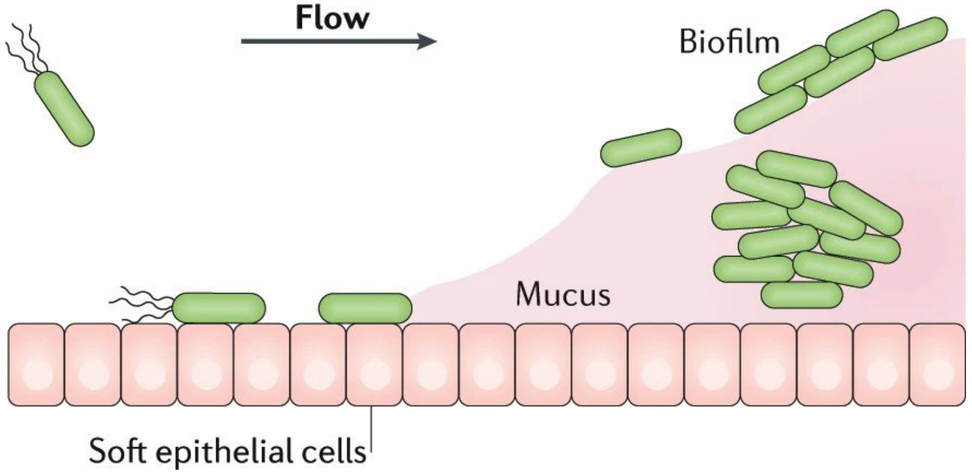

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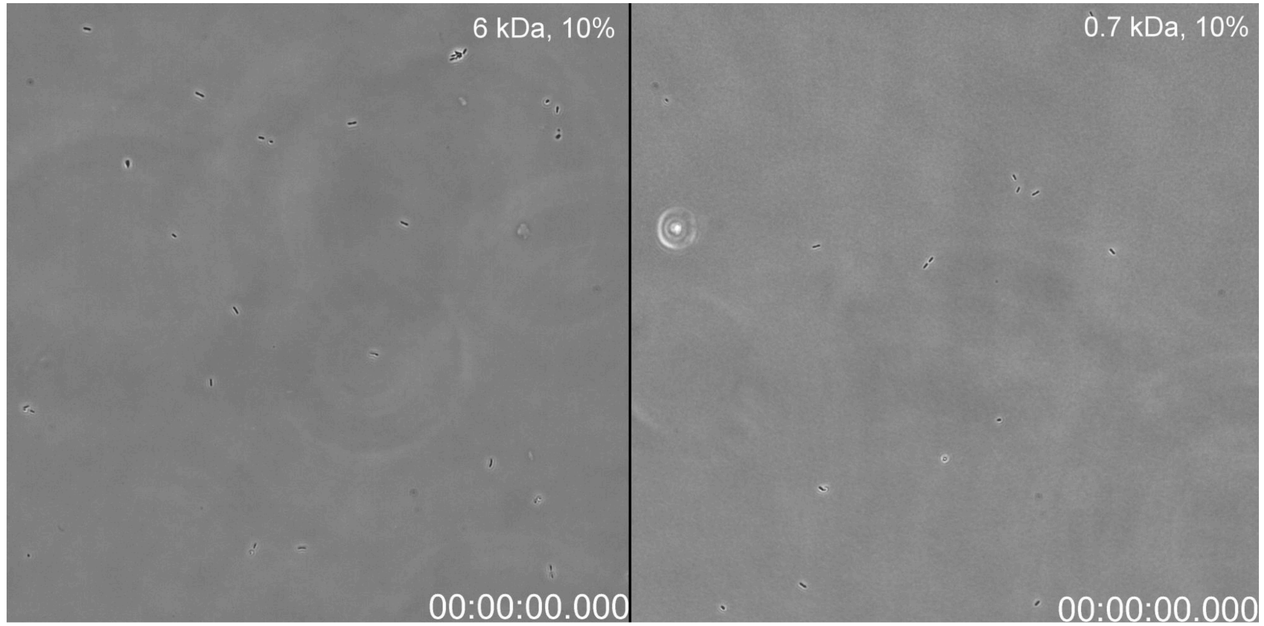
Mechanical properties impact biofilm formation



Cont, eLife 2020
Cont, mBio 2023

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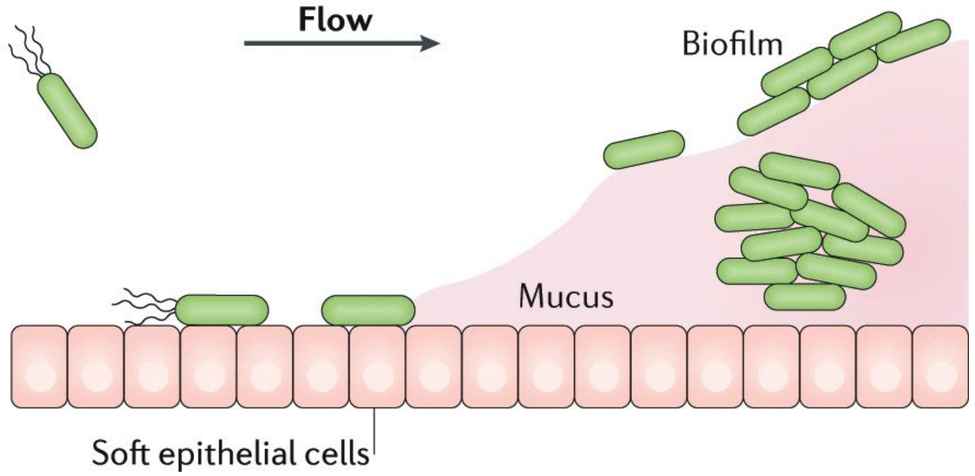

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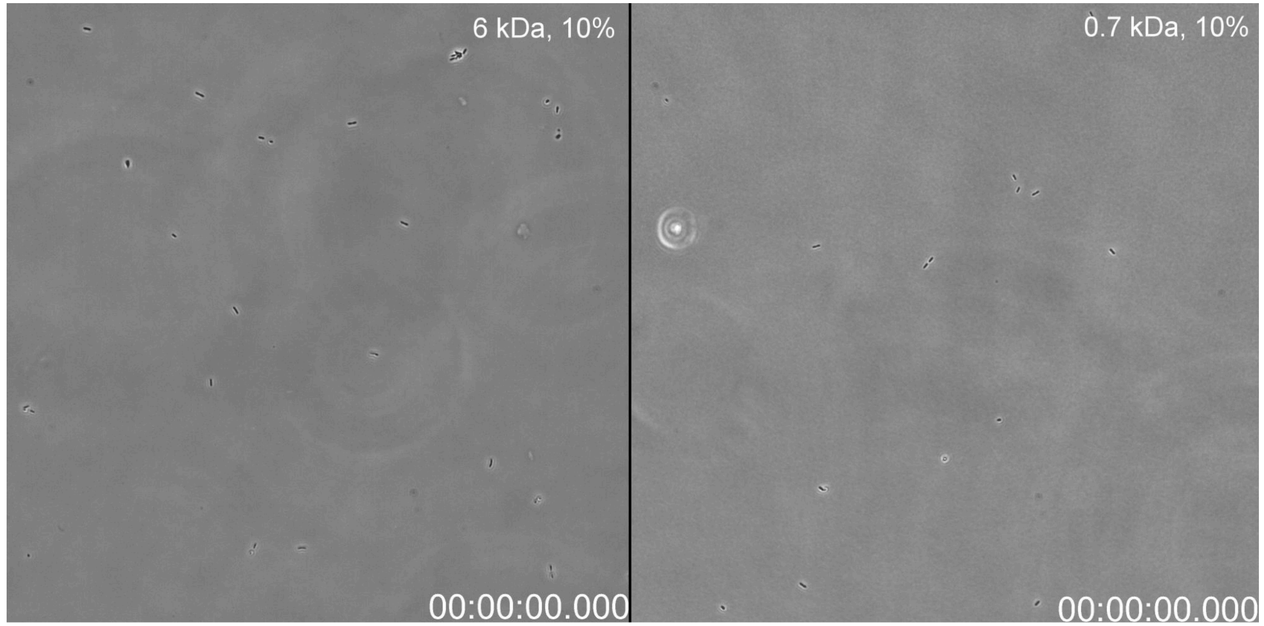


Cont, eLife 2020
Cont, mBio 2023

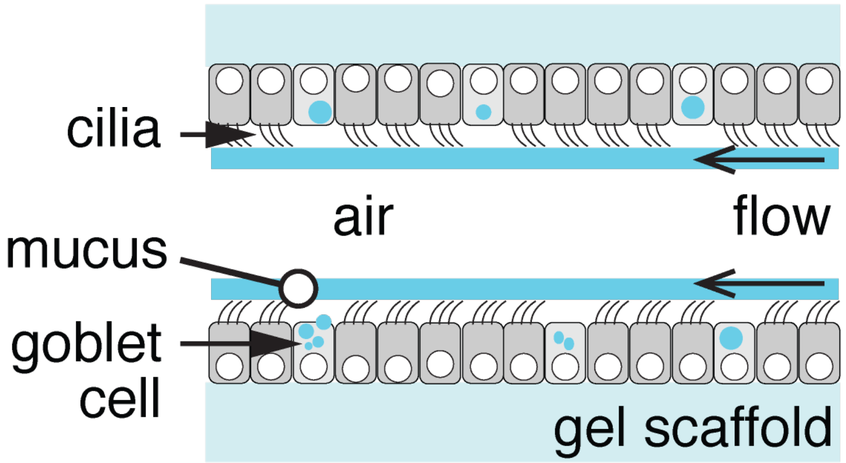
How do *P. aeruginosa* cells colonize and form biofilms *in vivo*?

Airgels: tube-shaped airway organoids

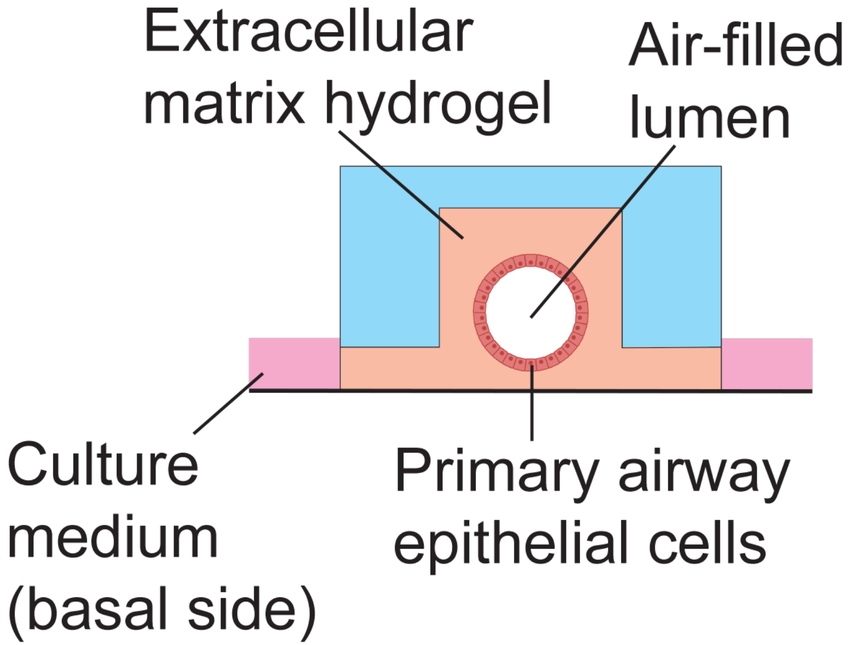
(**air**way in a **gel**)

Technical requirements:

- suitable for microscopy
- tube-shape



Cross-sectional view



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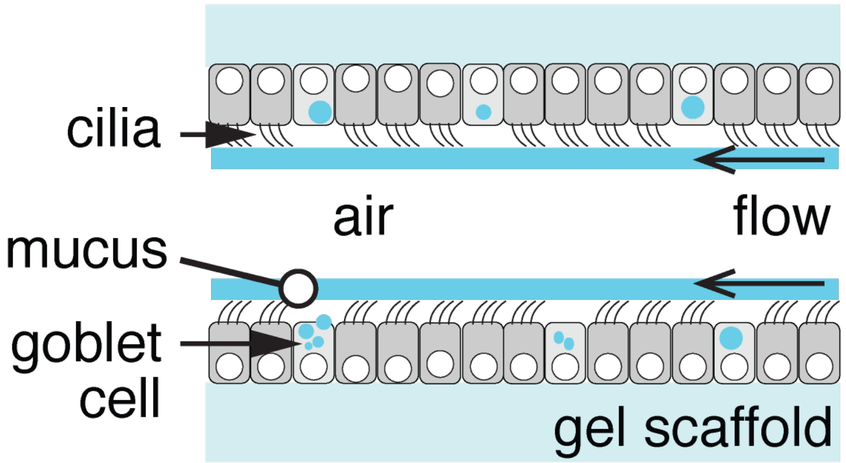

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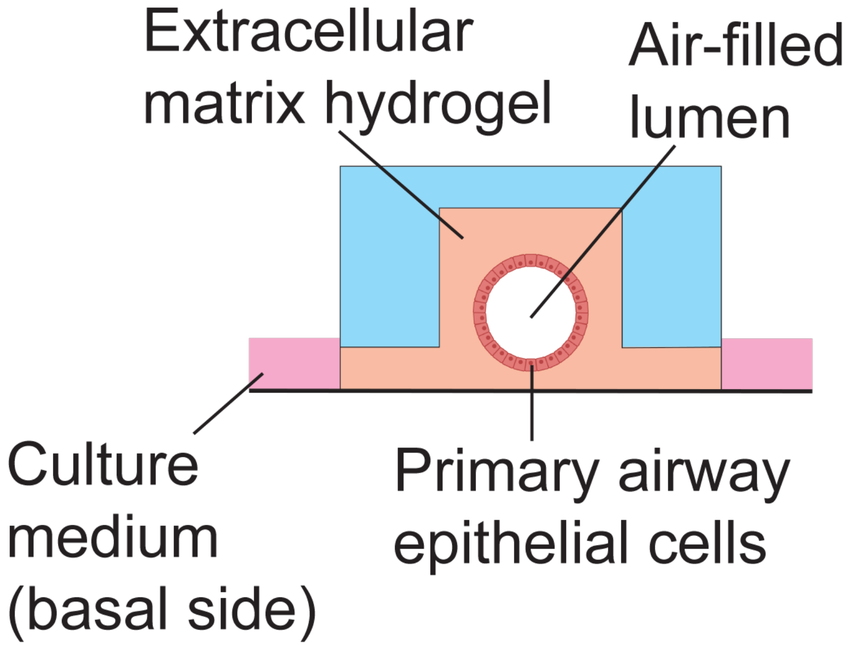
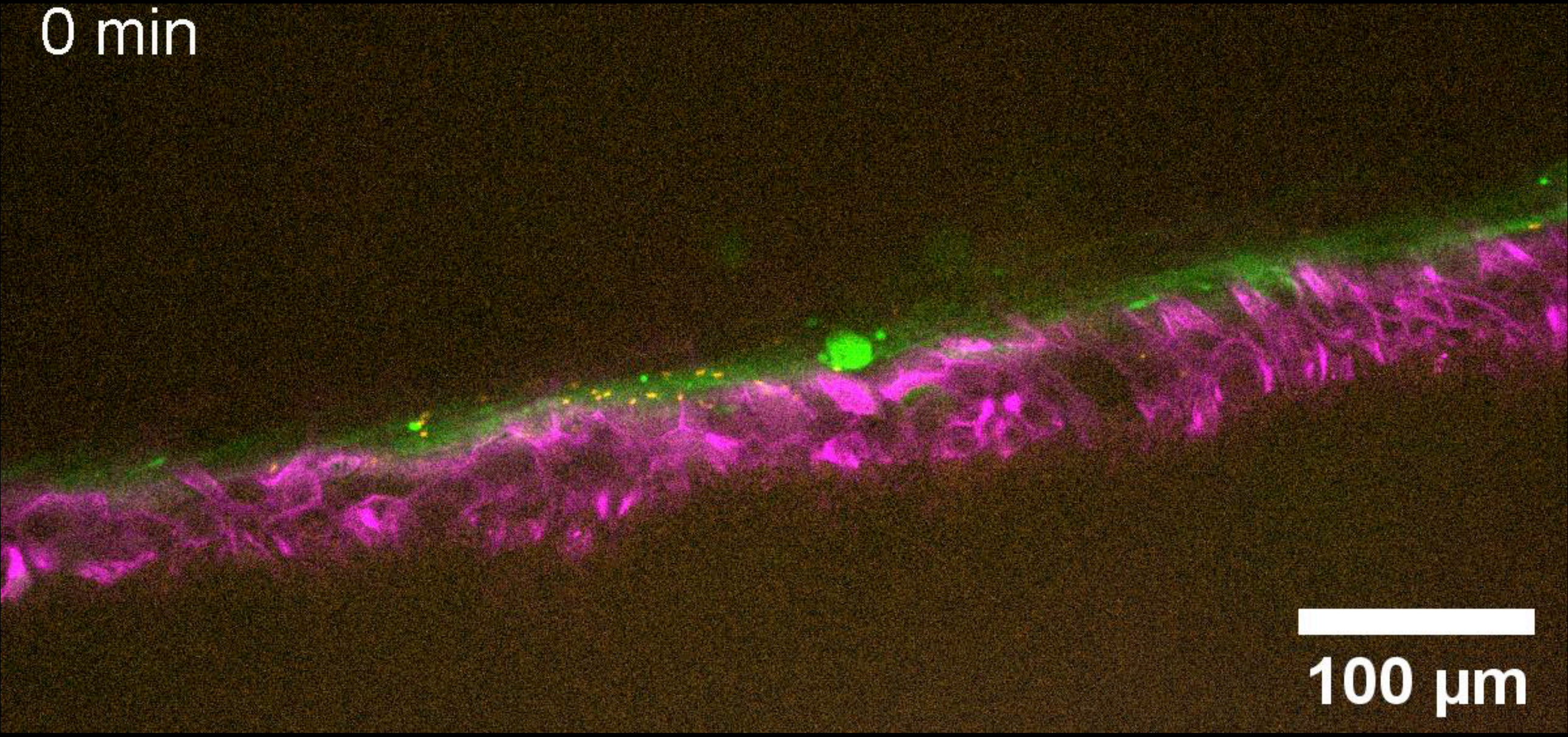
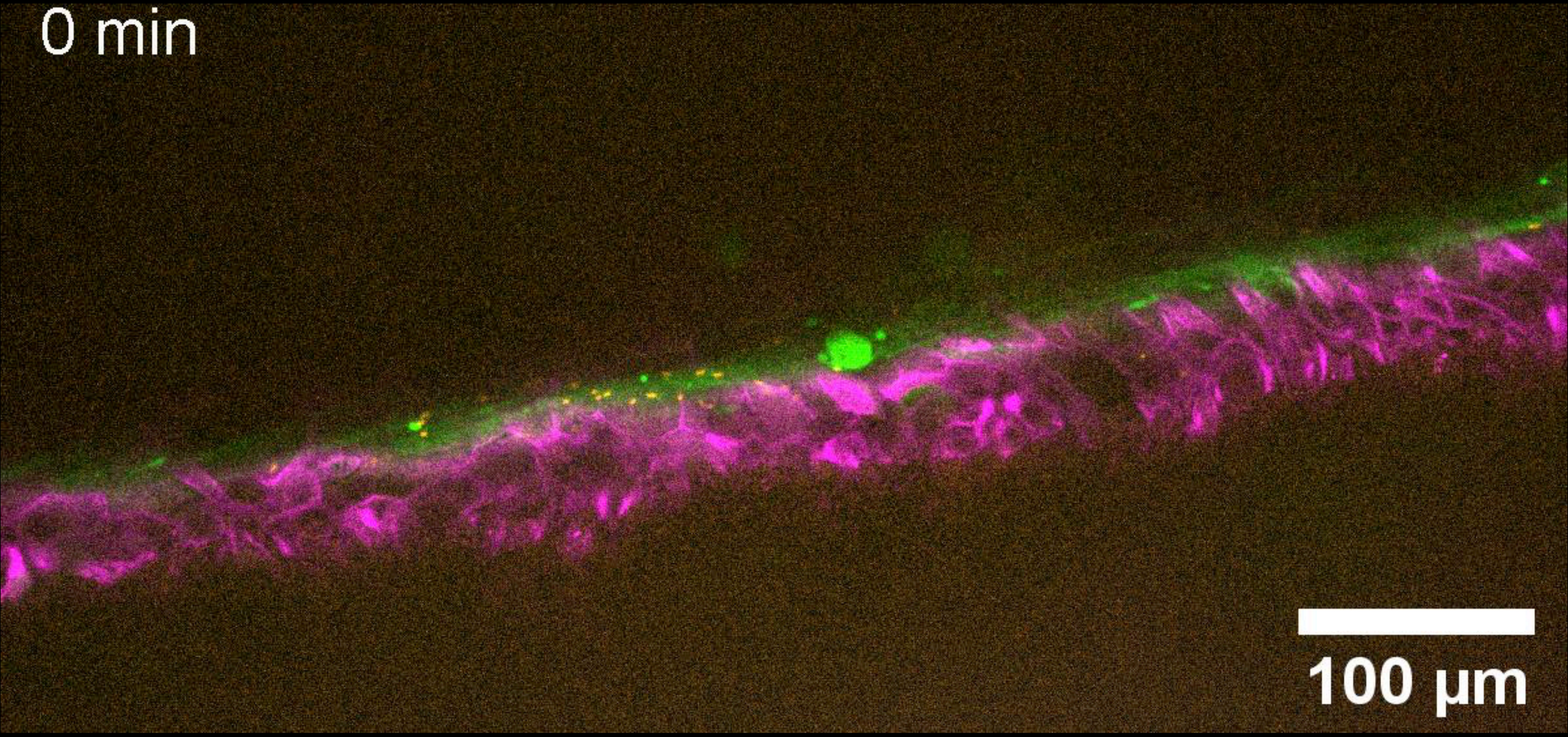


Rossy, Plos Bio 2023


0 min
100 µm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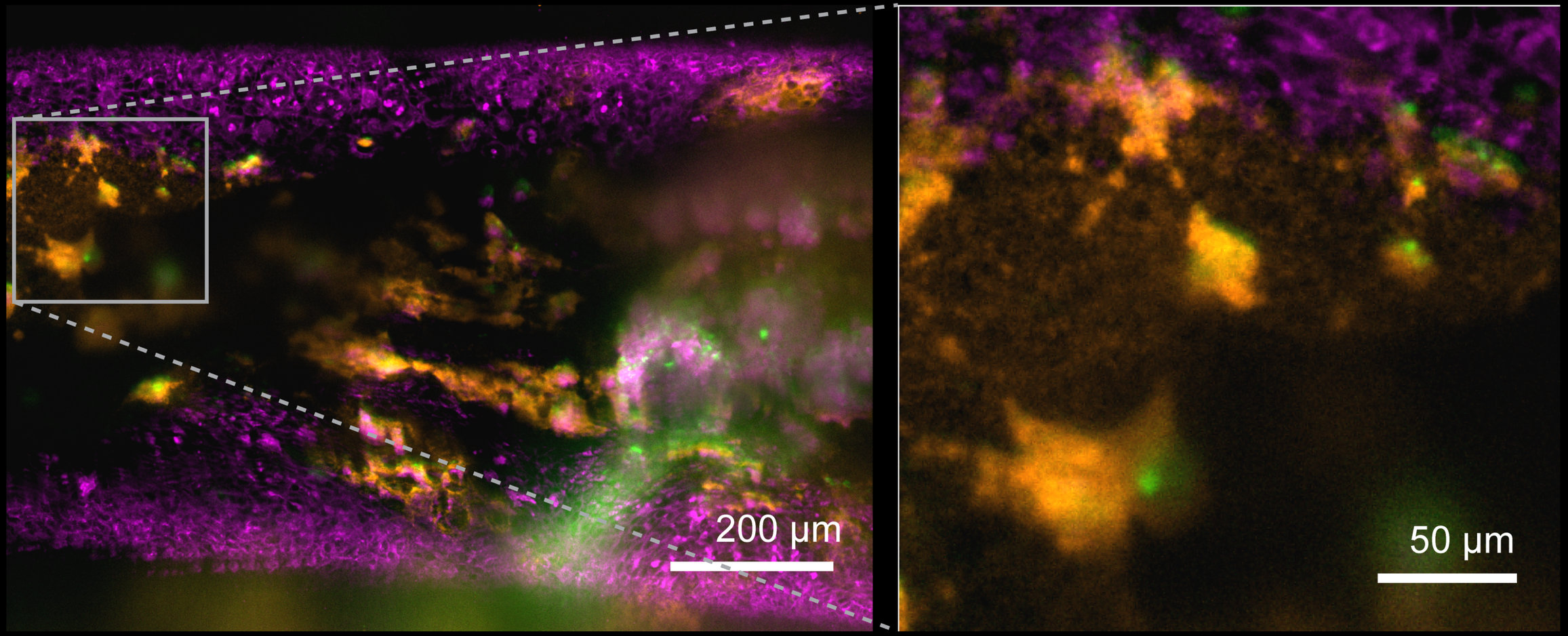
Live visualization of infection in Airgels

Mucus Plasma membrane / *P. aeruginosa*



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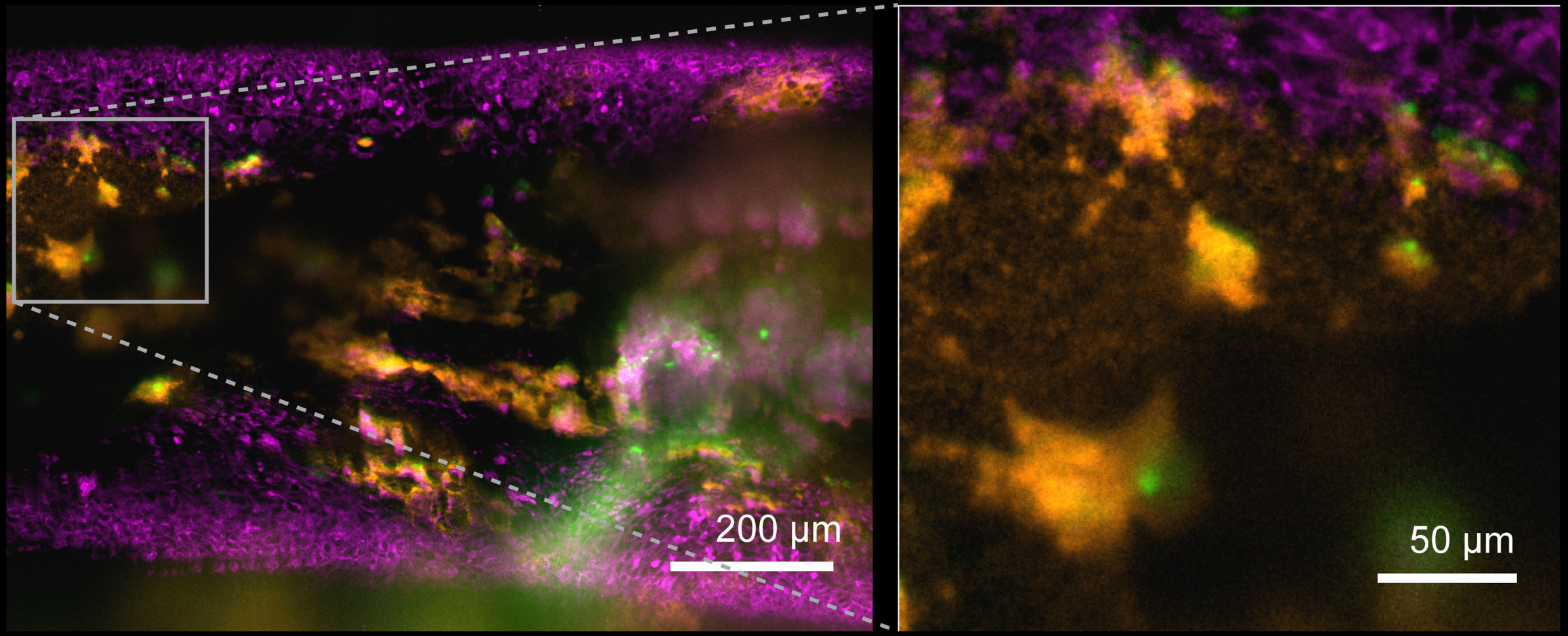
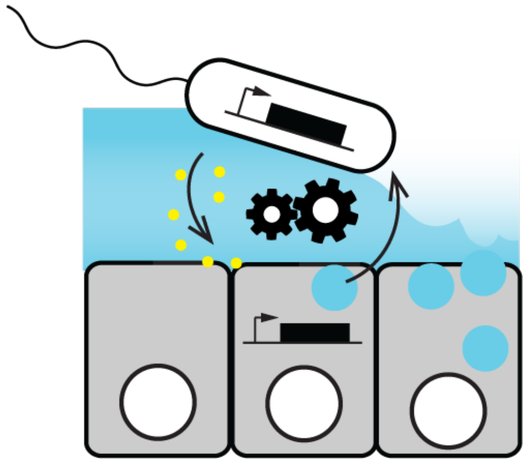


Rossy, Plos Bio 2023

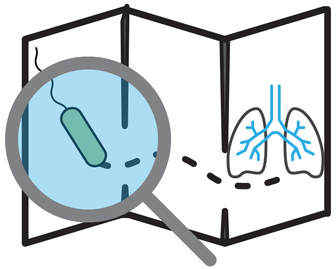
A new perspective on infections



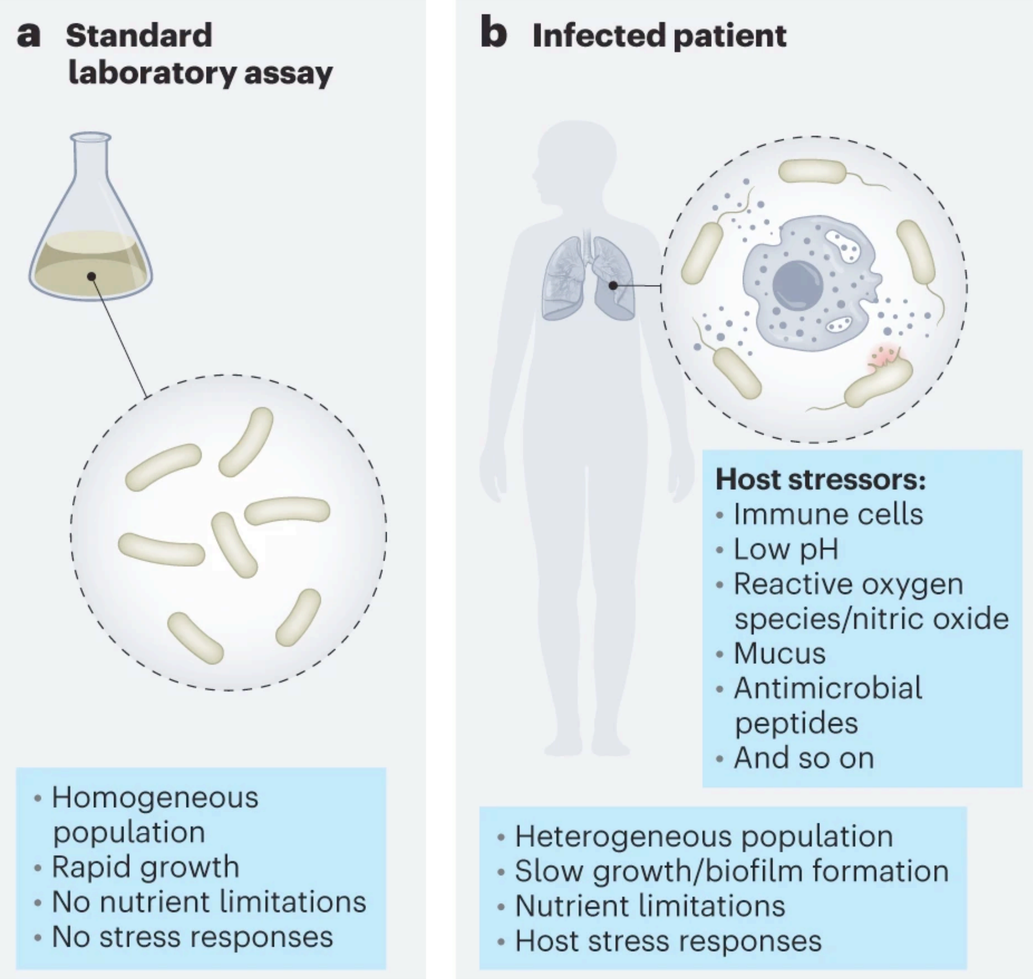
- How **mechanical signals** contribute to pathogenicity
- Generate **new data** to identify alternative therapeutic targets
- Current efforts: use predictive power of AI to design compounds interfering with new targets.

Microbiology

Engineering



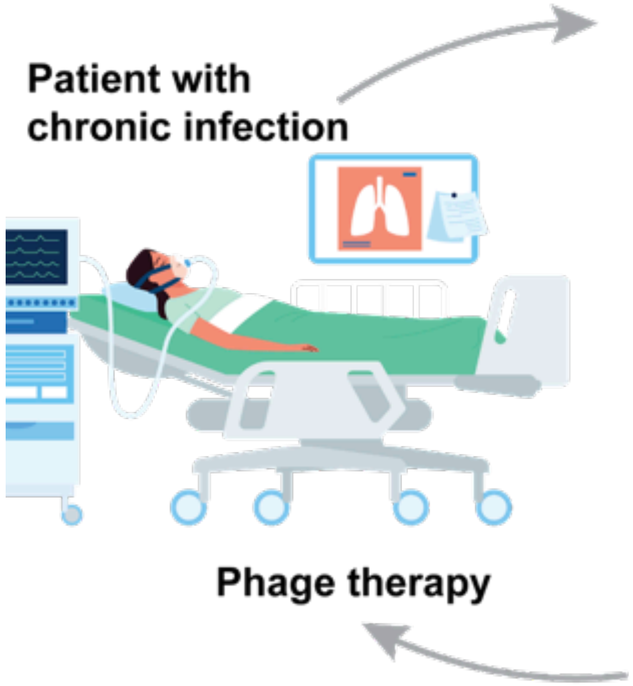
The patient environment: a missing link in therapy



- Most antibiotics are discovered *in vitro*
- Bacterial physiological adapation *in vivo* may treatment efficacy

Sollier, Nat Micro 2024

Personalized phage therapy against antibiotic-resistant *Pseudomonas aeruginosa* respiratory infections



Pneumology

Dr. Angela Koutsokera
& Dr. Georgia Mitropoulou

Phage production

Dr. Gregory Resch

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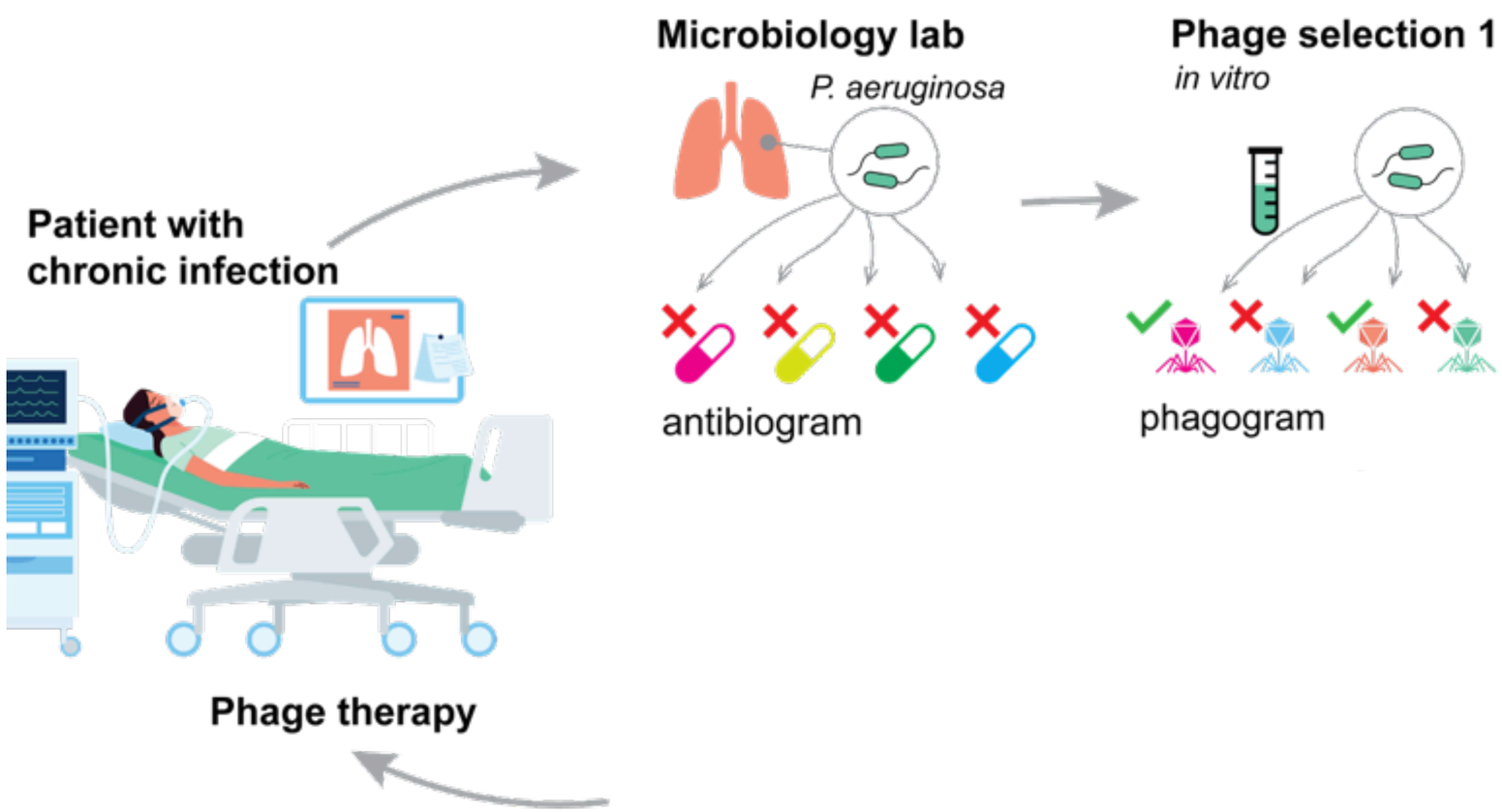

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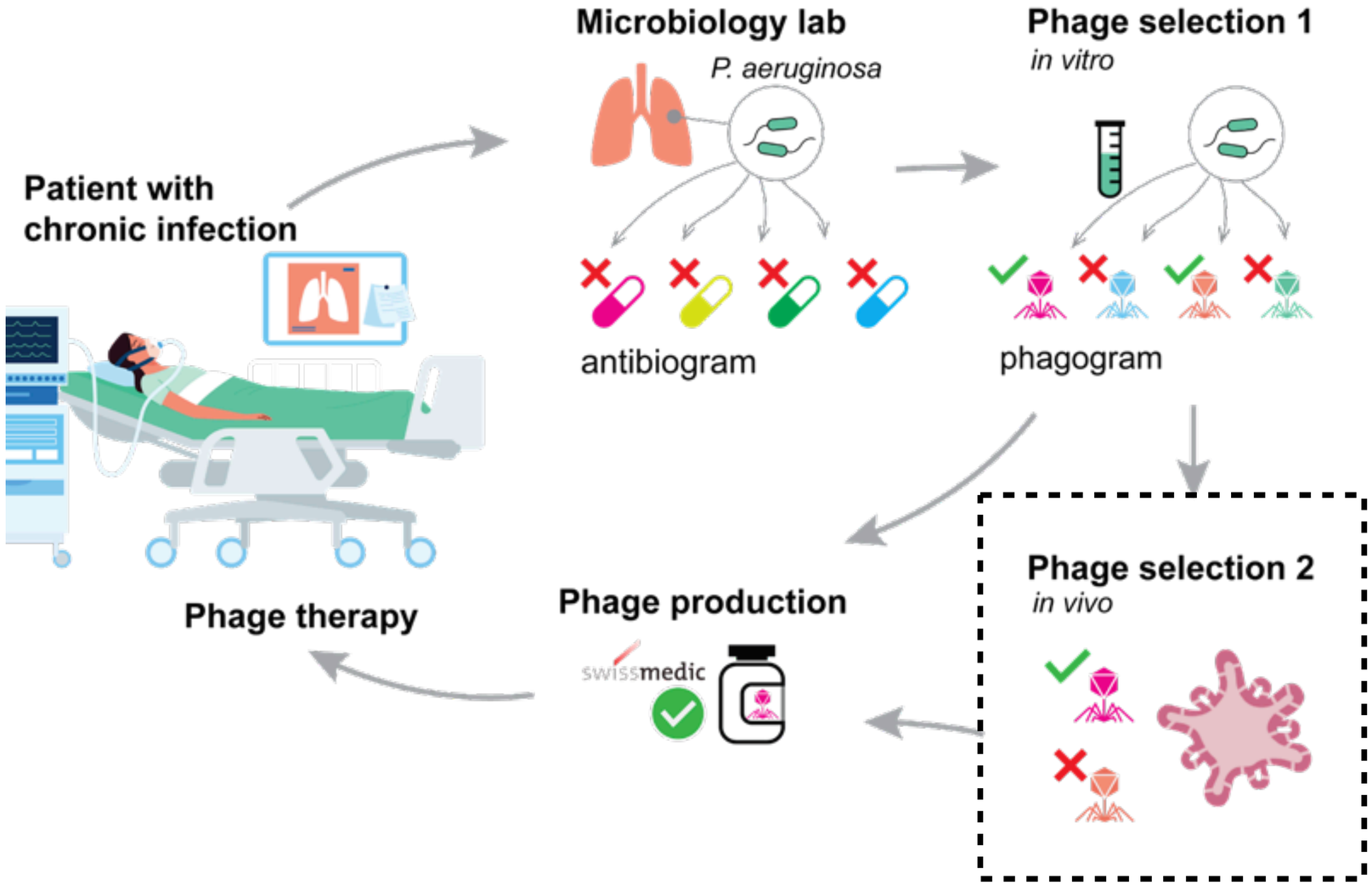

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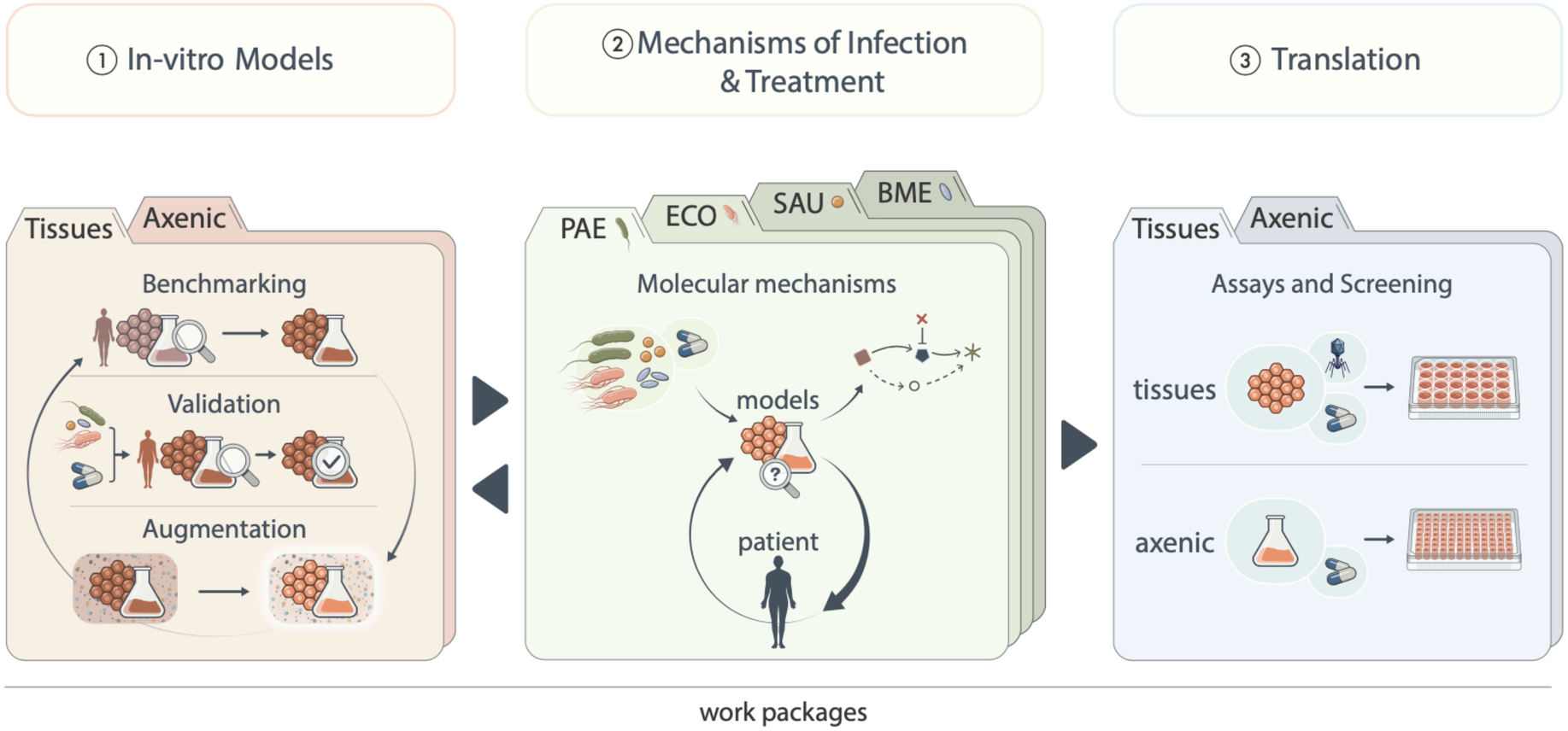
NCCR AntiResist

New Approaches to Combat Antibiotic-Resistant Bacteria

- To bring a **paradigm shift** in antibiotic discovery
- To **close the gap** between the **bedside and the bench**
- To **bridge disciplines** and **institutions** within **Switzerland**
- To stimulate **long-lasting partnership** with the **private sector**
- To equip **future generations of scientists** with **interdisciplinary expertise**

NCCR AntiResist

Connecting clinical data and models development – phase 2



NCCR AntiResist

NCCR data catalog - Promoting data sharing within and outside the NCCR

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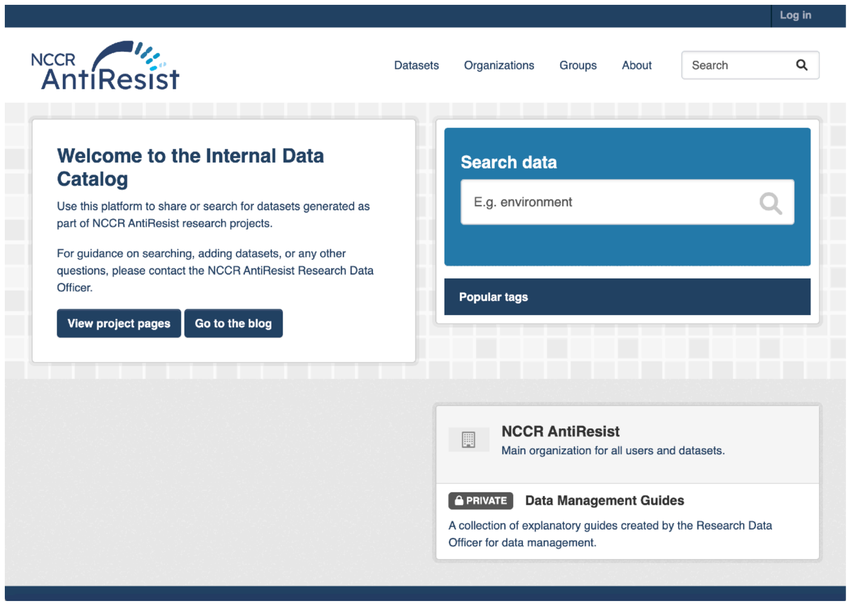
About

- Unifying platform for data stored in resources across institutions
- Accessible from any institution with a custom user account



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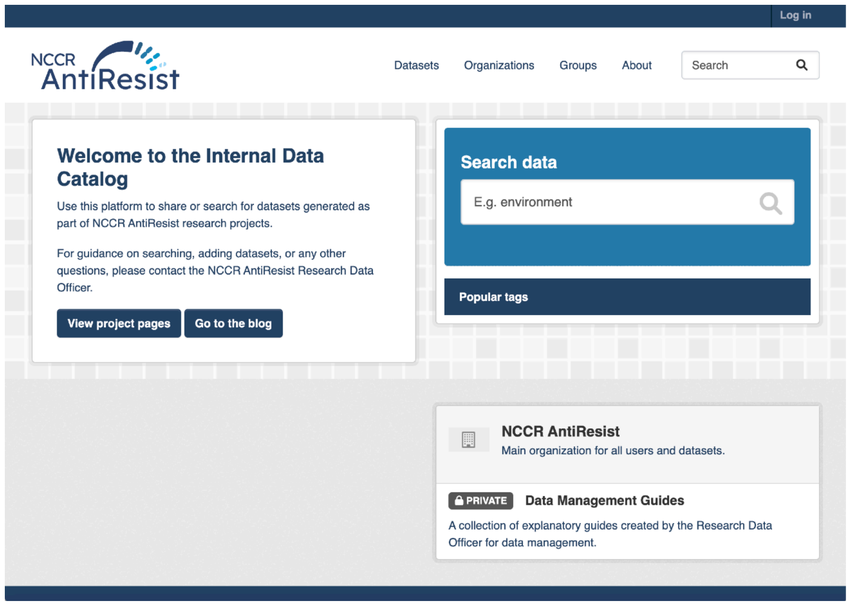

Recording Data

- Customized metadata
- Complements lab records
- Can include protocols and supporting documents

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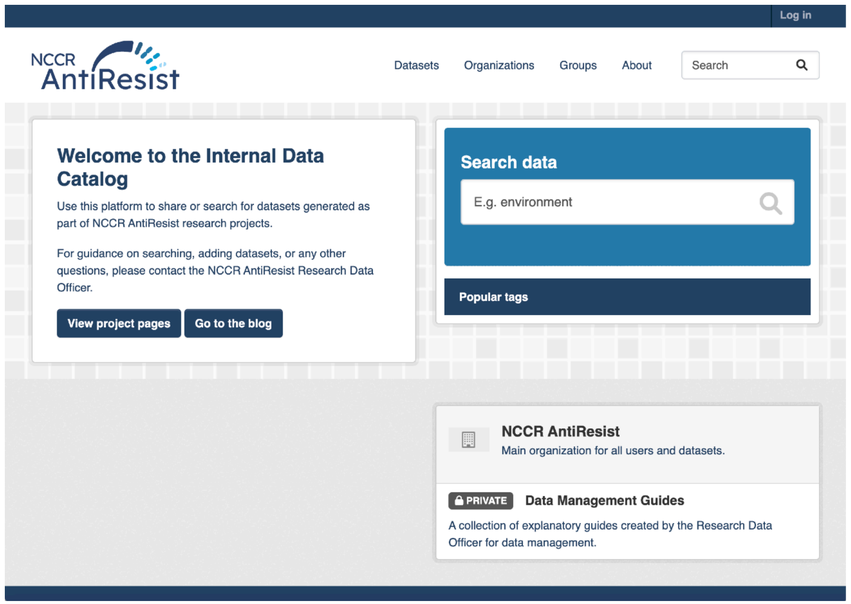

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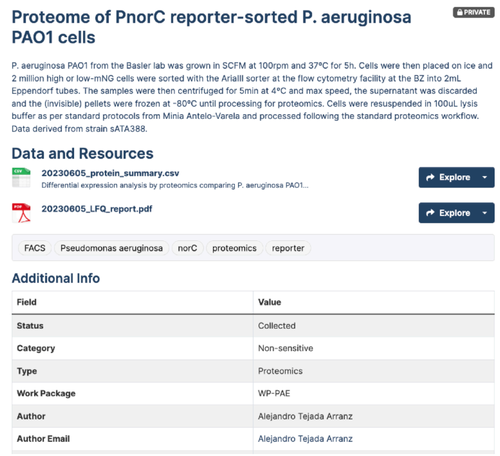
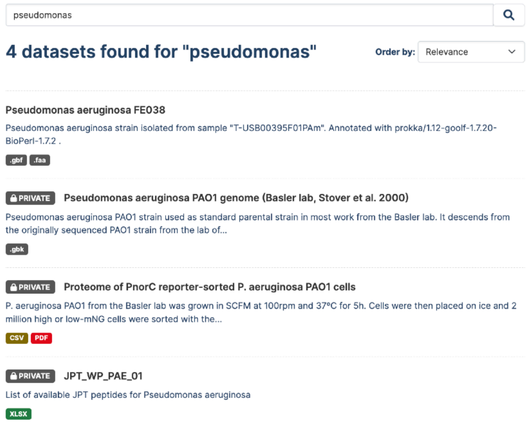


Finding Data

- Search by any fields
- Organized with groups, tags
- Contents of many filetypes become searchable



PERSATLAB

http://p-lab.science

@alexpersat

Team:

Marco Kühn
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Jeremy Wong
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Sourabh Monnappa
Sofya Mikhaleva
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Chia-Ni Tsai
Han-Yi Huang
Po-Long Hsiao
Elke Holderbeke

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