

Mechano-microbiology: how bacteria sense and respond to forces

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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



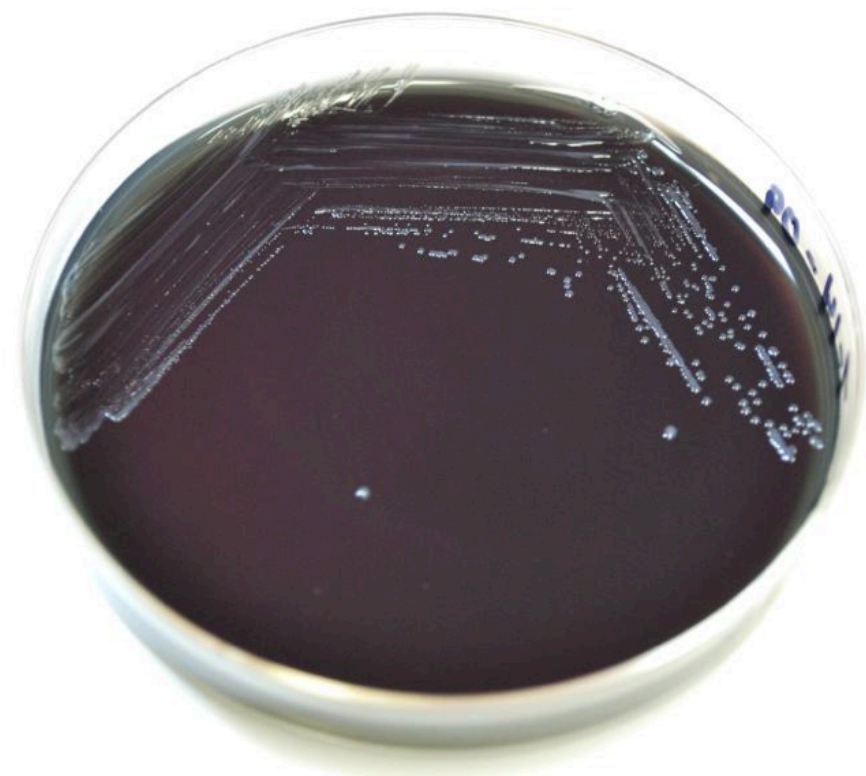
Mechanics: a missing link in microbiology



The functions of many bacterial genes are unknown

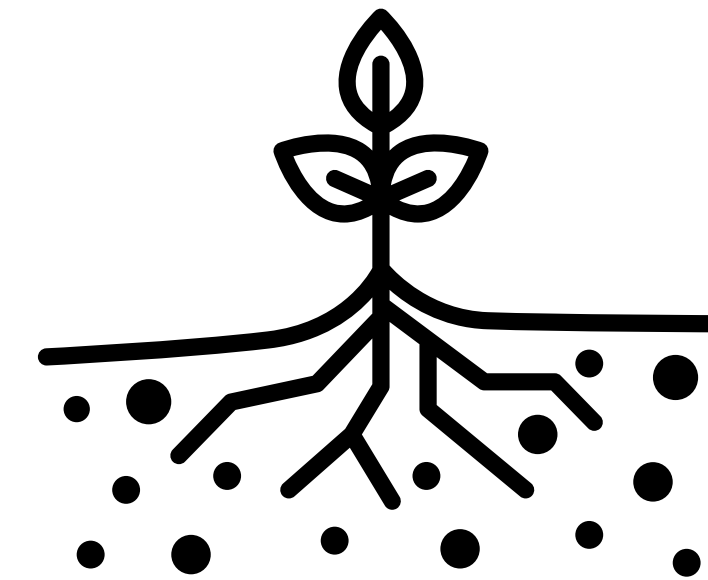
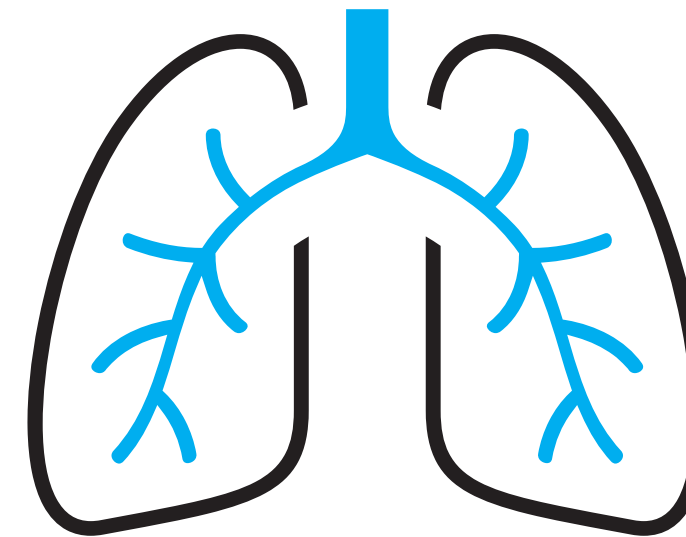
—————> New antibiotics 

LAB



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ENVIRONMENT



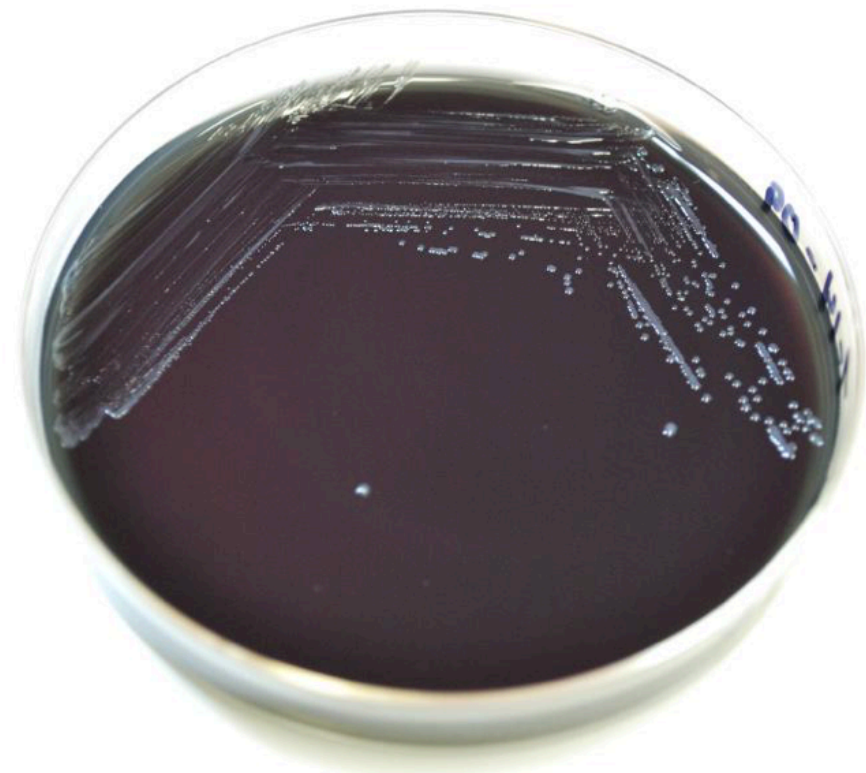
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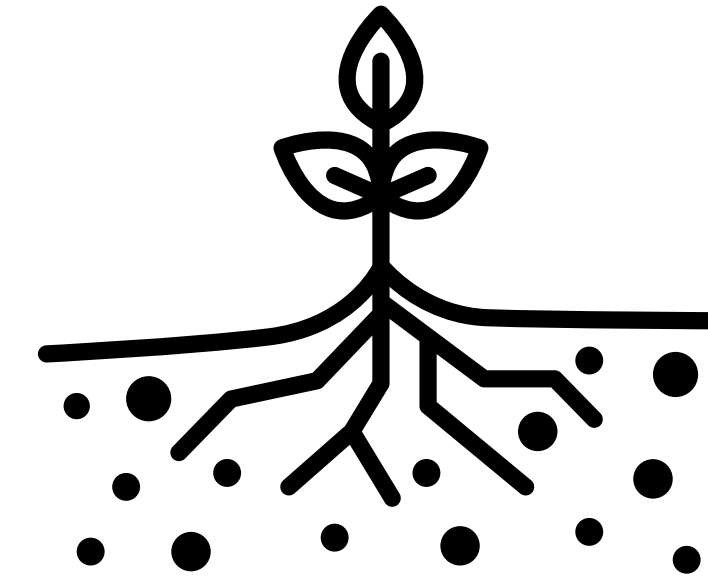
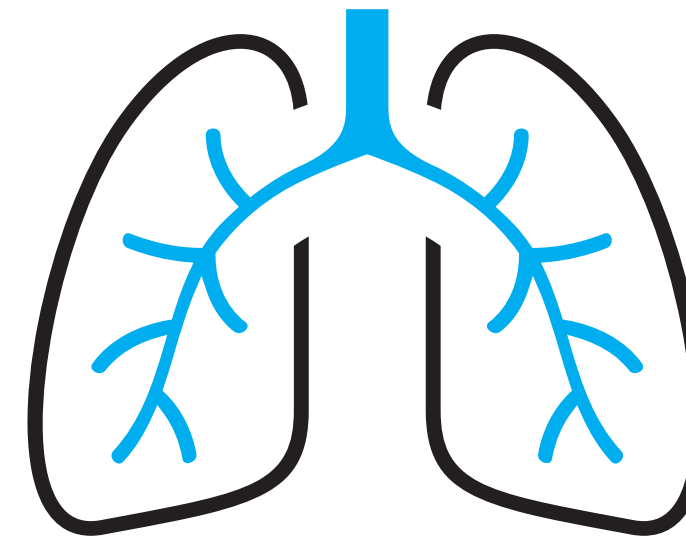
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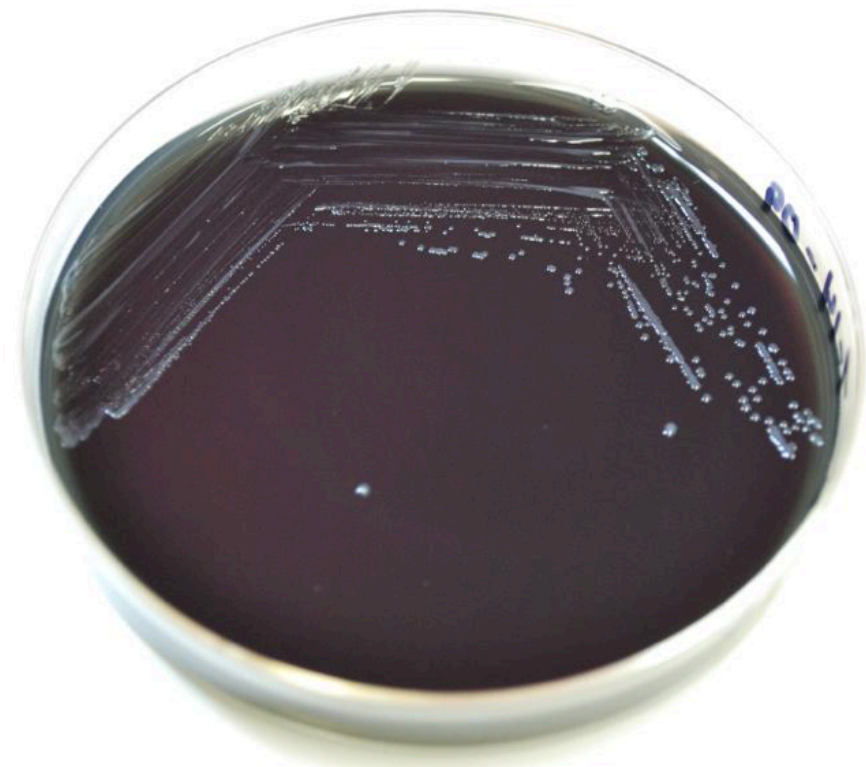
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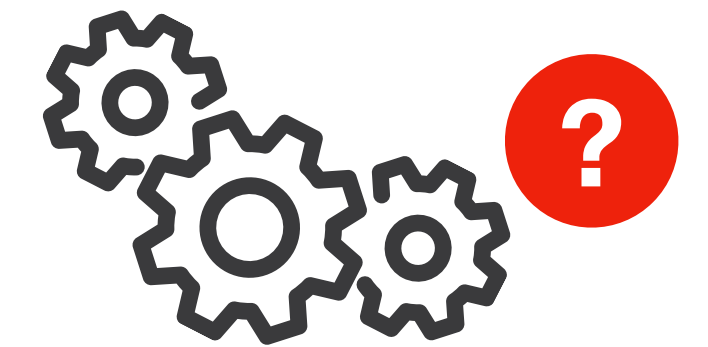
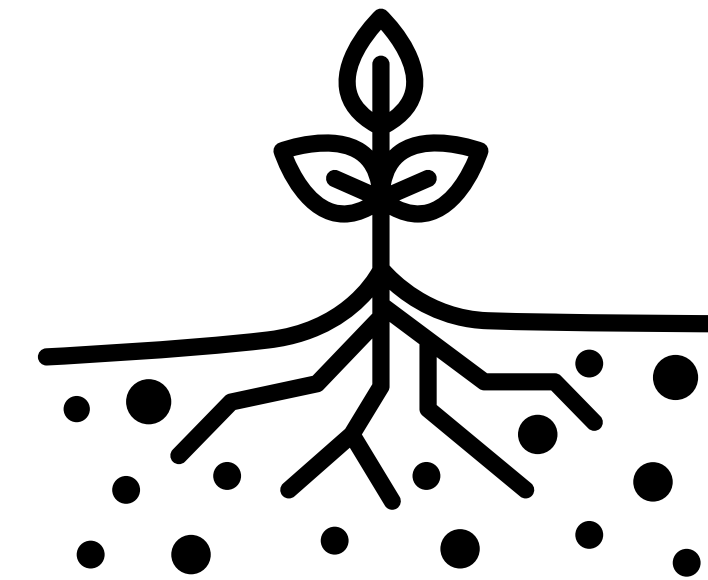
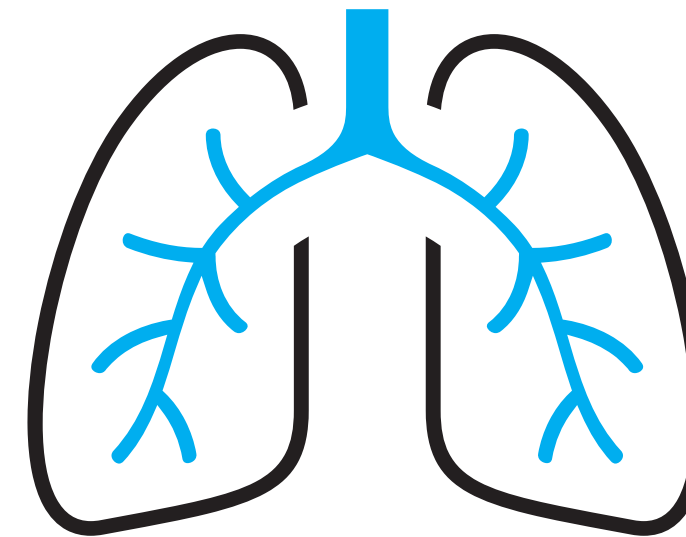
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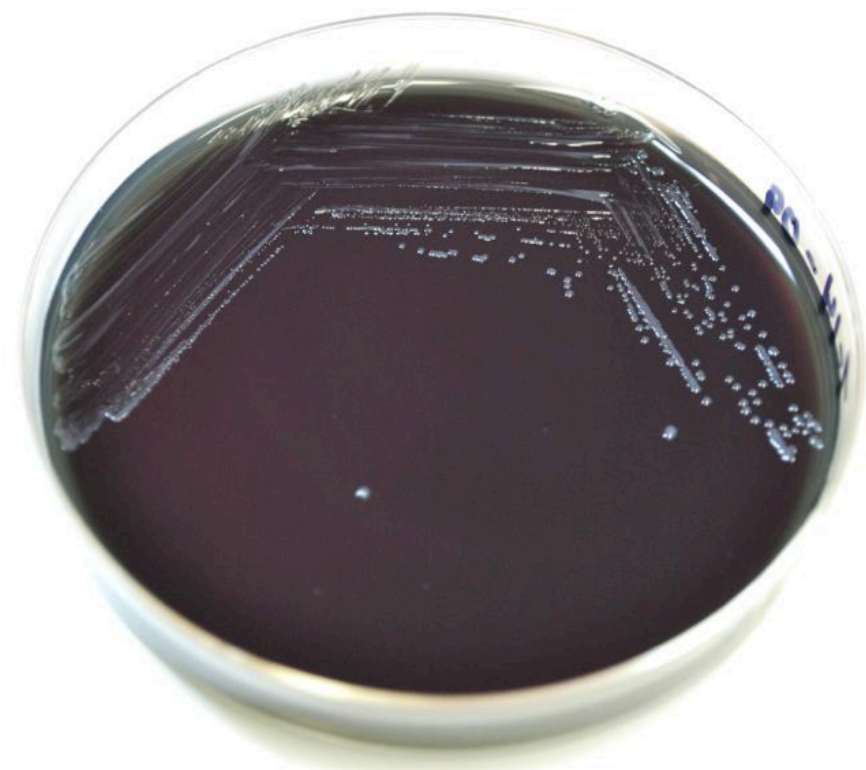
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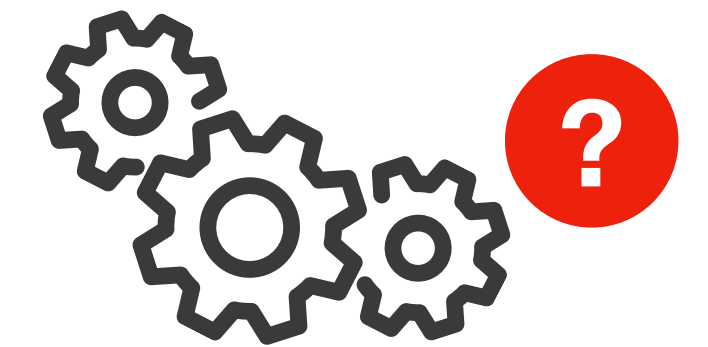
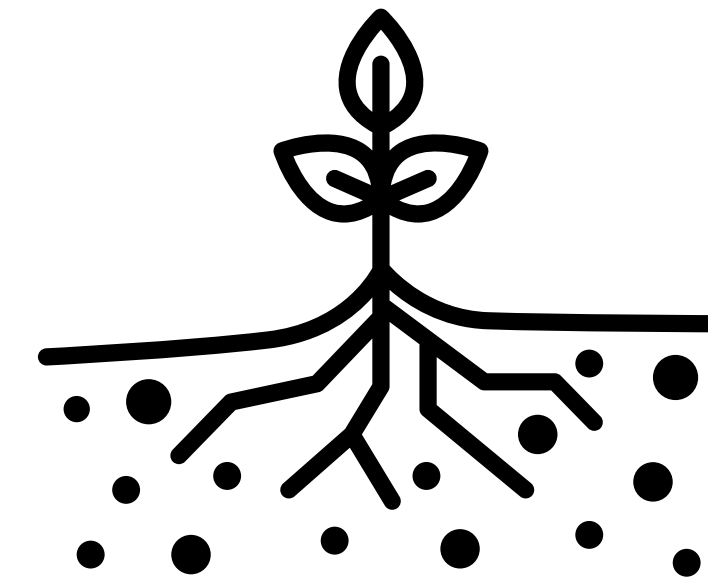
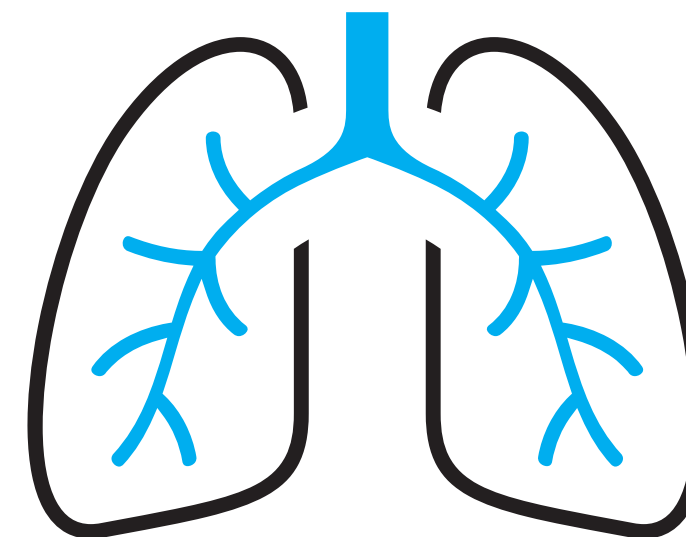
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My lab's interdisciplinary approach:



Engineer mechanical microenvironments

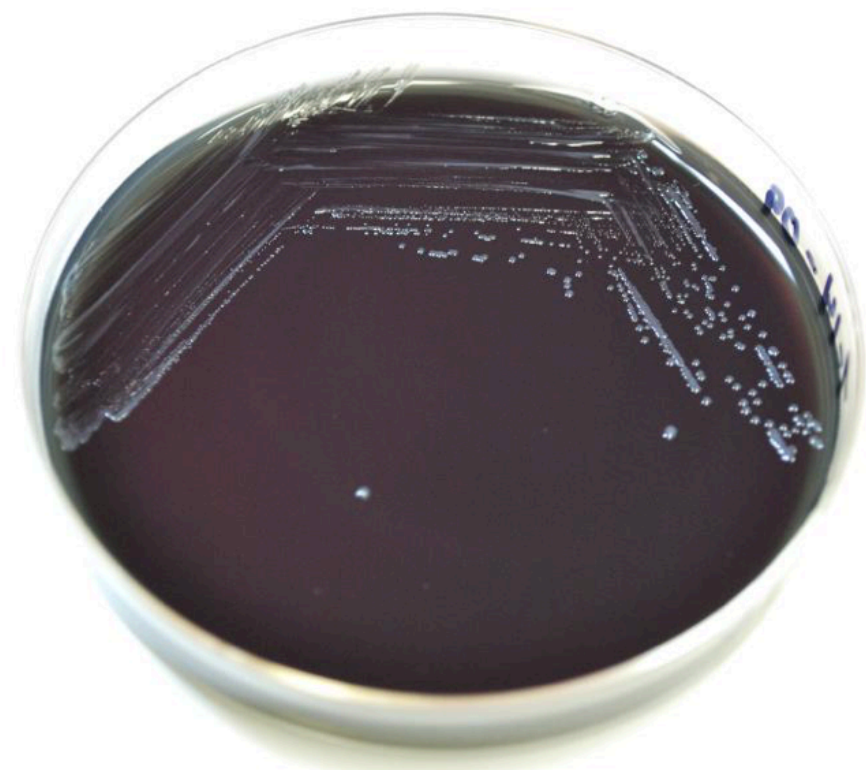
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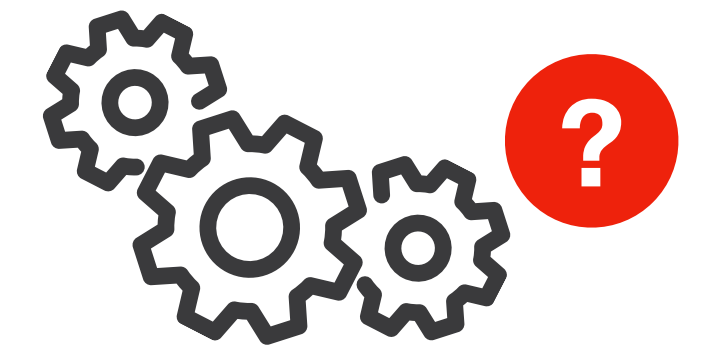
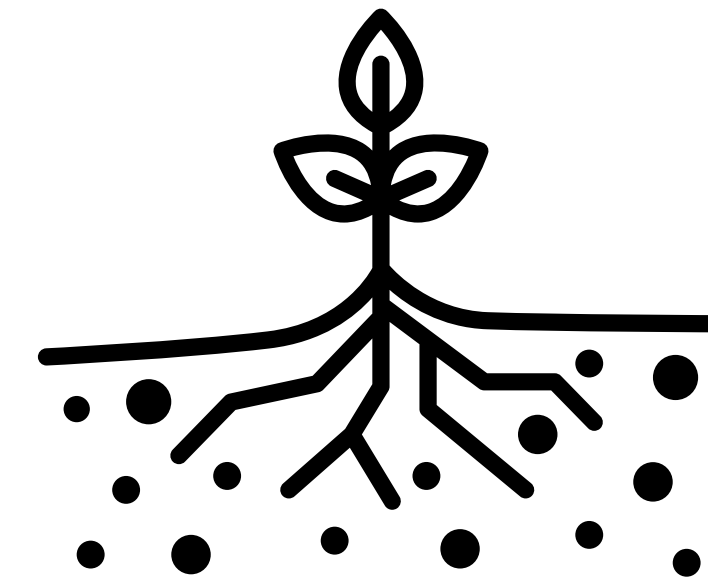
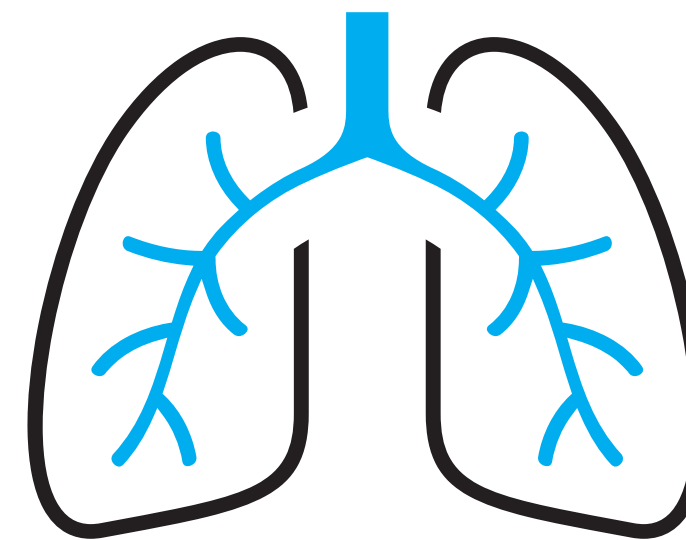
—→ New antibiotics 

LAB



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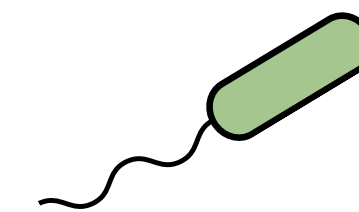
ENVIRONMENT



My lab's interdisciplinary approach:

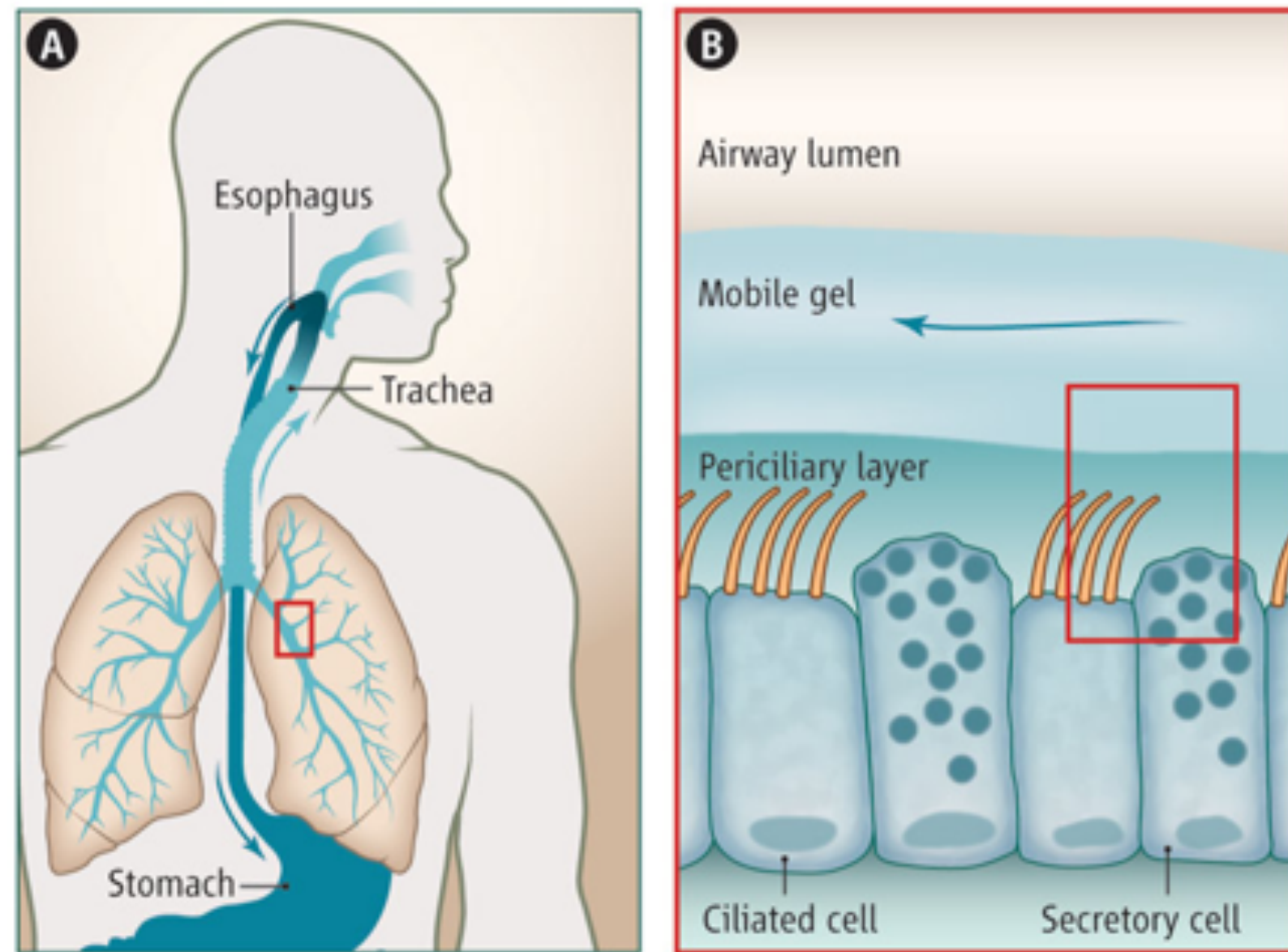


Engineer mechanical microenvironments



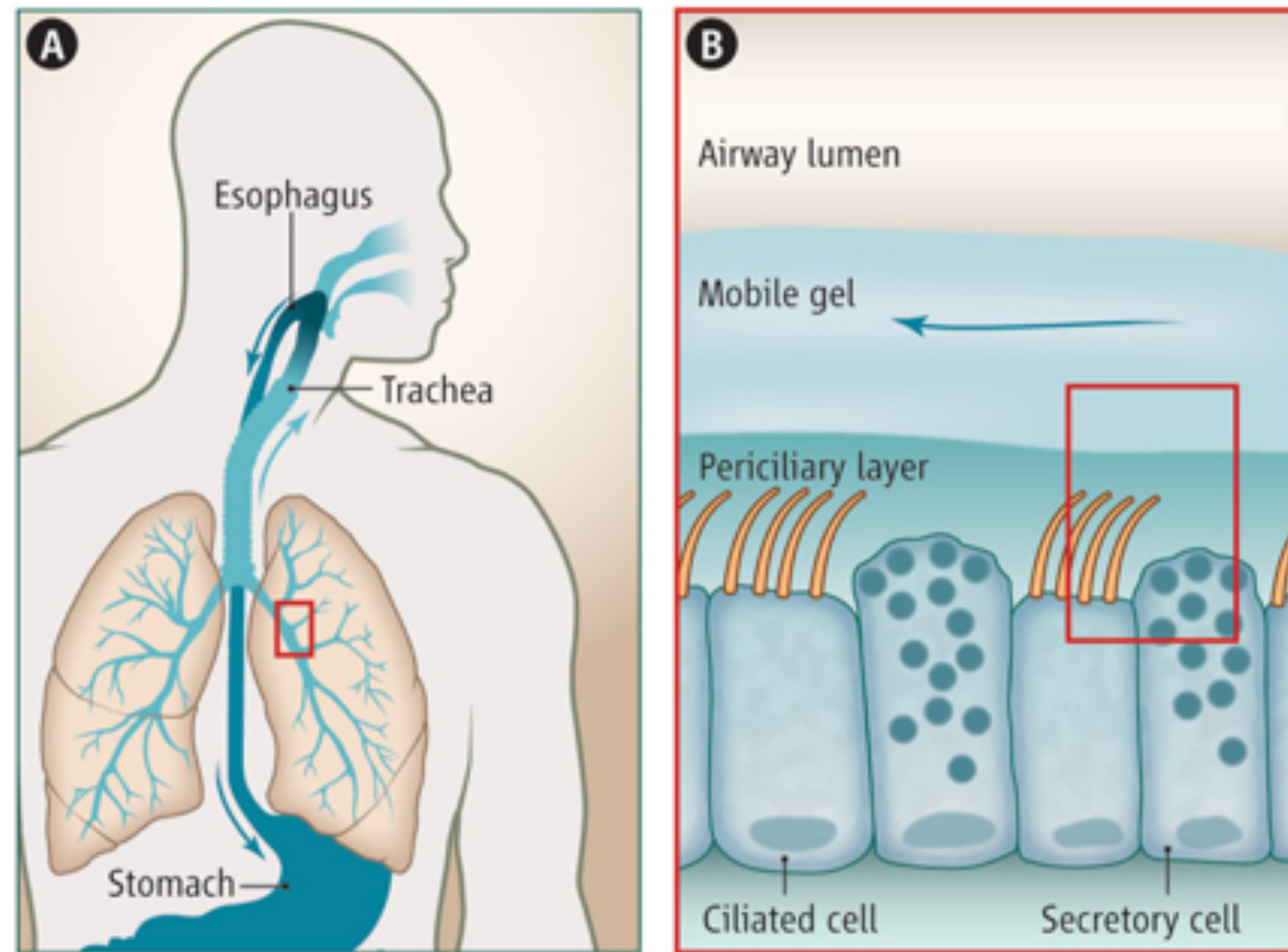
Investigate how forces regulate **bacterial physiology**

The airway is a mechanically complex environment

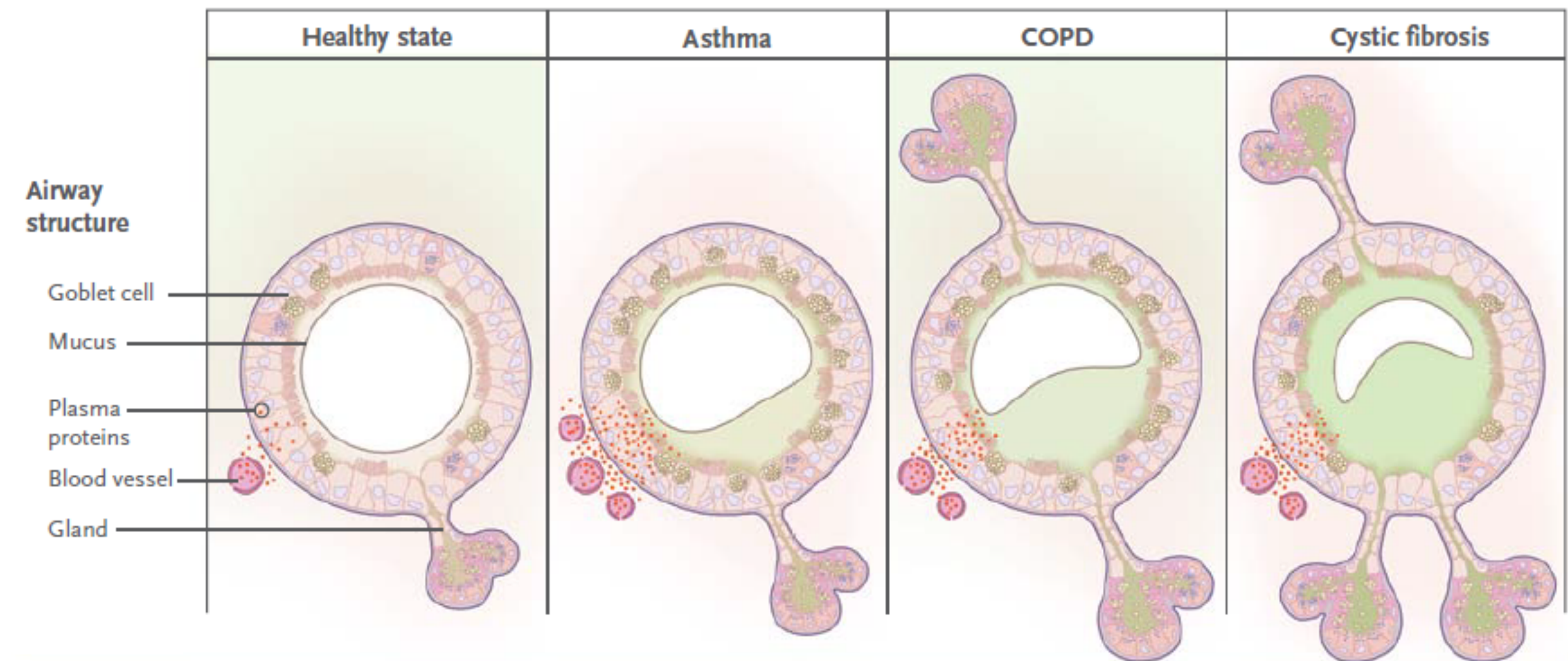


Dickey, 2012, Science

The airway is a mechanically complex environment

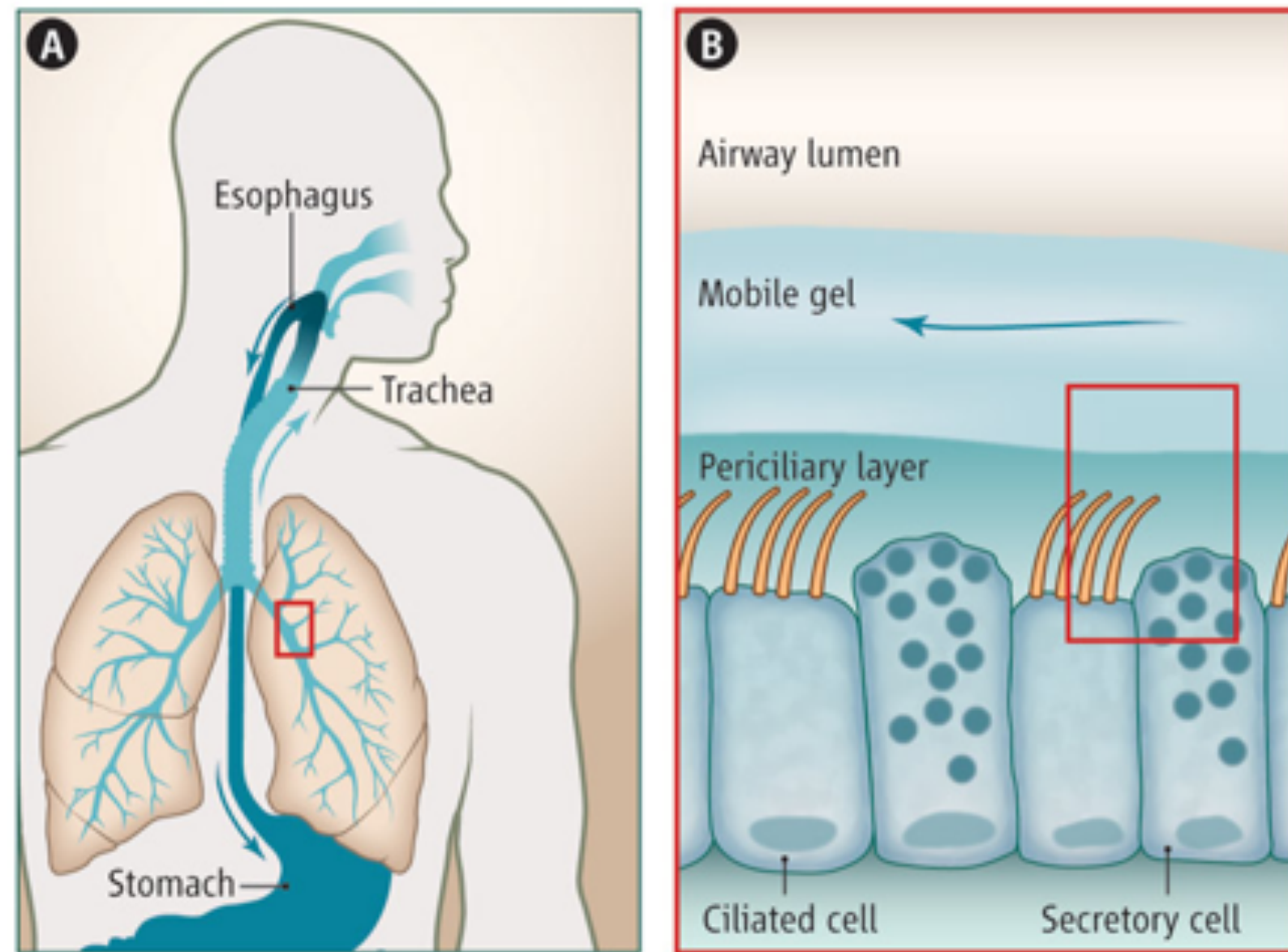


Dickey, 2012, Science

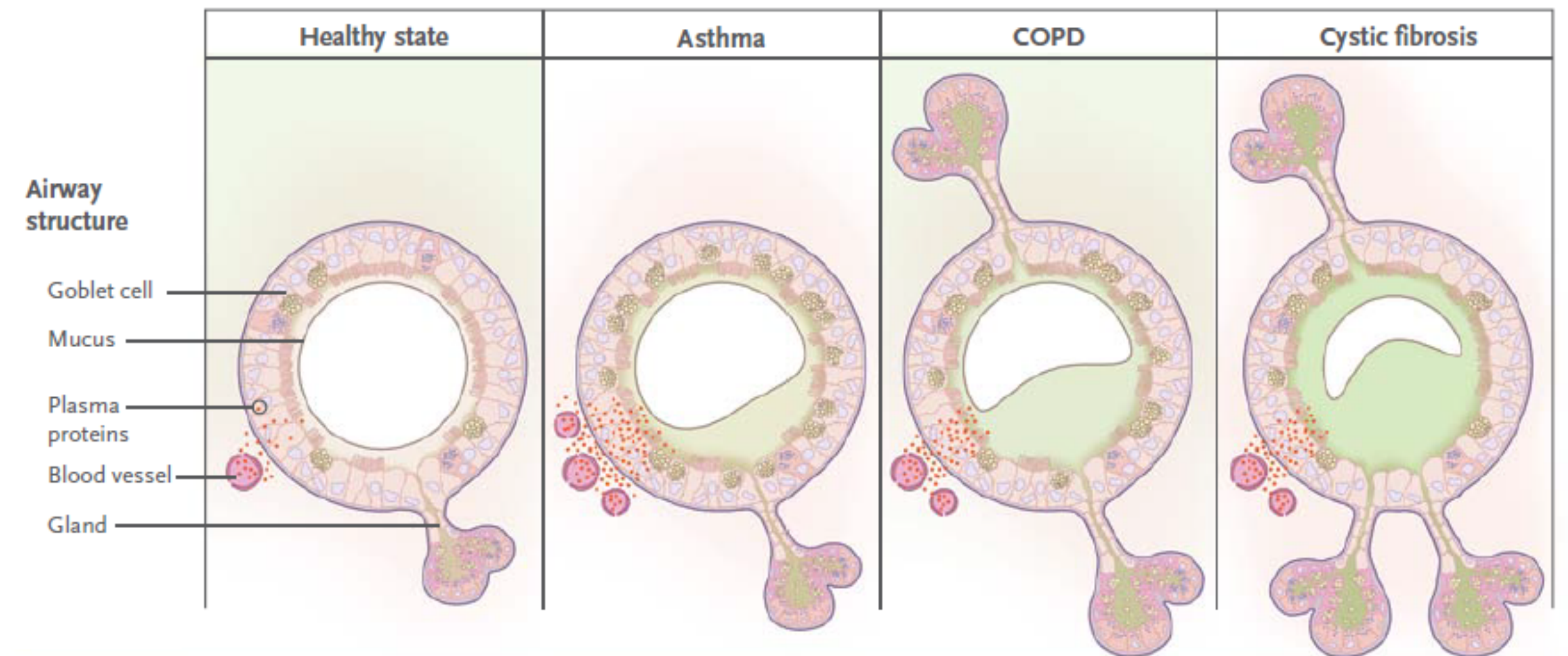


Fahy and Dickey, 2010, NEJM

The airway is a mechanically complex environment



Dickey, 2012, Science

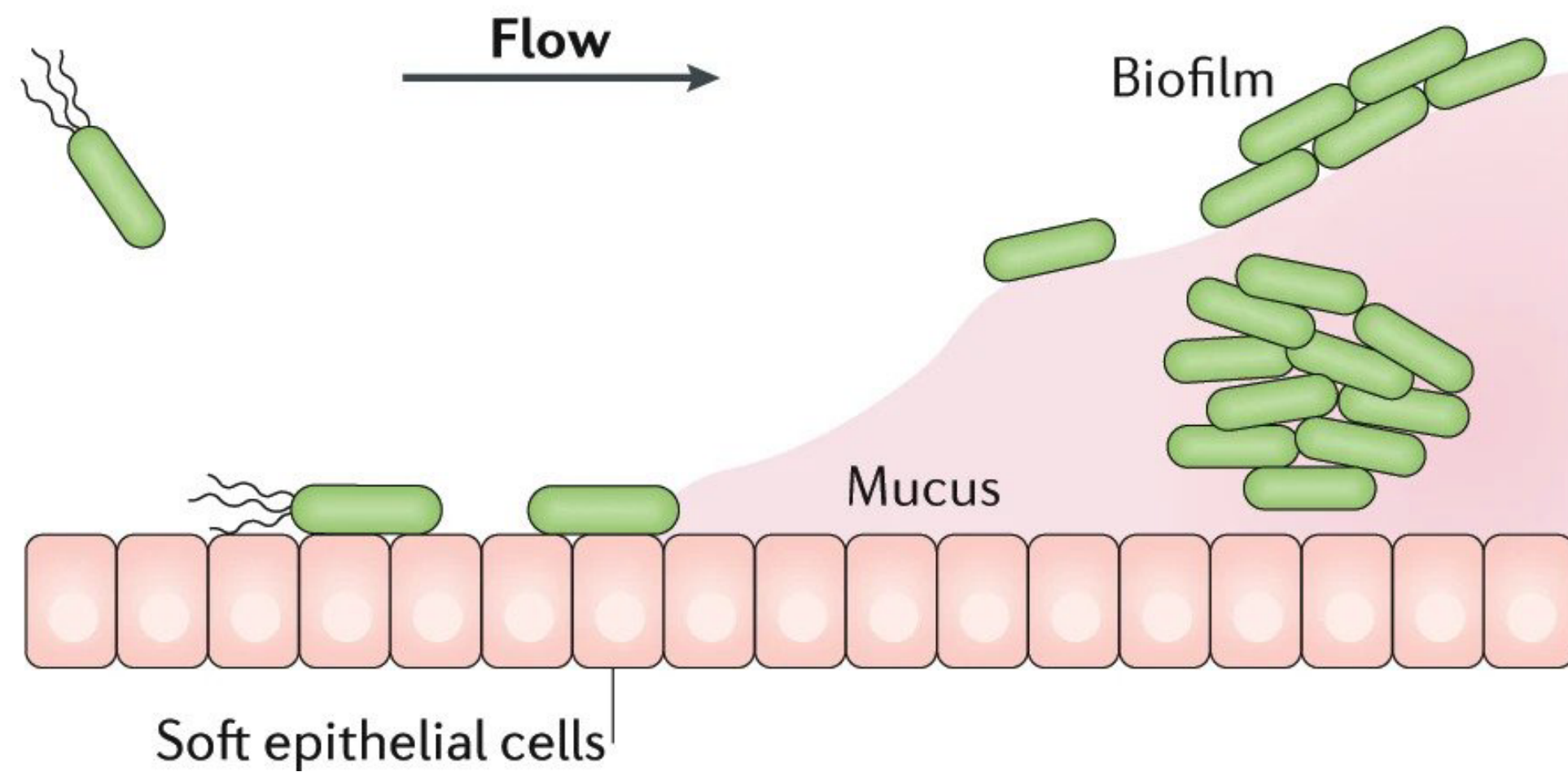


Fahy and Dickey, 2010, NEJM

Mucus is the most accessible material in the airway

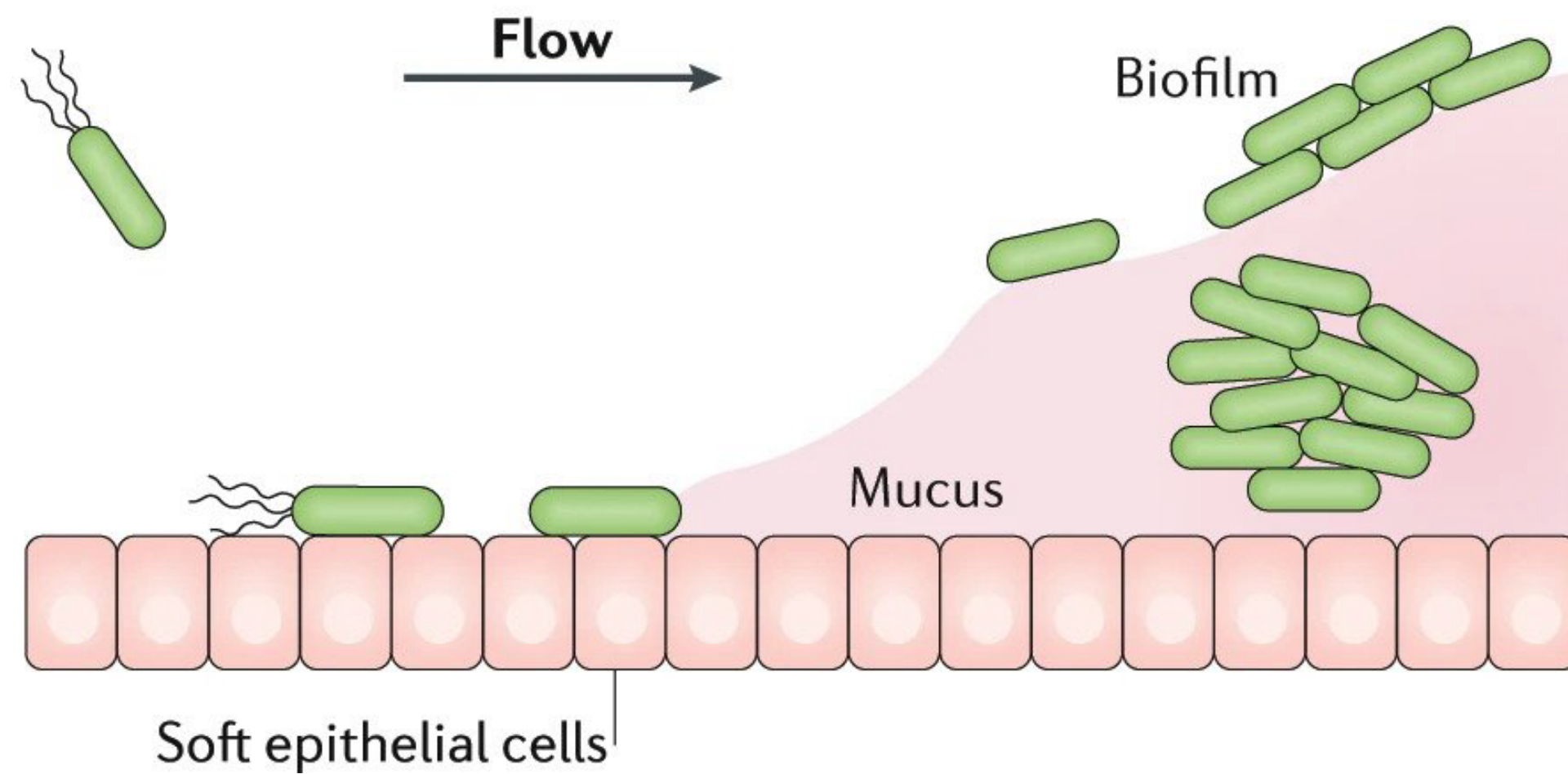
Compromised mucus is associated with sensitivity to *P. aeruginosa* infections

Mechanobiology in the soft world



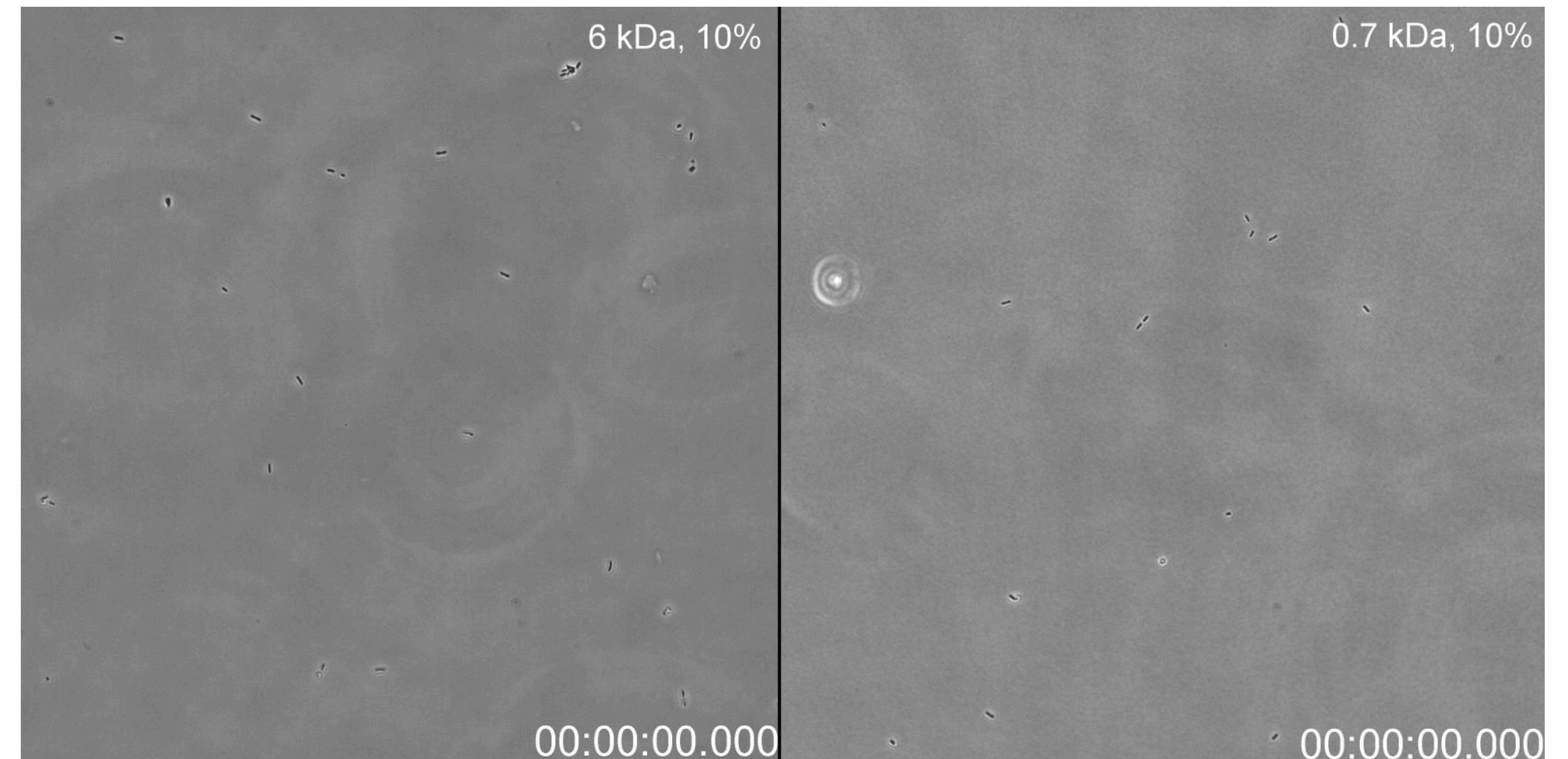
Dufrêne and Persat, *Nat. Rev. Micro.* 2020

Mechanobiology in the soft world



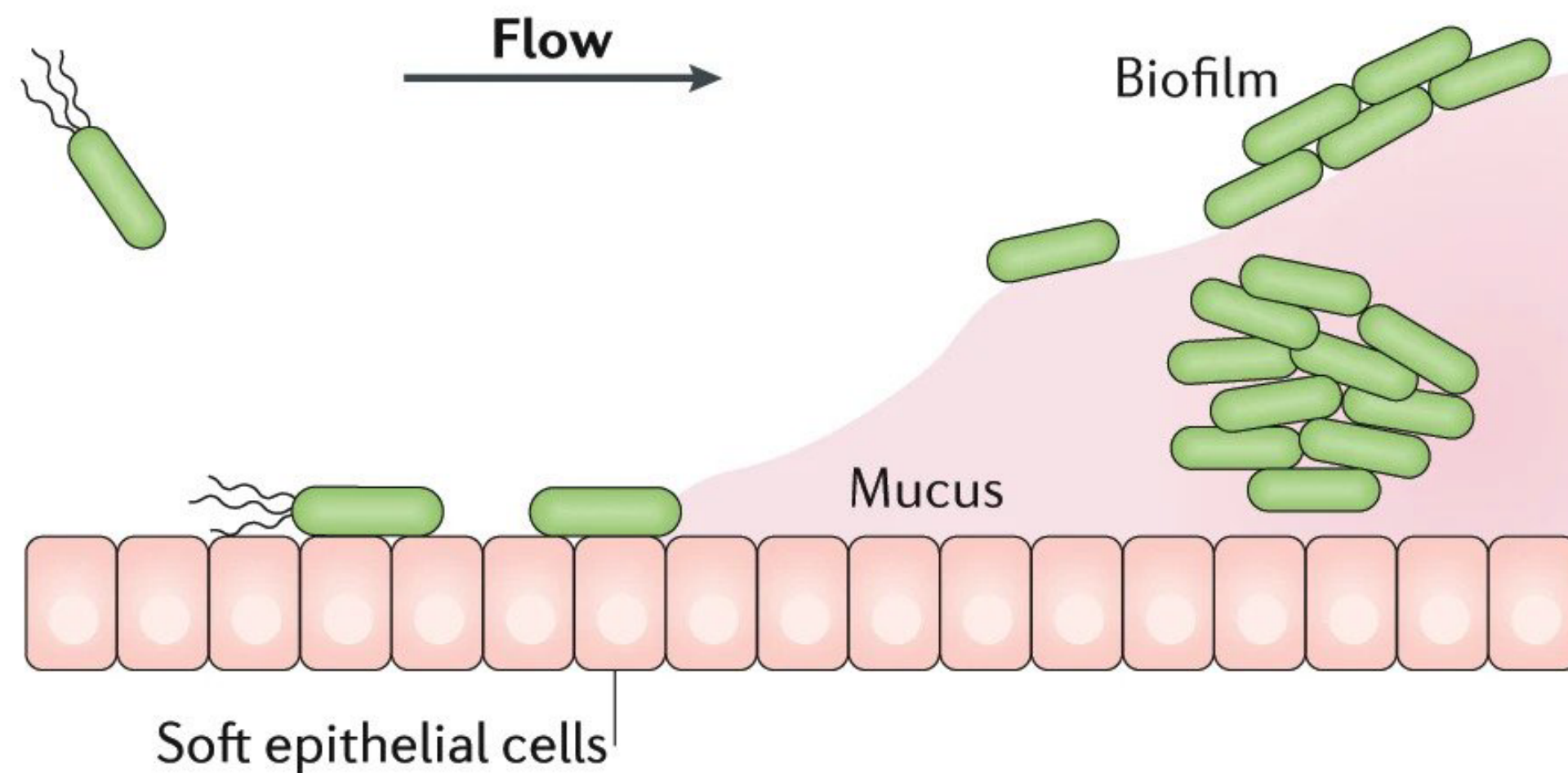
Dufrêne and Persat, *Nat. Rev. Micro.* 2020

Mechanical properties impact biofilm formation



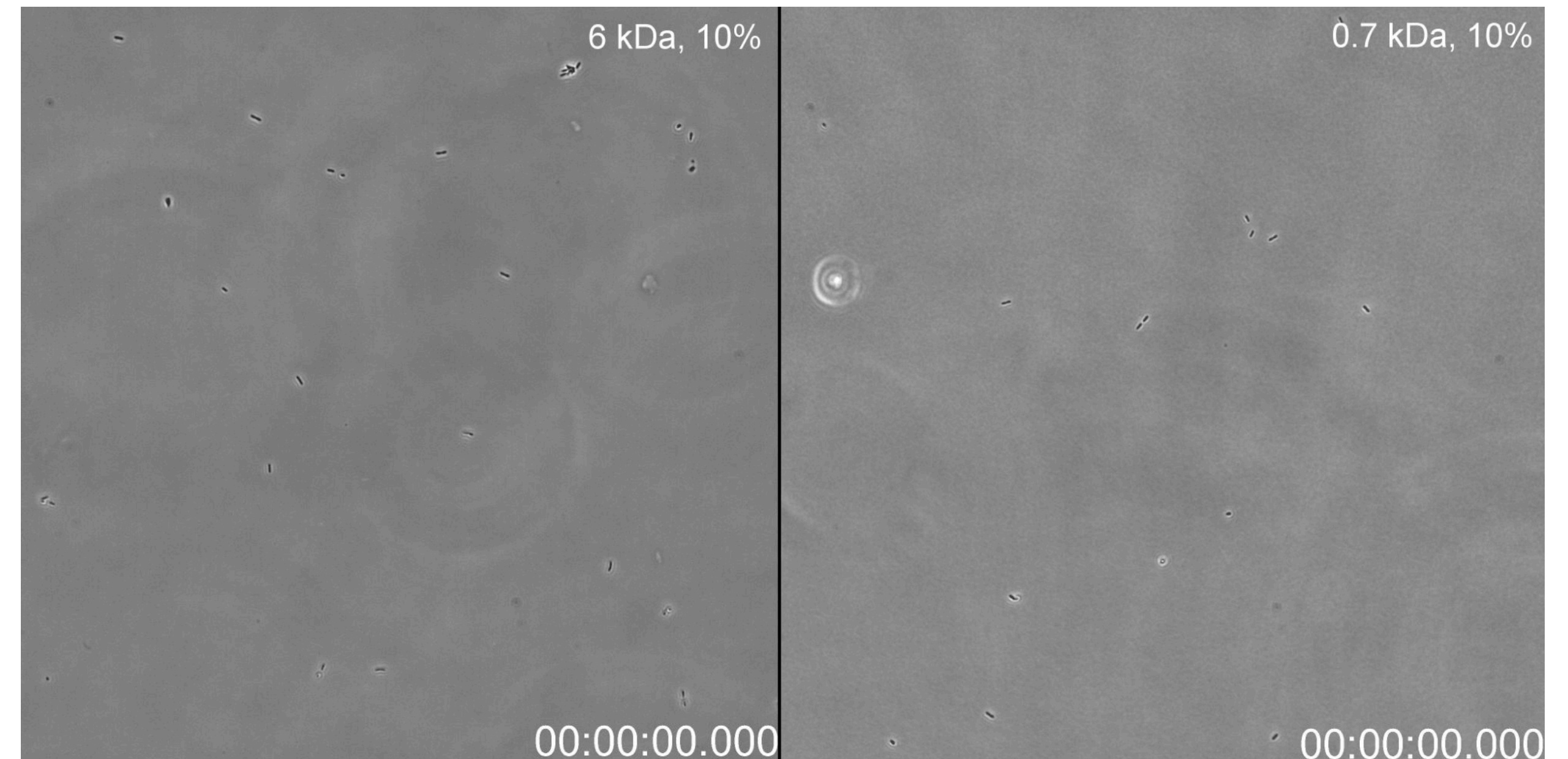
Cont, eLife 2020
Cont, mBio 2023

Mechanobiology in the soft world



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

Mechanical properties impact biofilm formation



Cont, eLife 2020
Cont, mBio 2023

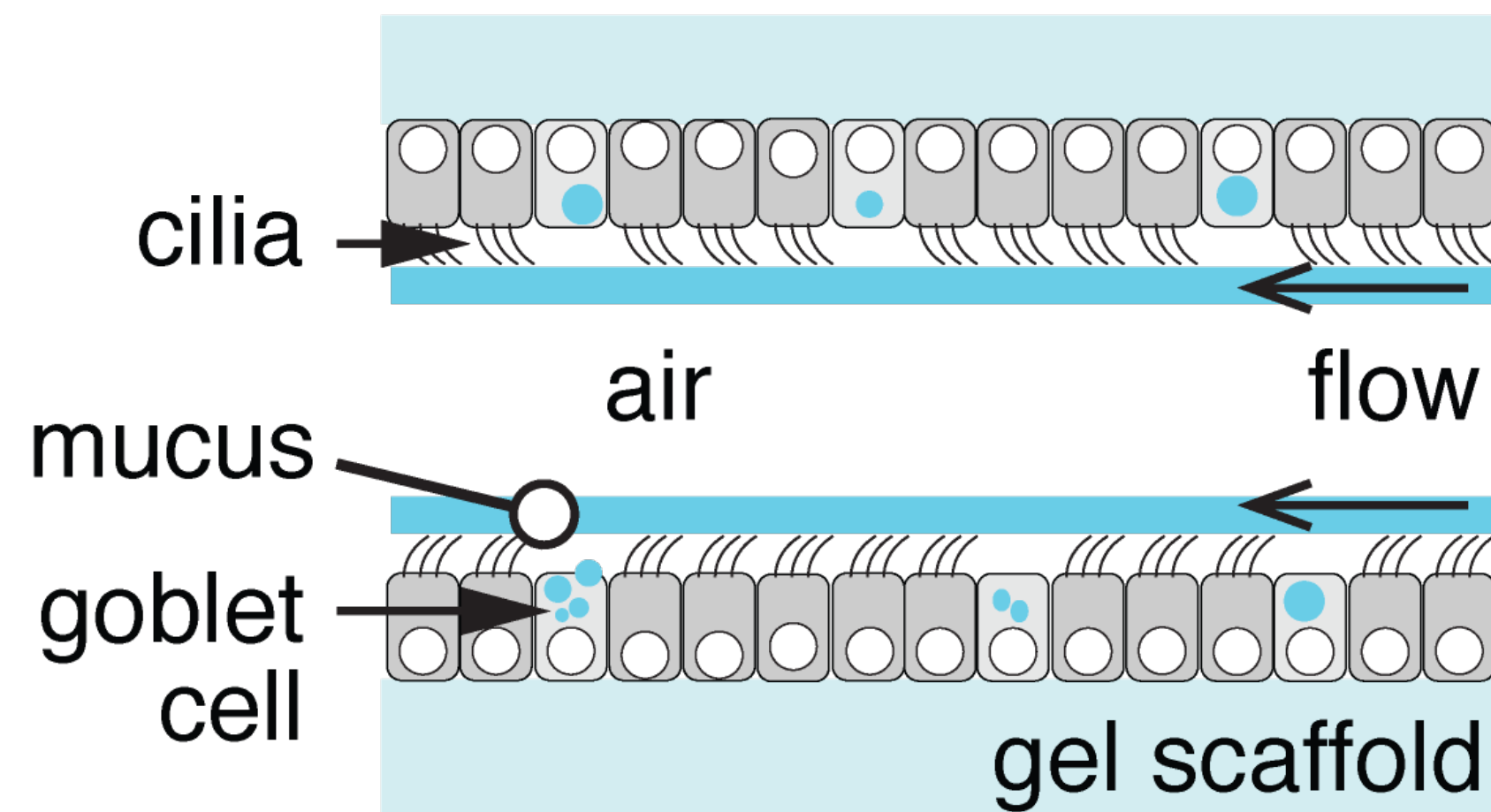
How do *P. aeruginosa* cells colonize and form biofilms *in vivo*?

Airgels: tube-shaped airway organoids

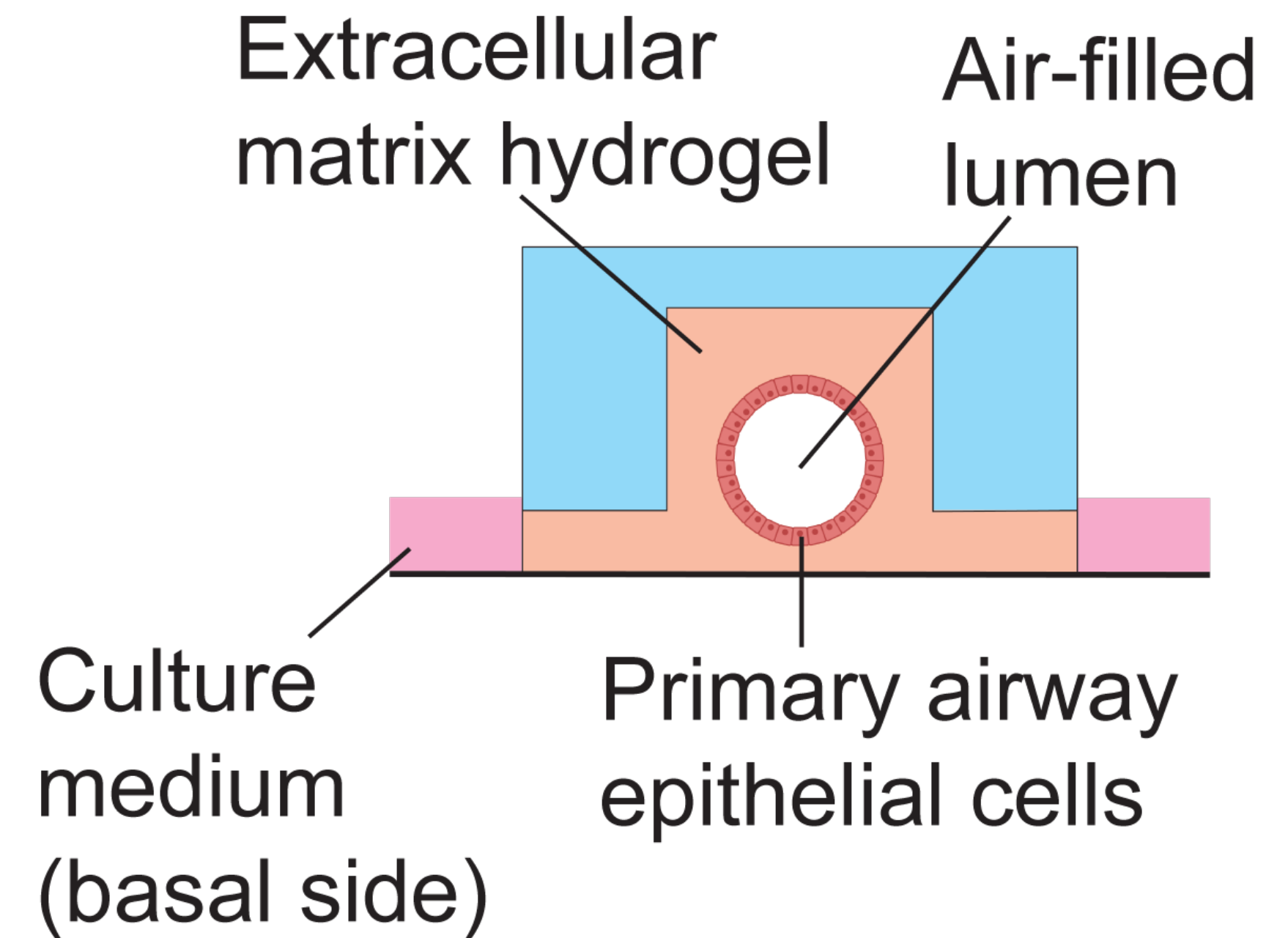
(airway in a gel)

Technical requirements:

- suitable for microscopy
- tube-shape



Cross-sectional view

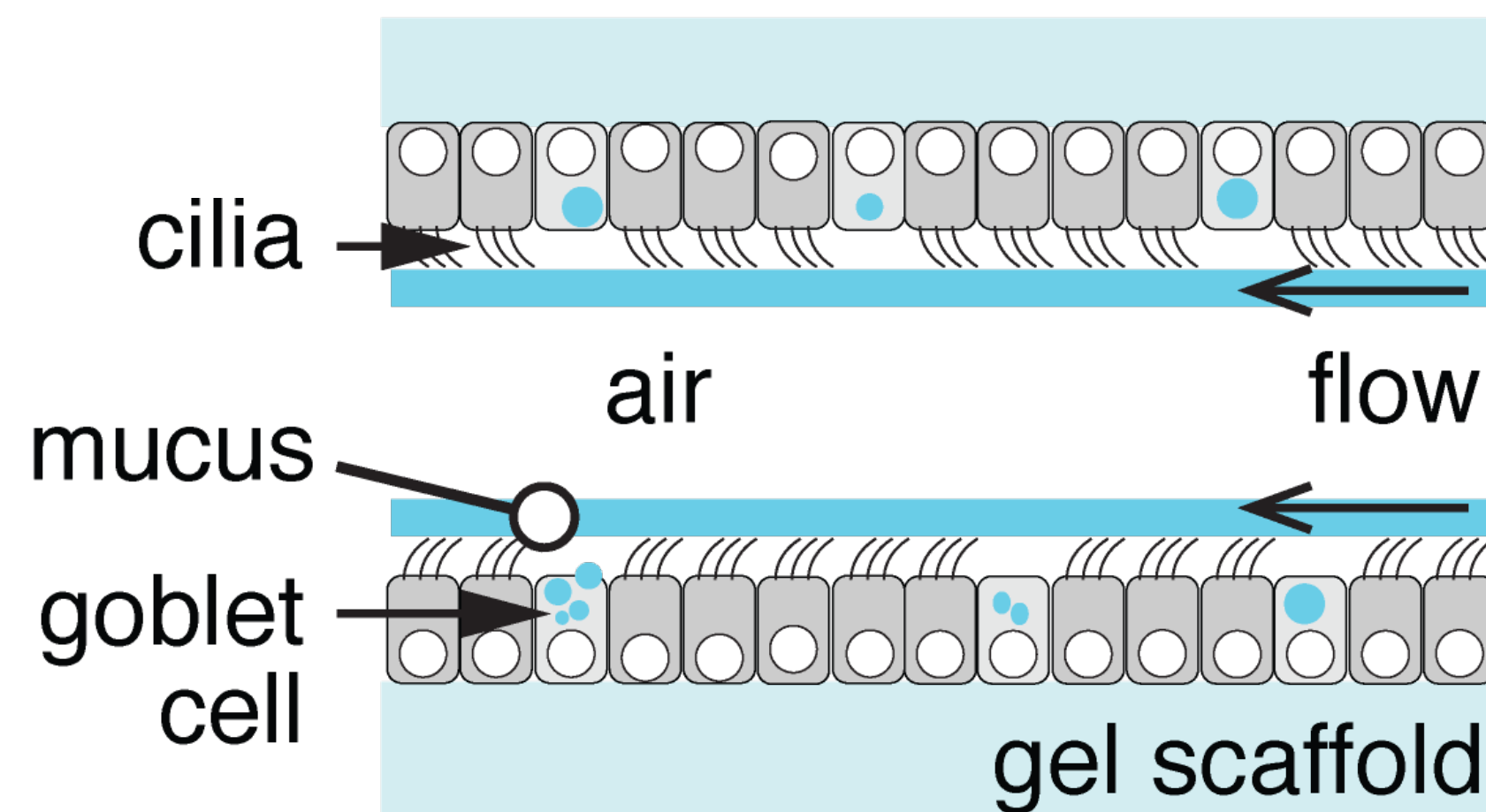


Airgels: tube-shaped airway organoids

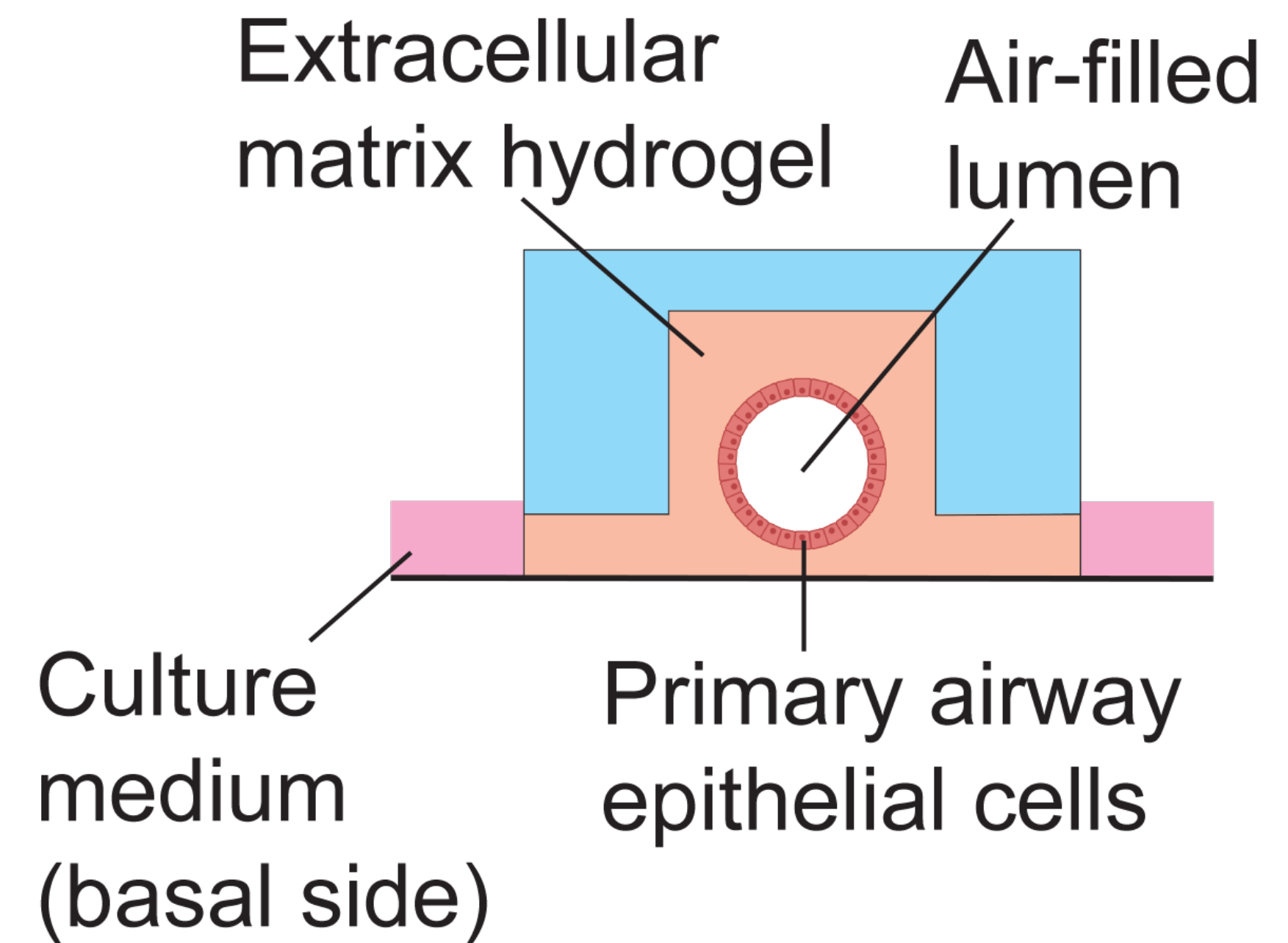
(airway in a gel)

Technical requirements:

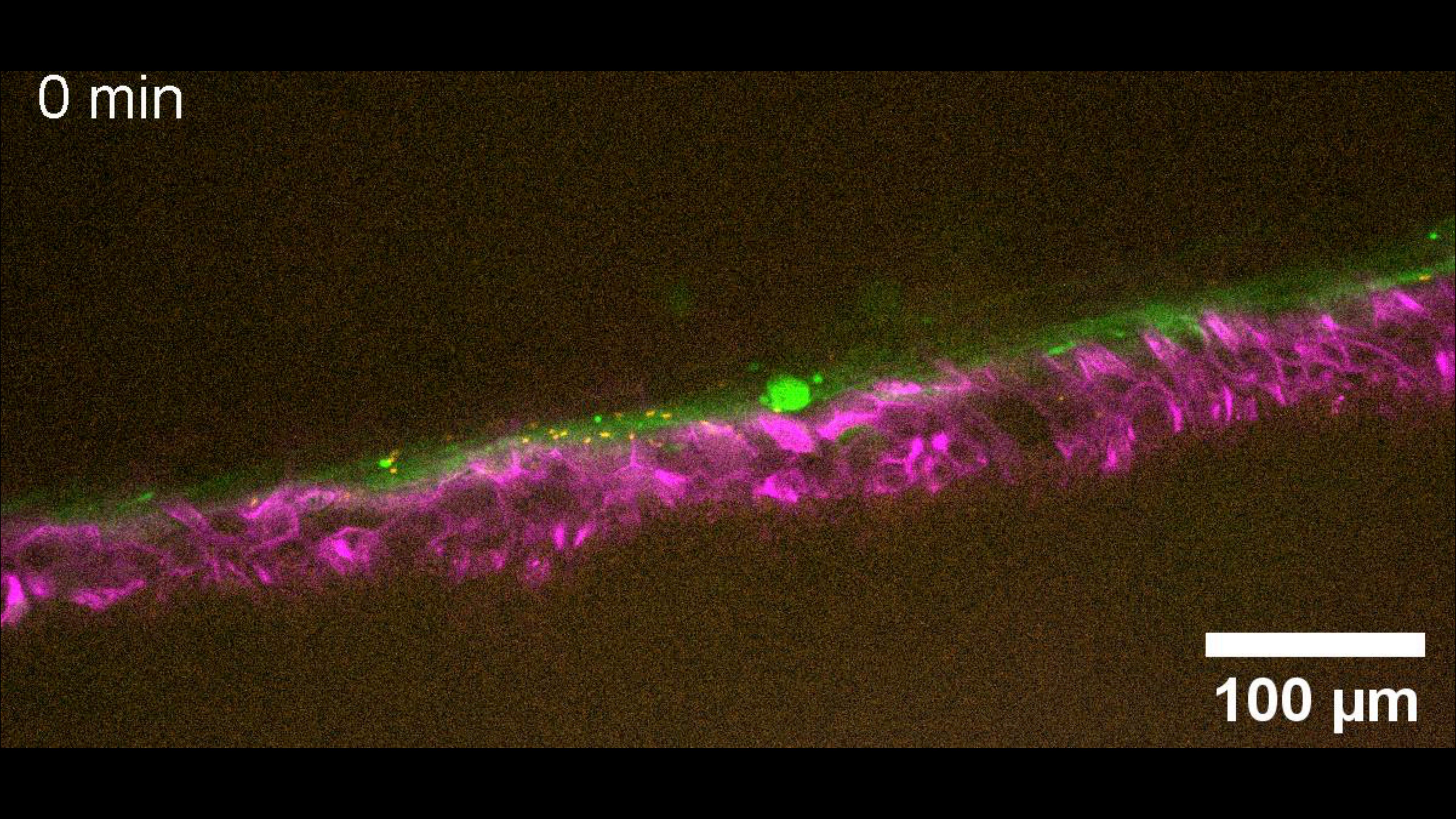
- suitable for microscopy
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Cross-sectional view

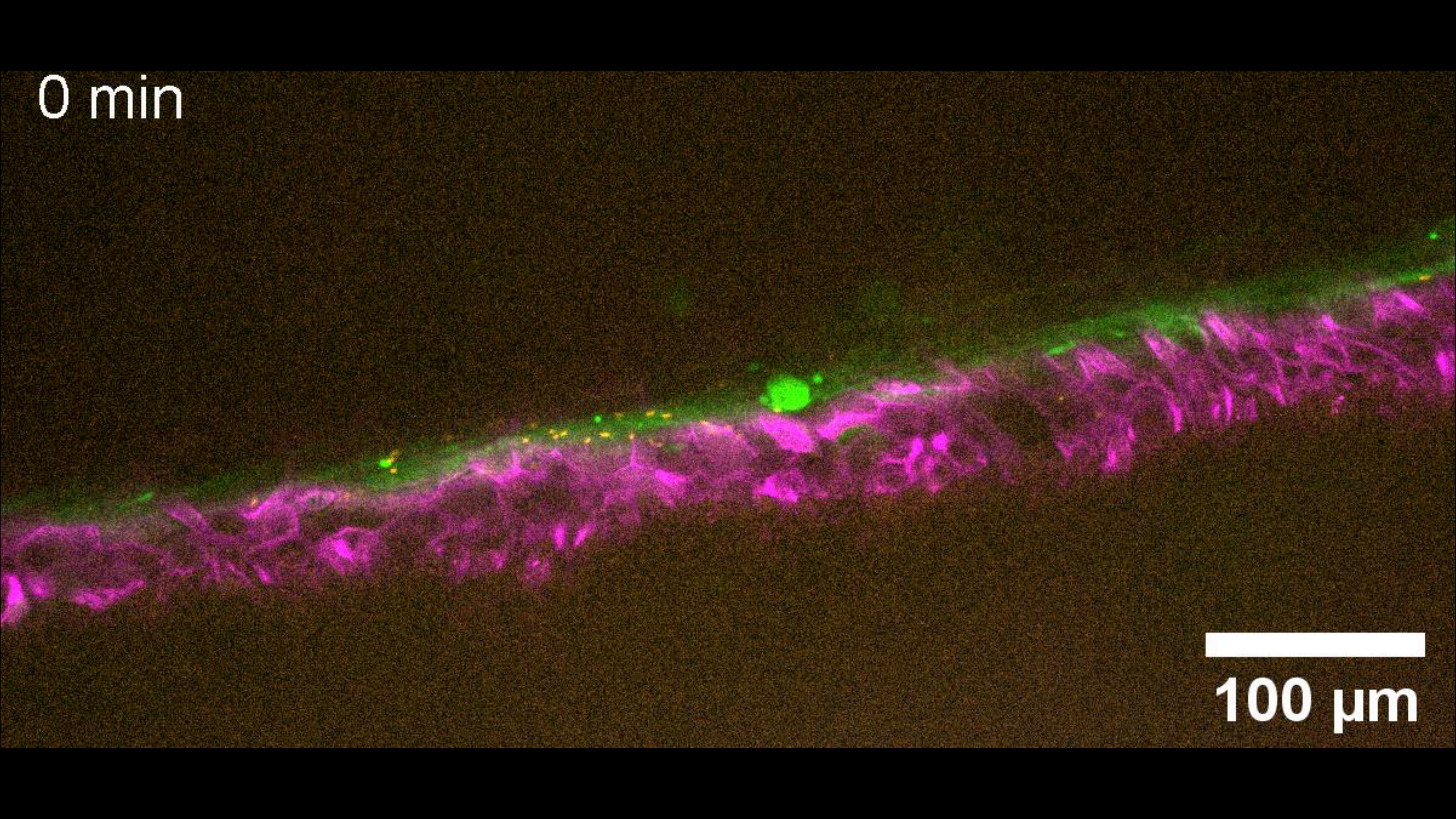


0 min



100 μm

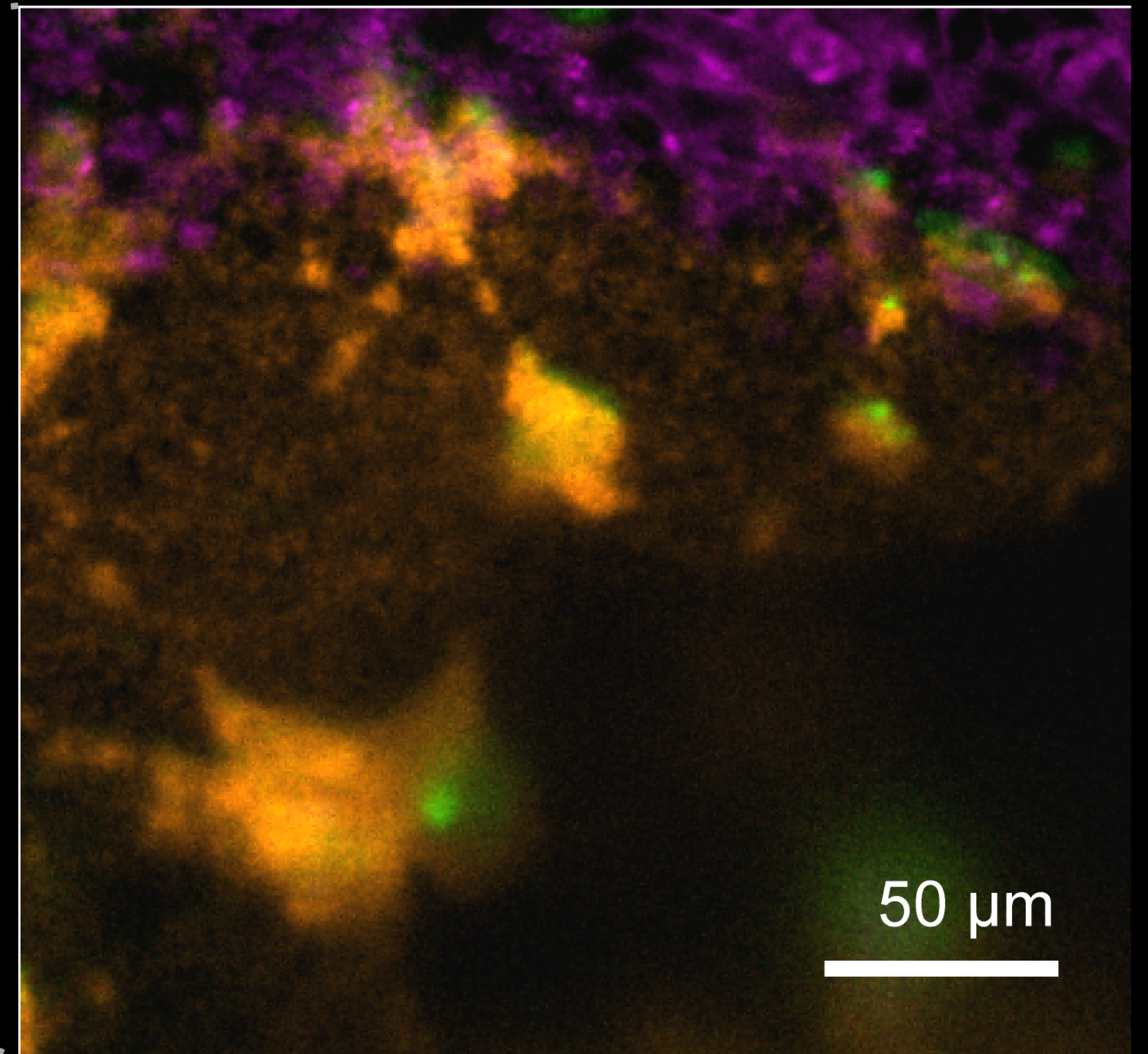
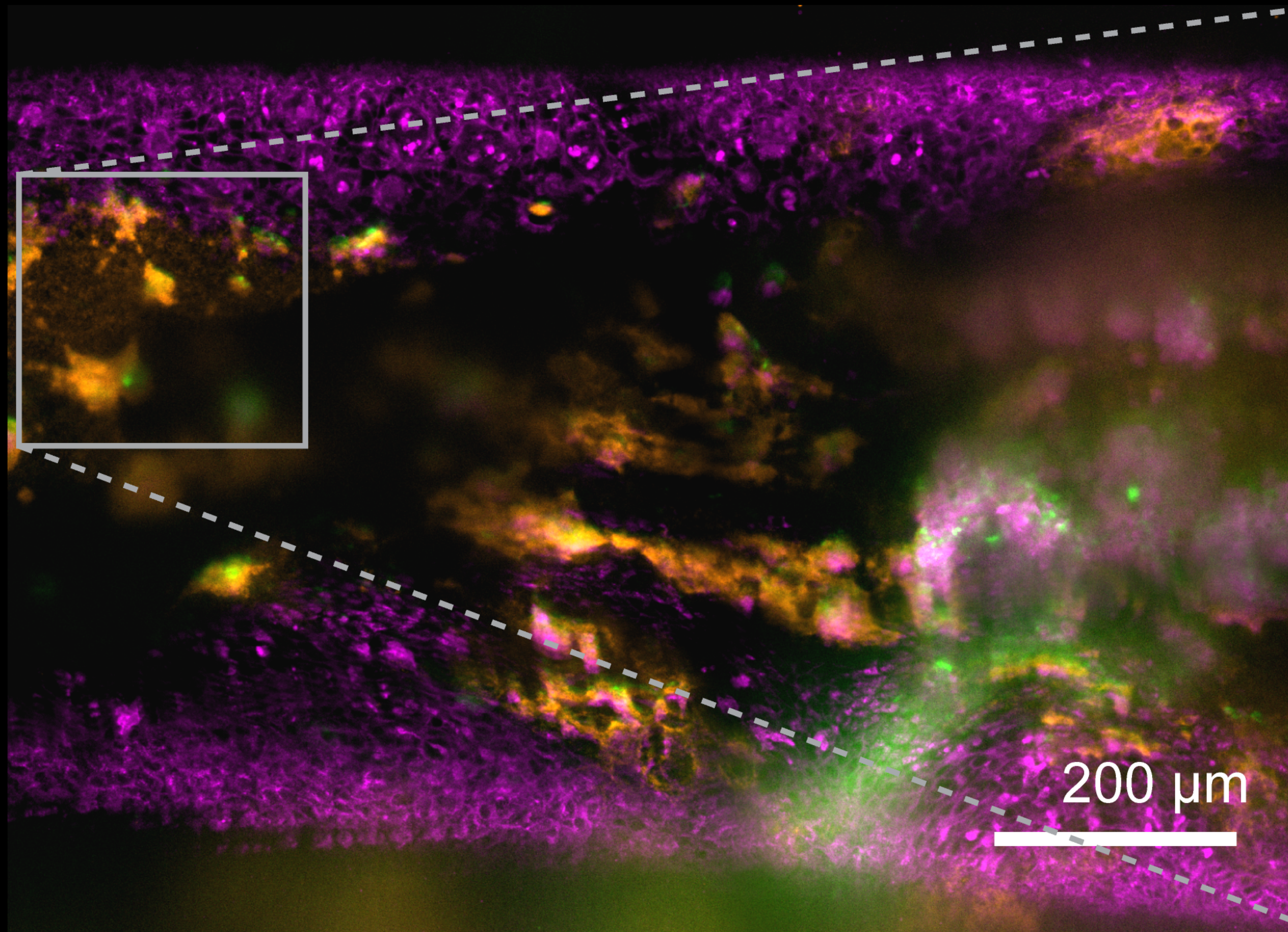
0 min



100 μm

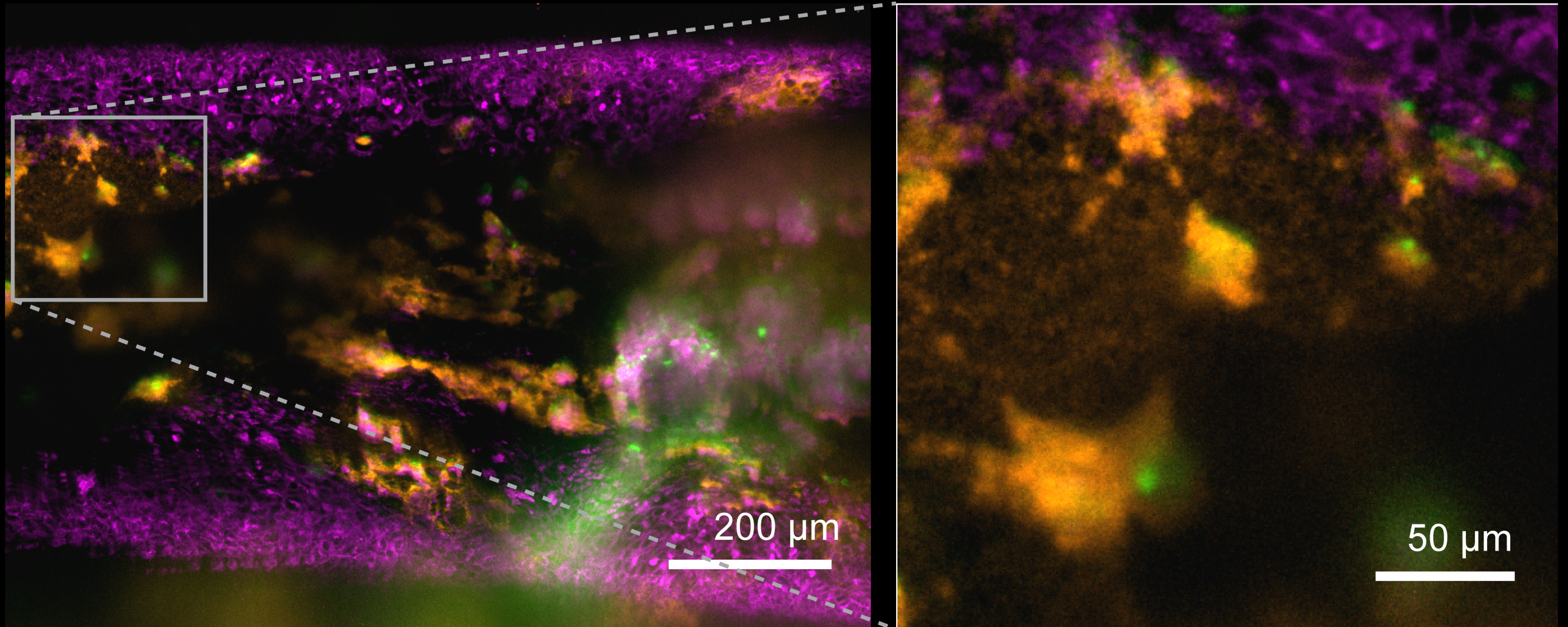
Live visualization of infection in Airgels

Mucus Plasma membrane / *P. aeruginosa*

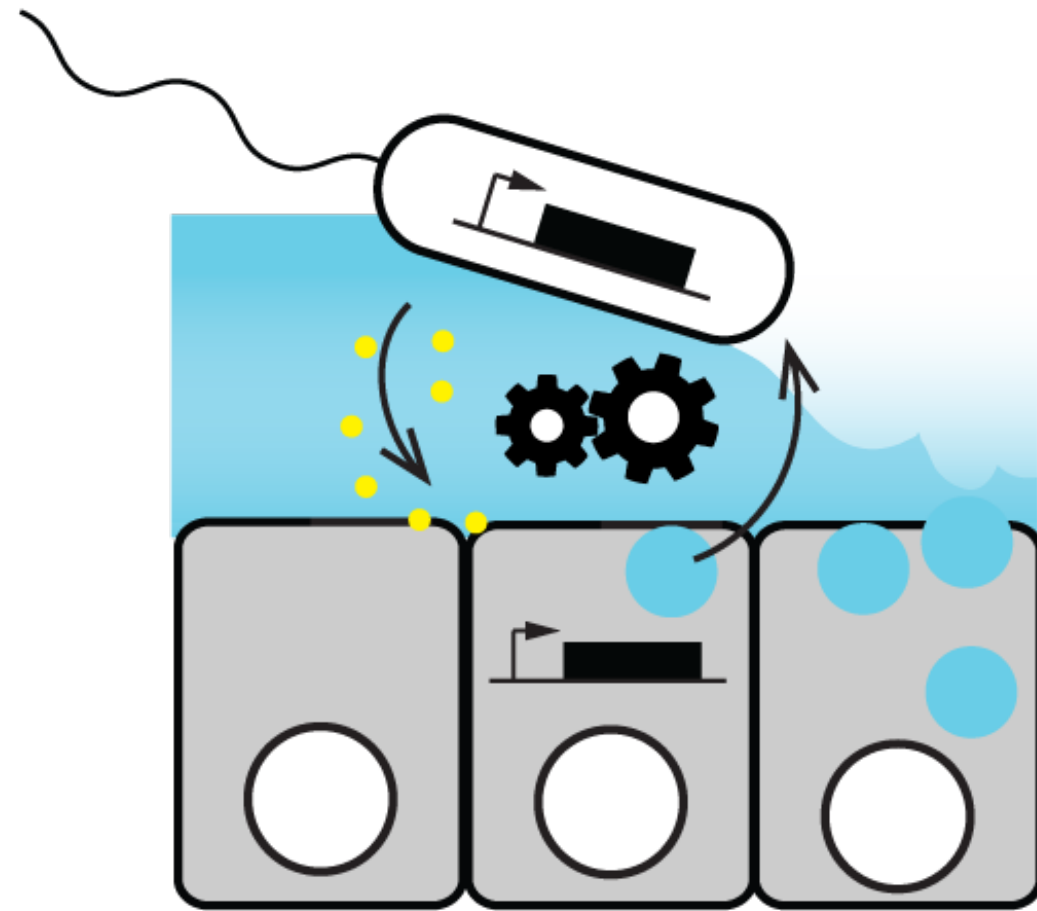


Live visualization of infection in Airgels

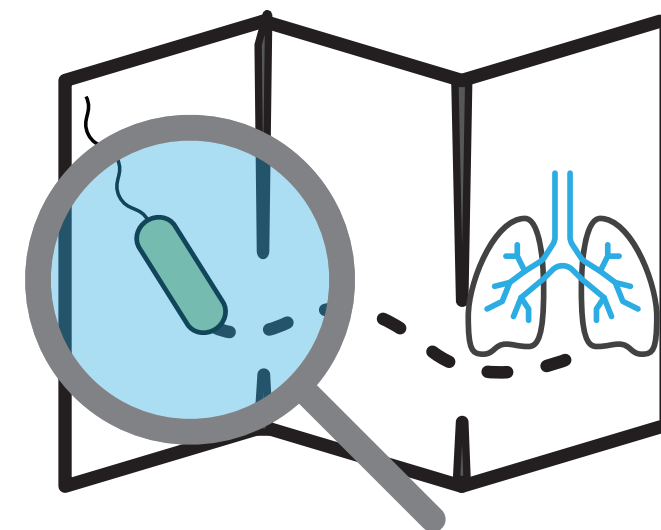
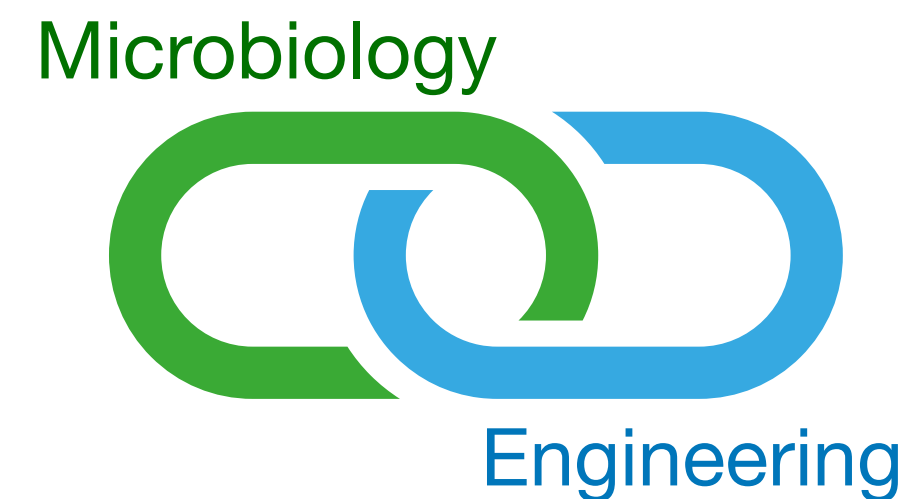
Mucus Plasma membrane / *P. aeruginosa*



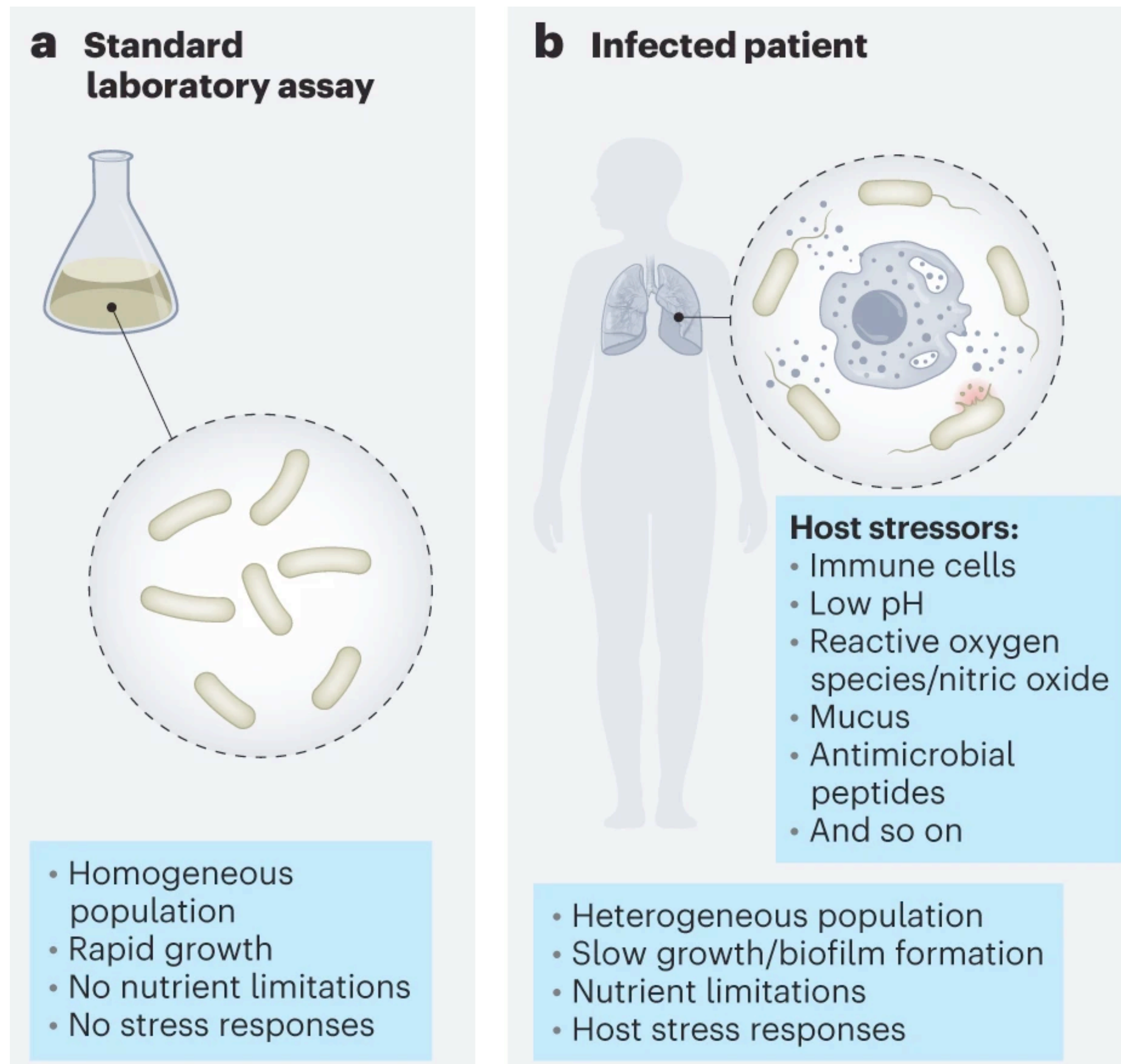
A new perspective on infections



- 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.

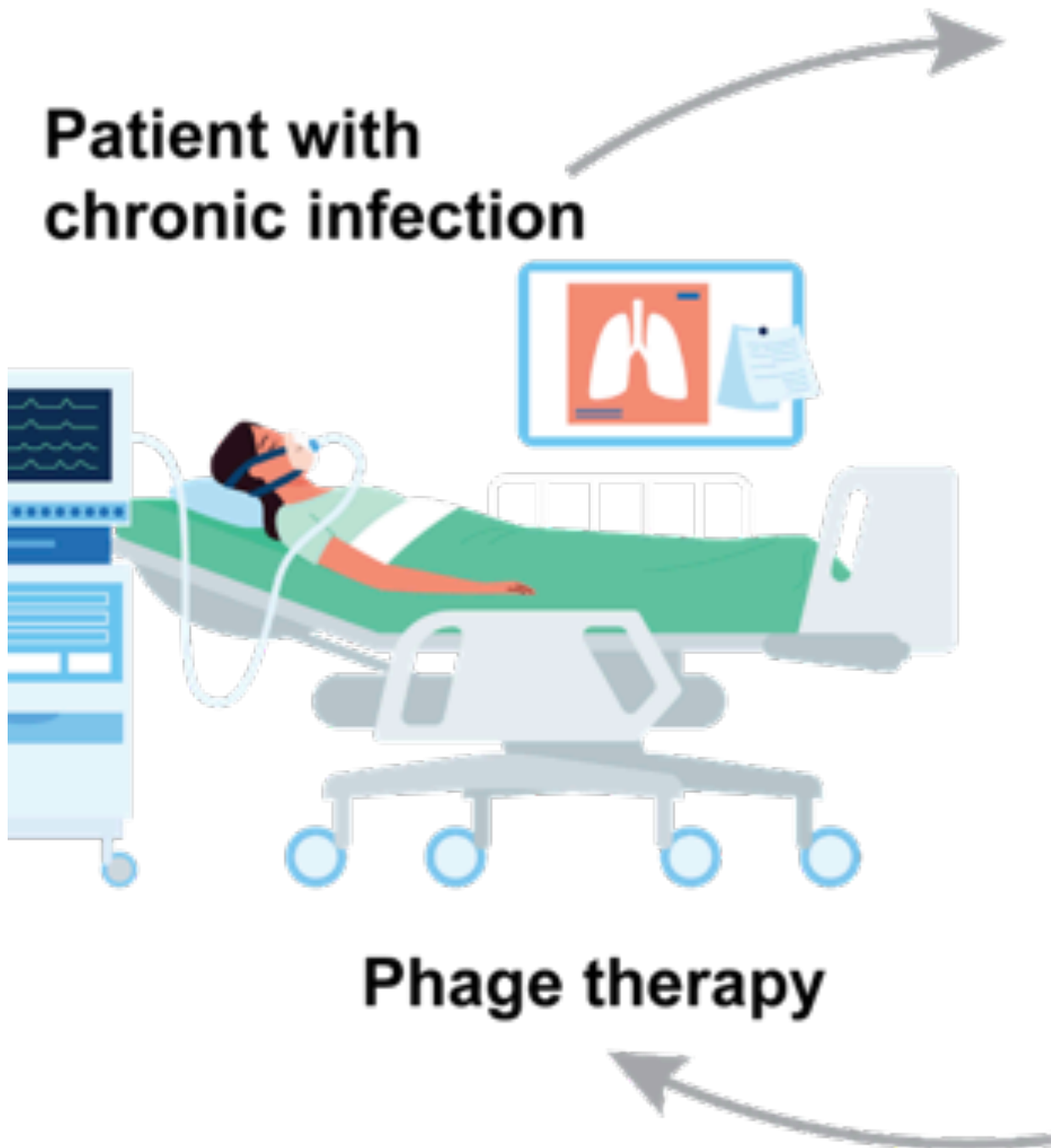


The patient environment: a missing link in therapy



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

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



Pneumology

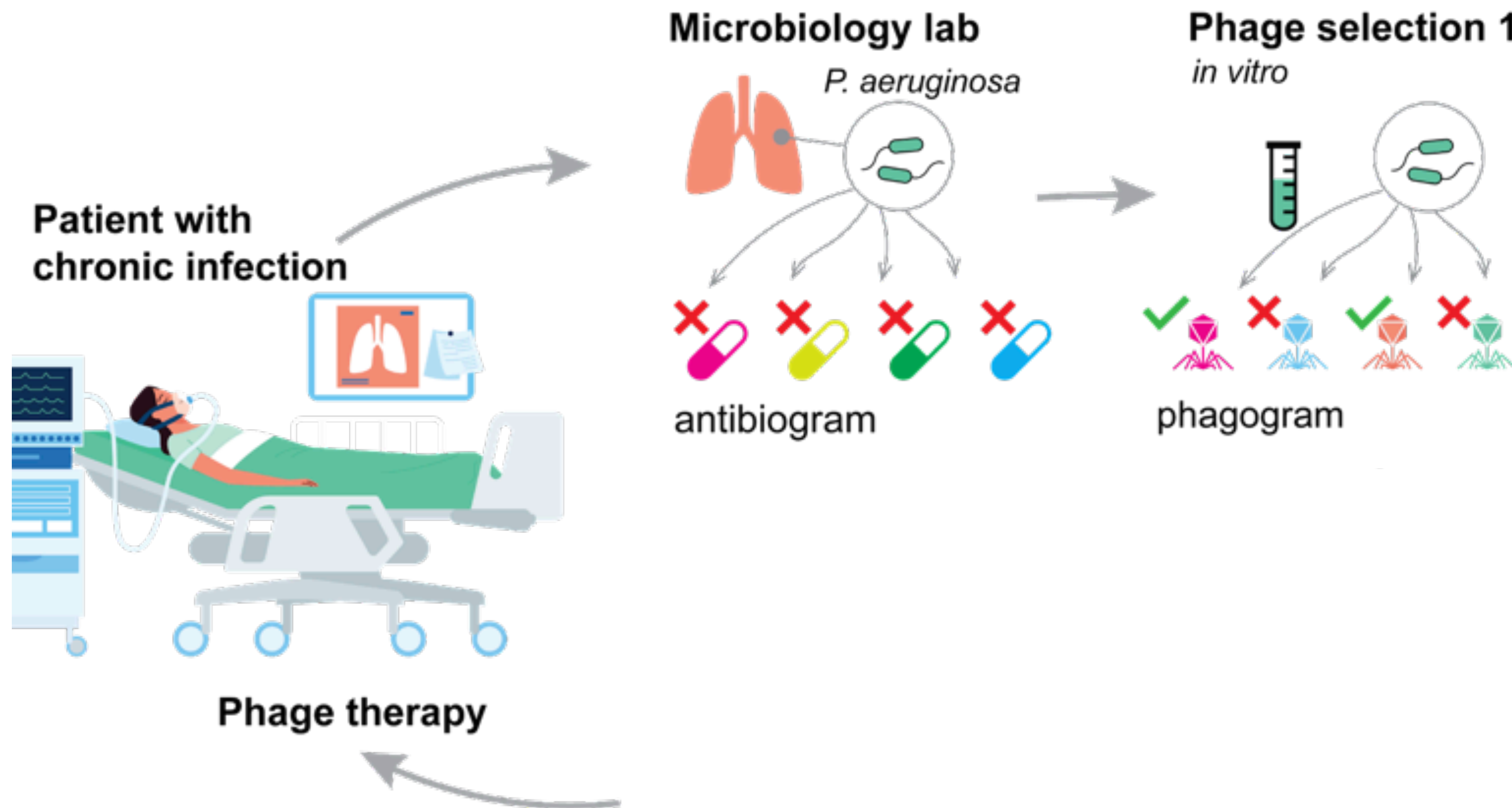
Dr. Angela Koutsokera
& Dr. Georgia Mitropoulou



Phage production

Dr. Gregory Resch

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



Pneumology

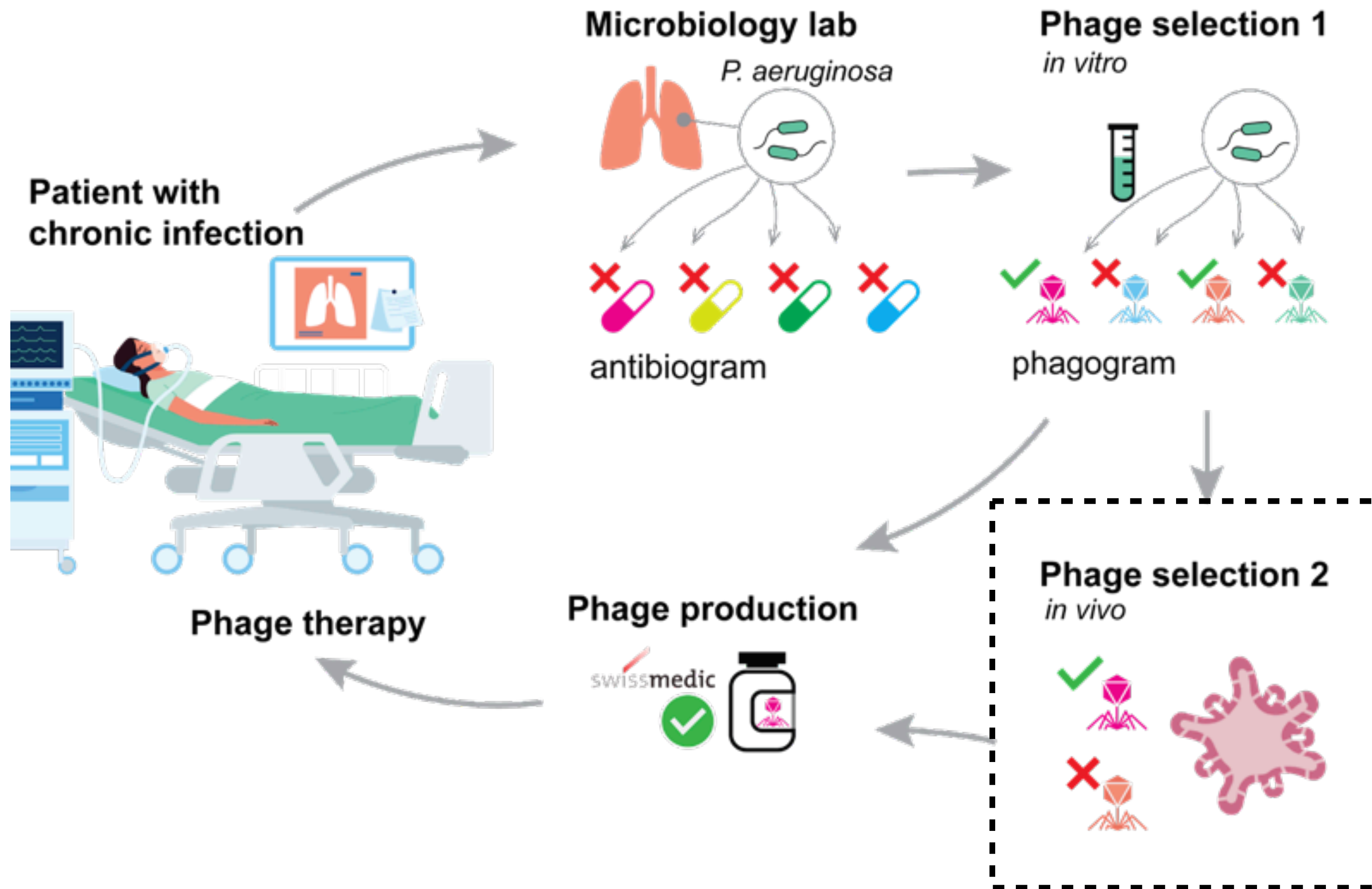
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Pneumology

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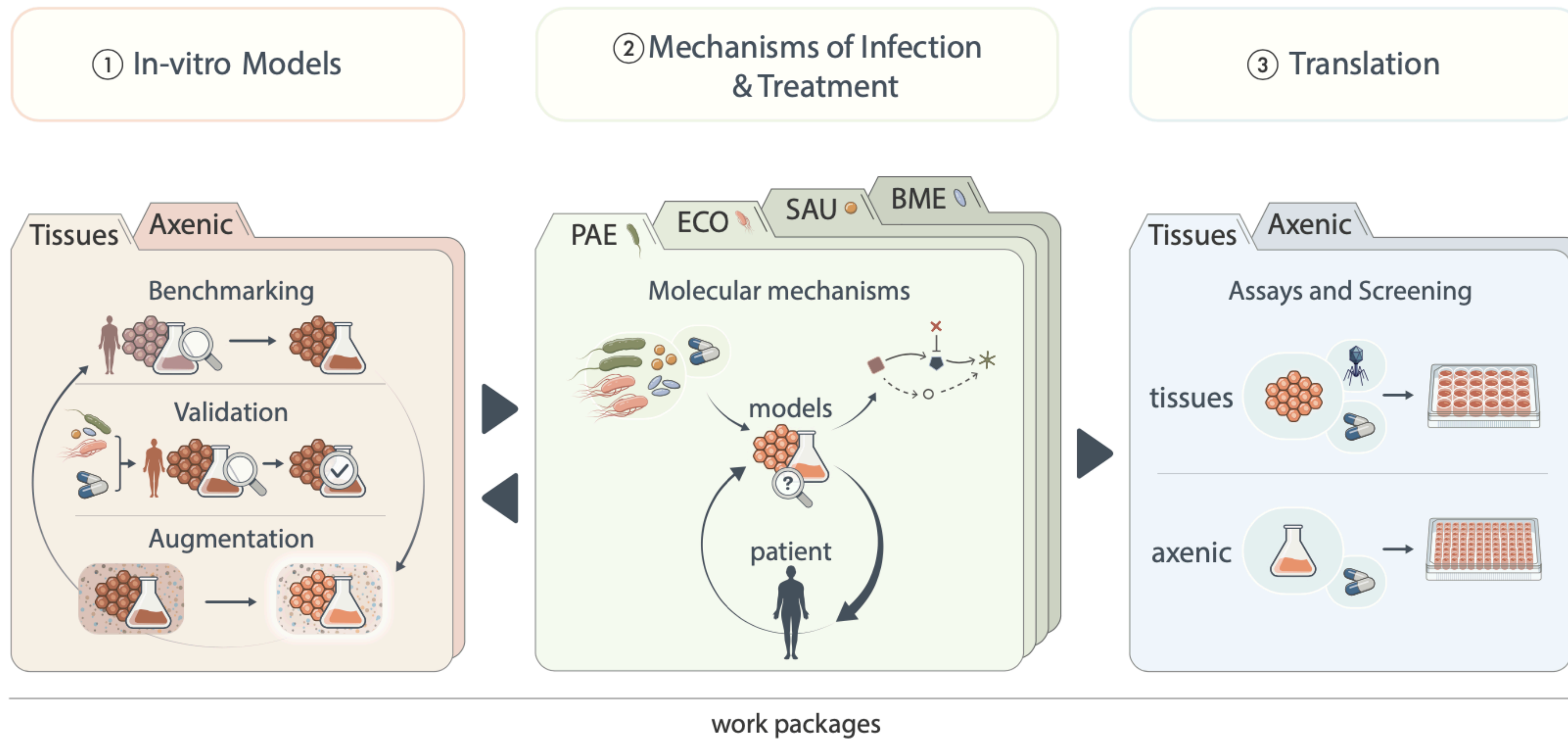


Phage production

Dr. Gregory Resch

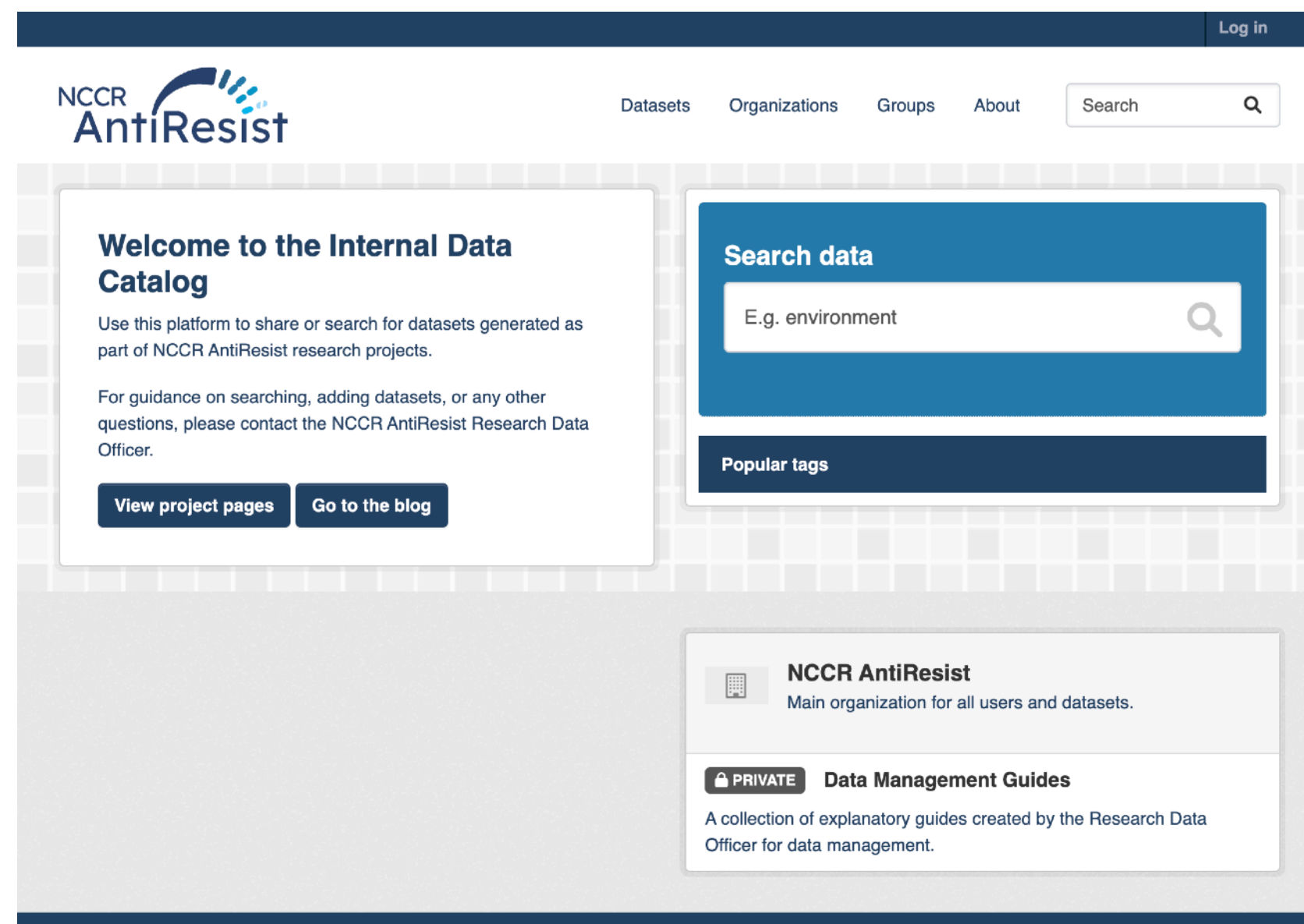
- To bring a **paradigm shift** in antibiotic discovery
- To **close the gap** between the **bedside and the bench**
- To **bridge disciplines** and **institutions** within **Switzerland**
- To stimulate **long-lasting partnership** with the **private sector**
- To equip **future generations of scientists**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

Connecting clinical data and models development – phase 2



About

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

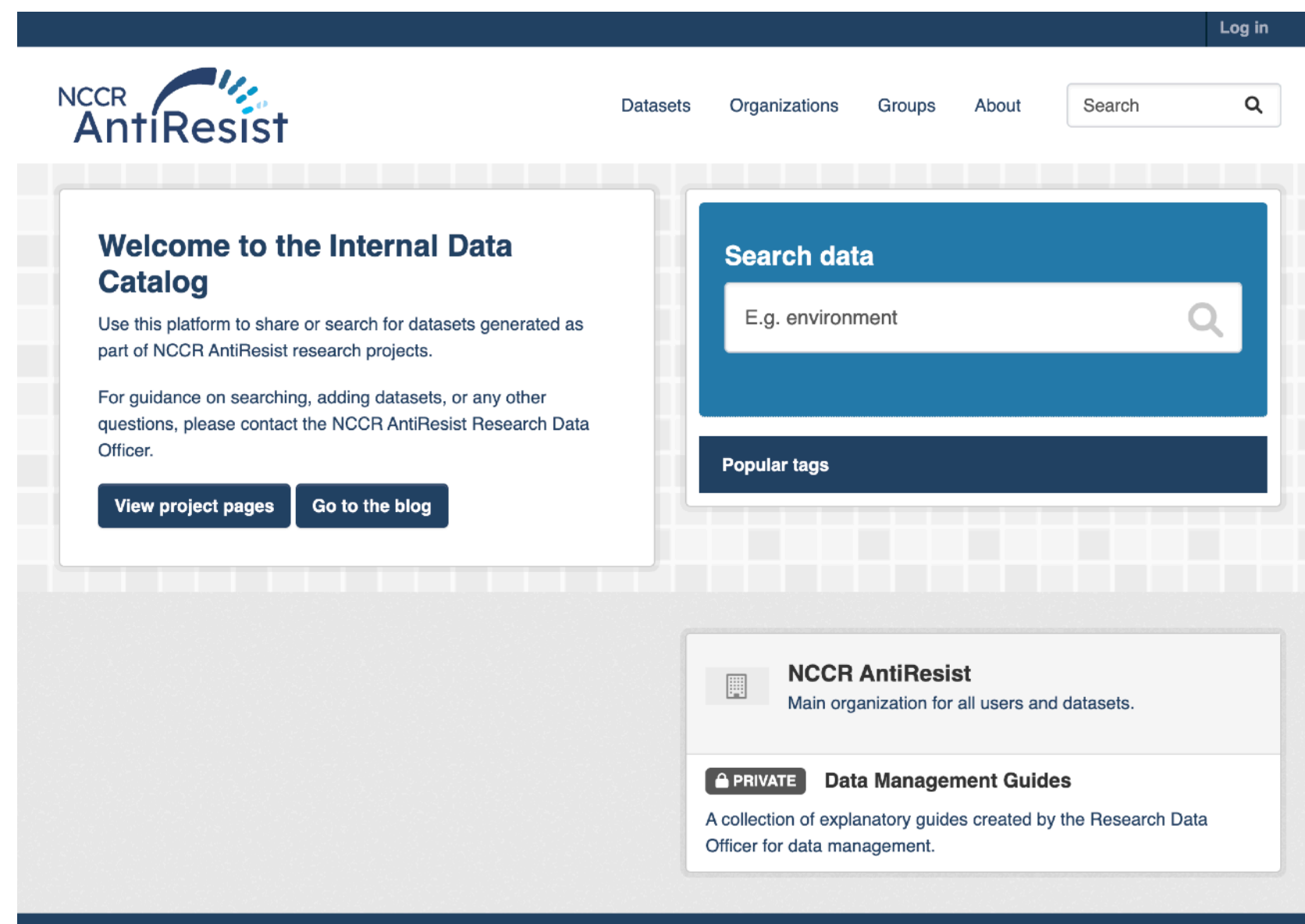


The screenshot shows the NCCR AntiResist data catalog website. At the top right is a "Log in" button. The navigation menu includes "Datasets", "Organizations", "Groups", "About", and a search bar with a magnifying glass icon. The main content area is divided into several sections:

- Welcome to the Internal Data Catalog:** A white box with a blue header. It contains the text: "Use this platform to share or search for datasets generated as part of NCCR AntiResist research projects." and "For guidance on searching, adding datasets, or any other questions, please contact the NCCR AntiResist Research Data Officer." Below this are two buttons: "View project pages" and "Go to the blog".
- Search data:** A blue box with a white search input field containing the text "E.g. environment" and a magnifying glass icon.
- Popular tags:** A dark blue box with white text.
- NCCR AntiResist:** A white box with a blue header and a grid icon. It contains the text: "Main organization for all users and datasets."
- PRIVATE Data Management Guides:** A white box with a blue header and a lock icon. It contains the text: "A collection of explanatory guides created by the Research Data Officer for data management."

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The screenshot shows the NCCR AntiResist website home page. At the top, there is a navigation bar with 'Log in' on the right and 'NCCR AntiResist' on the left. Below the navigation bar, there are links for 'Datasets', 'Organizations', 'Groups', and 'About', along with a search bar. The main content area features a 'Welcome to the Internal Data Catalog' section with a description and two buttons: 'View project pages' and 'Go to the blog'. To the right, there is a 'Search data' section with a search input field containing 'E.g. environment' and a search icon, and a 'Popular tags' section below it. At the bottom, there is a 'NCCR AntiResist' section with the text 'Main organization for all users and datasets.' and a 'Data Management Guides' section with a 'PRIVATE' label and the text 'A collection of explanatory guides created by the Research Data Officer for data management.'

Recording Data

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

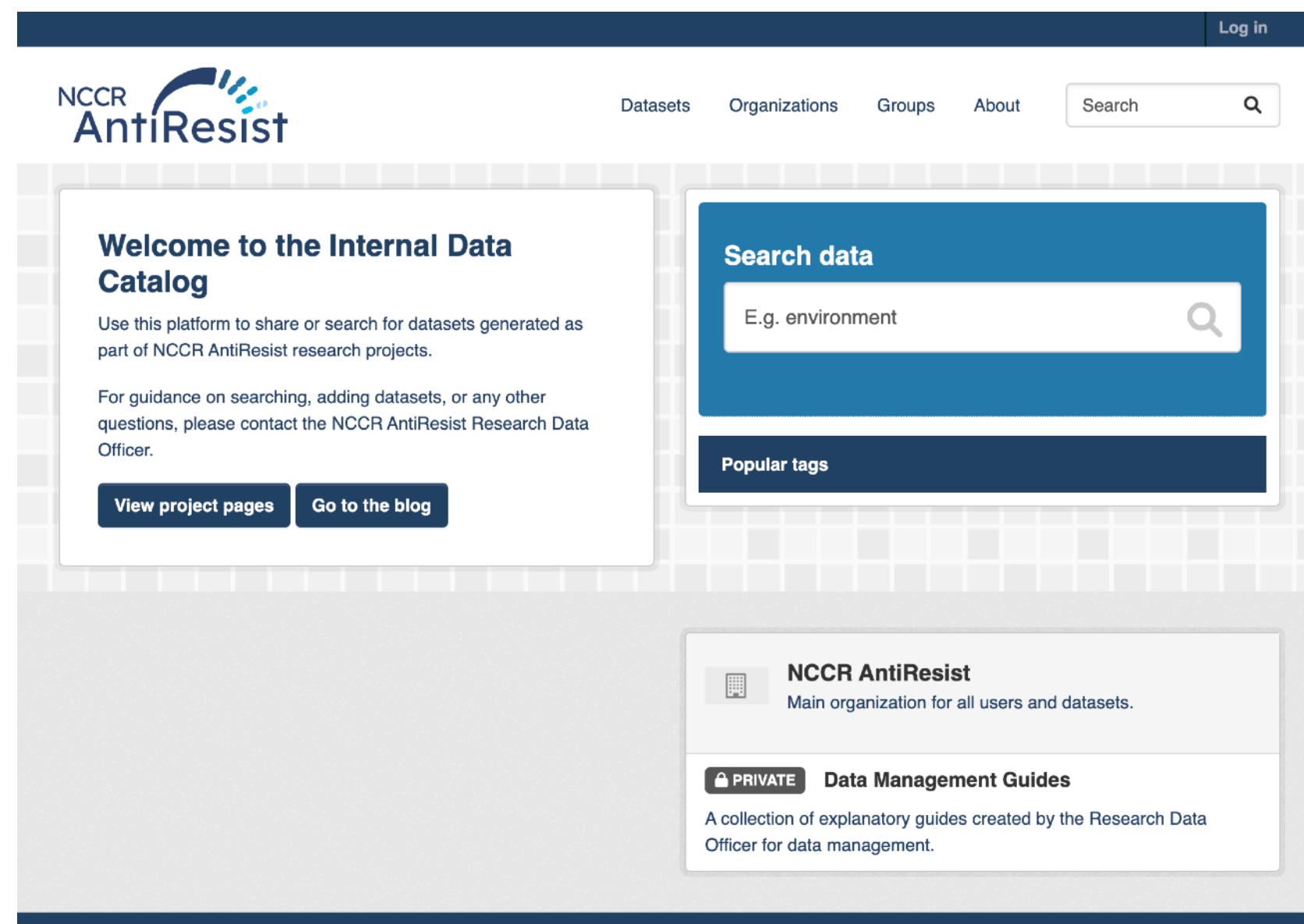


The screenshot shows a dataset page for 'Proteome of PnorC reporter-sorted P. aeruginosa PAO1 cells'. The page includes a 'PRIVATE' label, a description of the dataset, and a 'Data and Resources' section with two items: '20230605_protein_summary.csv' and '20230605_LFQ_report.pdf', each with an 'Explore' button. Below this, there is a breadcrumb trail: 'FACS > Pseudomonas aeruginosa > norC > proteomics > reporter'. The 'Additional Info' section contains a table with the following data:

Field	Value
Status	Collected
Category	Non-sensitive
Type	Proteomics
Work Package	WP-PAE
Author	Alejandro Tejada Arranz
Author Email	Alejandro Tejada Arranz

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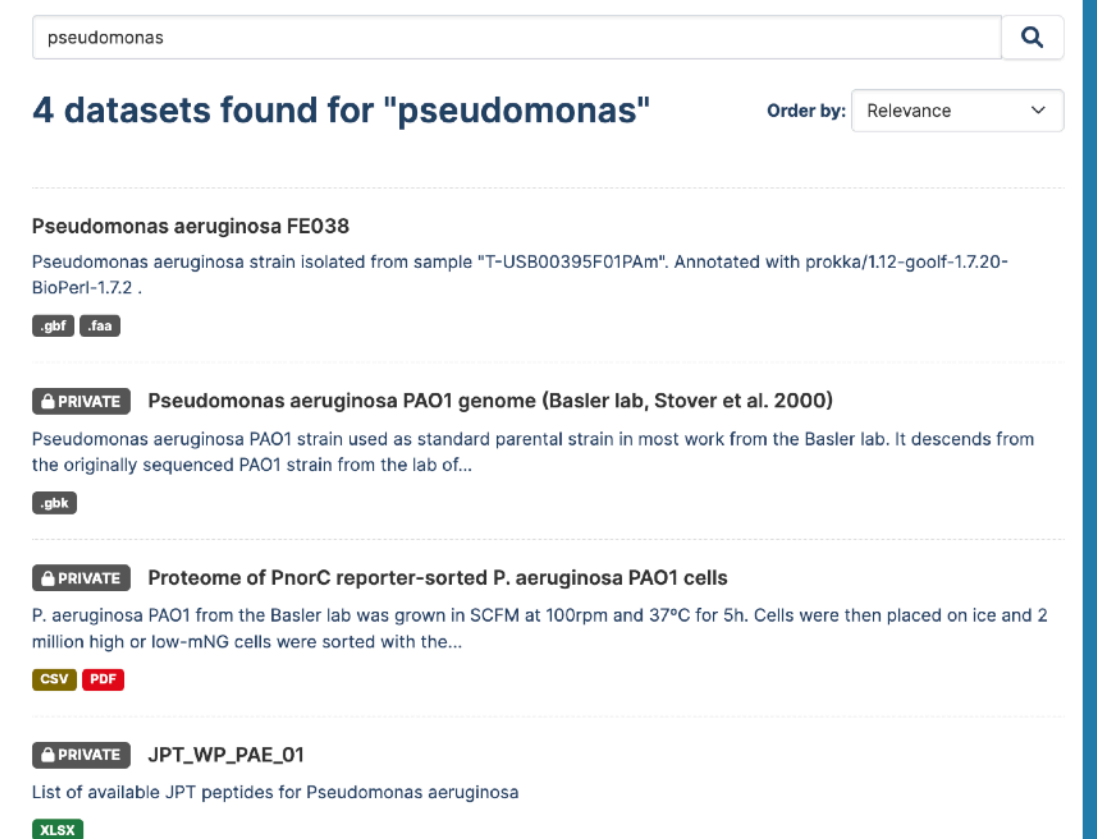
Recording Data

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- Complements lab records
- Can include protocols and supporting documents



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
Lorenzo Talà
Jeremy Wong
Zainebe Al-Mayyah
Sourabh Monnappa
Sofya Mikhaleva
Tania Distler
Lucas Meirelles
Chia-Ni Tsai
Han-Yi Huang
Po-Long Hsiao
Elke Holderbeke

Funding:

Swiss Ntl Science Foundation
NCCR AntiResist
Giorgi Cavaglieri Foundation
Beytout Foundation
HFSP
Gebert Rüt Stiftung
Enable
iPhD
EPFL-Imaging