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3D in vitro model of pancreatic cancer to study oncolytic virus infection

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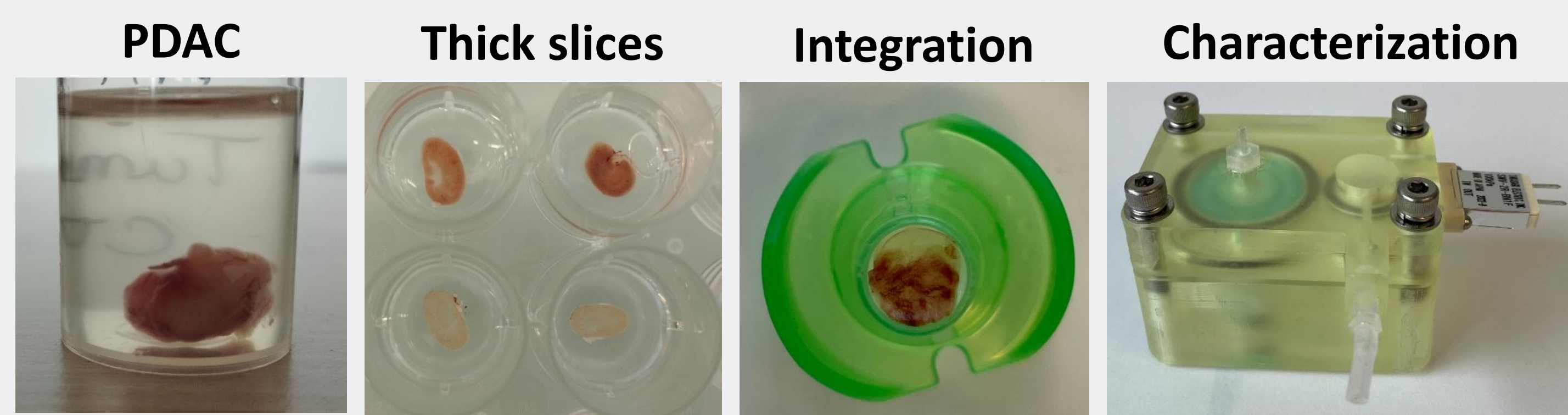
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Introduction

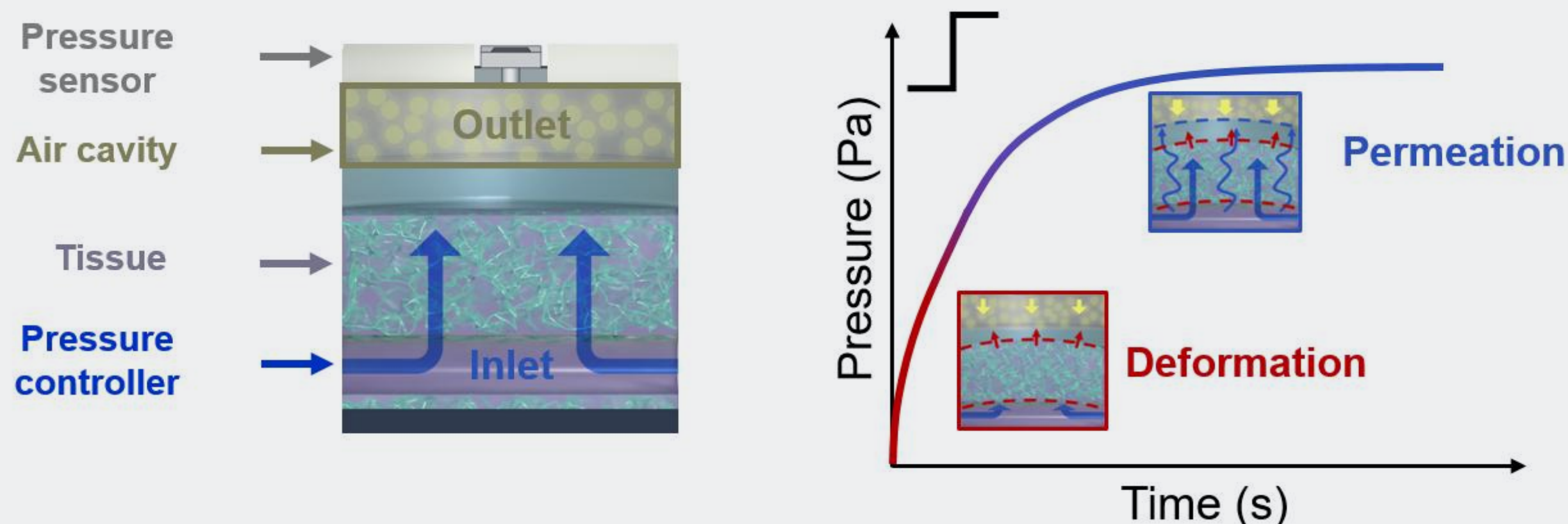
Pancreatic cancer (PDAC) is on track to become the second leading cause of cancer-related deaths worldwide, largely due to the lack of effective treatments beyond surgery. Oncolytic viruses represent a promising therapeutic strategy, as they specifically target and destroy tumor cells while activating antitumor immune responses. However, their efficacy could be limited by poor access to the tumor microenvironment, an area that remains underexplored. Our research aims to address this challenge by investigating the permeability of the pancreatic tumor environment and its impact on oncolytic virus delivery.

Poroelastic characterization of PDAC



PRESTO working principle

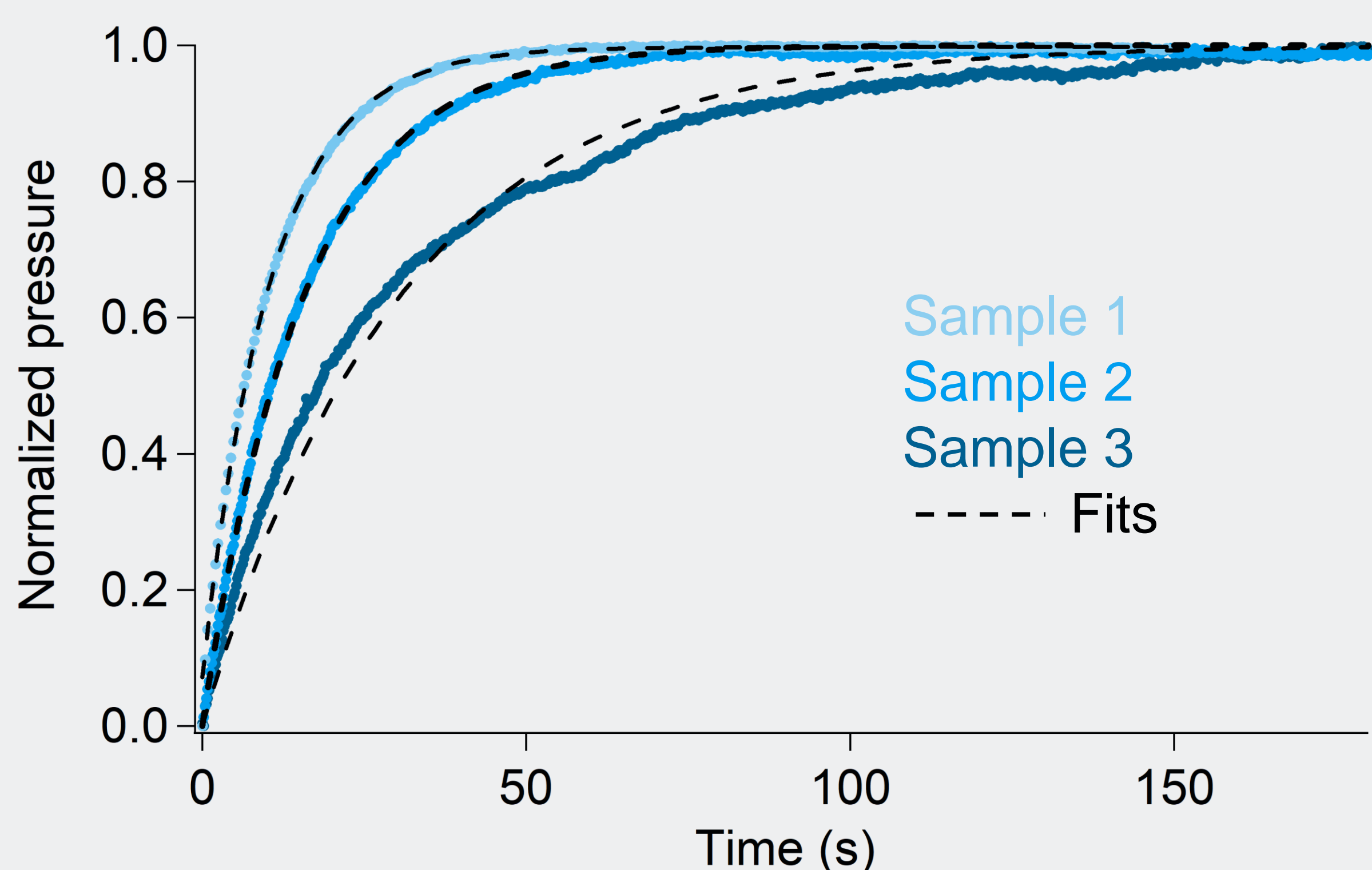
air cavity PREssure based poroelaSTometry



PRESTO allows the direct, contactless and real-time monitoring of tissue's elasticity and permeability.

Model and fits

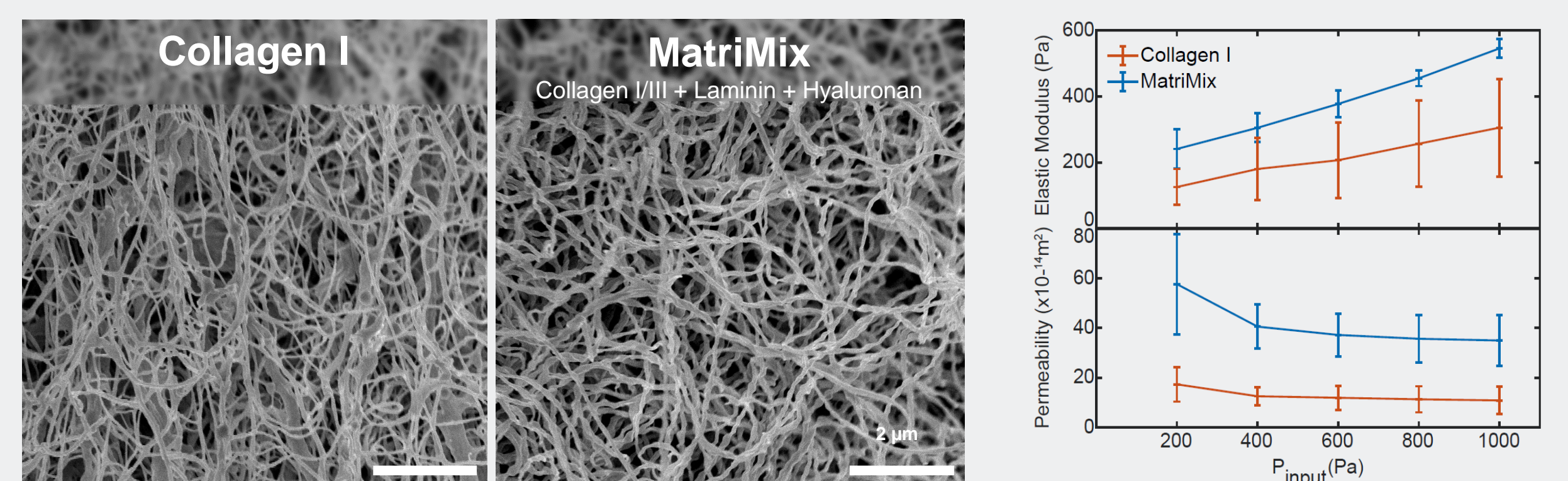
We fit the pressure response with a 1D model of poroelasticity, which allows us to extract the permeability and the elasticity of the tissue:



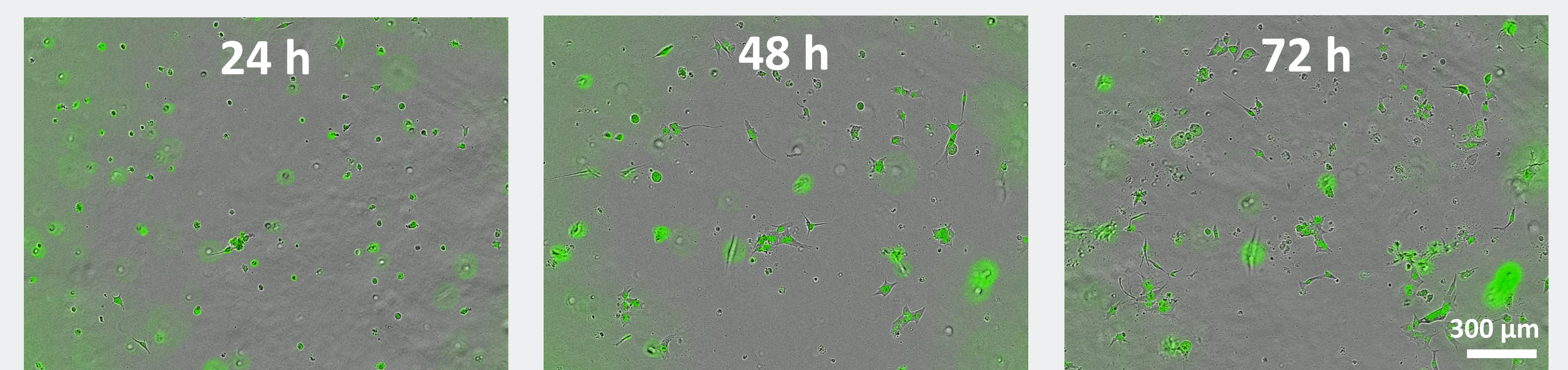
The permeability of PDAC is in the range of $1.5-5 \times 10^{-14} \text{ m}^2$, while its elasticity spans 3–7 kPa.

In vitro modelling of PDAC

Alcaide, Alric, Cacheux *et al.* Biochemical and Biophysical Research Communications (2024)

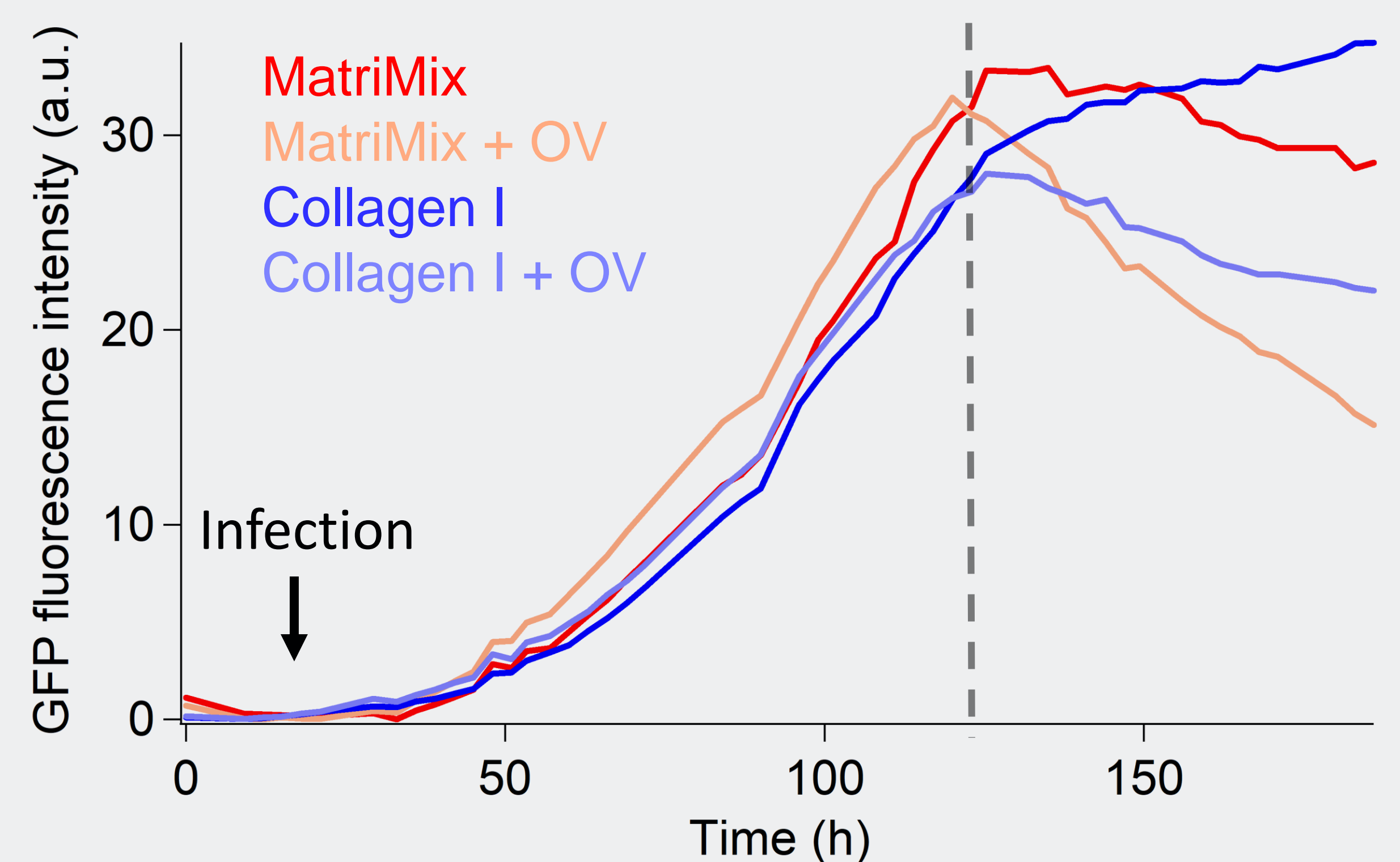


PDAC patient-derived primary cells (PDAC087T) embedded into hydrogels



PDAC cells express a nuclear histone fused to GFP, allowing live cells real-time fluorescence microscopy monitoring.

Infection with oncolytic viruses (OV)



- The proliferation rate decreases after 120 hours in both controls, with MatriMix showing a more pronounced slowdown, which may be due to its higher elastic modulus (*i.e.*, increased cell confinement).
- The virus increases the cell death rate in both hydrogels, with no significant difference between them.

Conclusions

- We demonstrate the ability of PRESTO to measure the elasticity and permeability of tissue explants.
- We developed a 3D *in vitro* model to replicate the physical microenvironment of PDAC cells.
- Infection of patient-derived primary cells (PDAC087T) reveals a delayed effect on cell death; we suggest that the size of OV (250 nm) limits their diffusion into the hydrogel and account for this delay.