



**PROGETTI DI RICERCA PER LO SVILUPPO  
DELLA SANITÀ DEL SUD**

*Biotecnologia – bioinformatica e sviluppo Farmaceutico*

**Puglia Life Science Hub: Il polo di LECCE**

Tecnologie abilitanti per la Medicina di Precisione

**Giuseppe Gigli**

CNR NANOTEC & Università del Salento

## Lecce High Tech Campus



**100 people**  
3000mq labs,  
start ups

**300 people**  
12000mq Labs,  
**1000 mq cleanroom, 6**  
**Open Facilities, joint labs**

**17k students,**  
9 departments.

**6000 mq,** living  
labs, spaces for  
companies, TT  
offices

**UNIVERSITÀ  
DEL SALENTO**

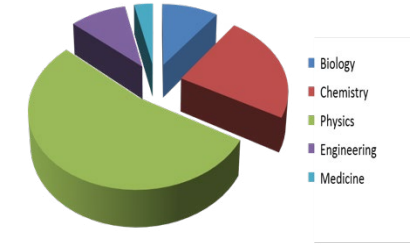
**GNR NANOTECH**  
INSTITUTE OF NANOTECHNOLOGY

**Dhitech**  
DISTRETTO TECNOLOGICO HIGH TECH

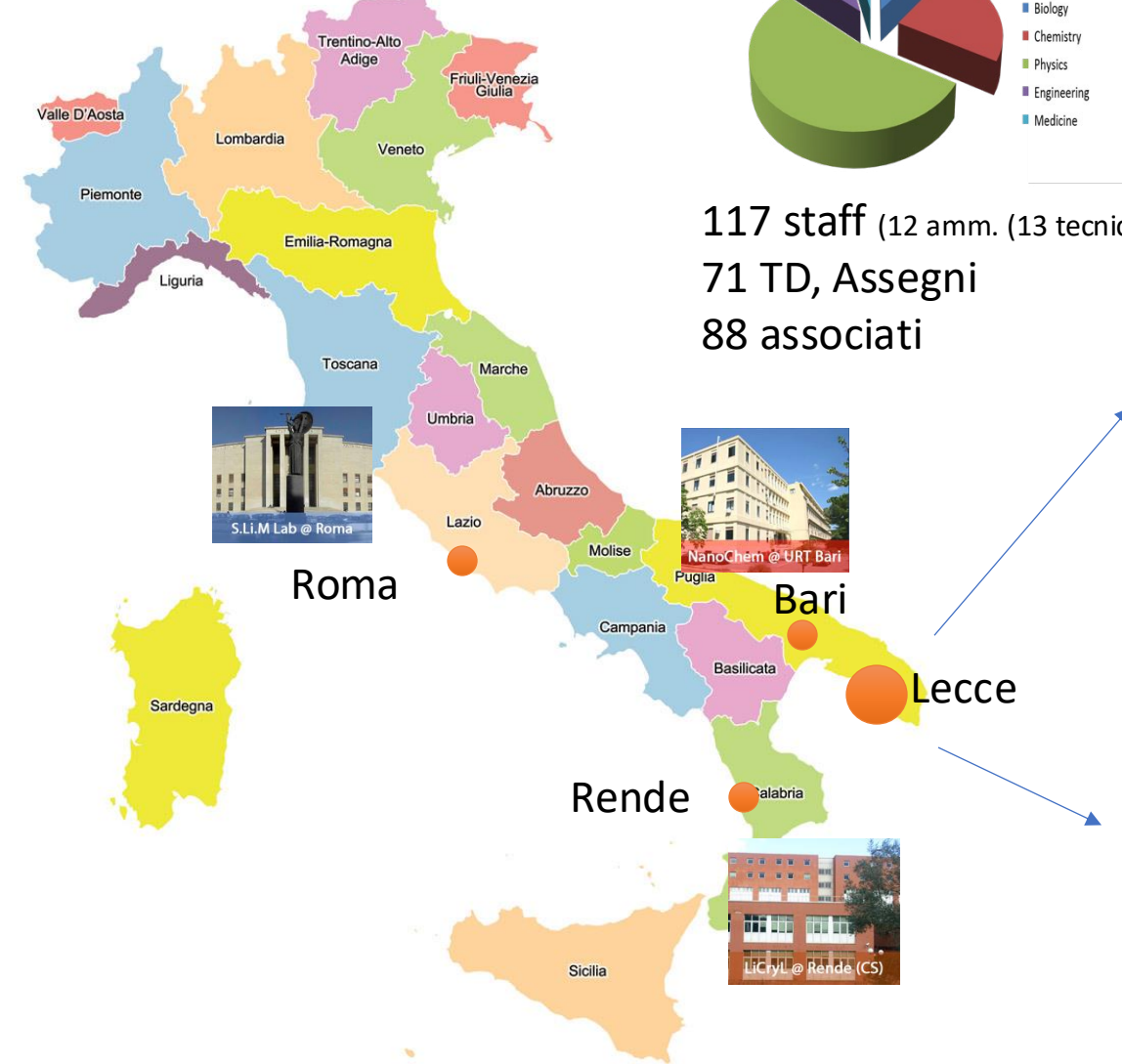
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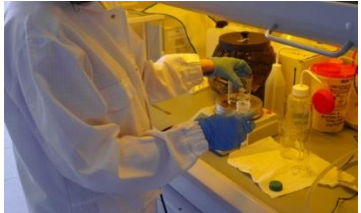
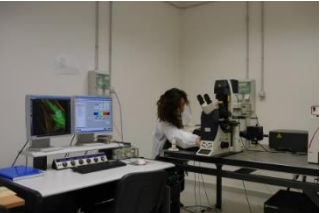



**interdisciplinary enviroment  
from physics to medicine**



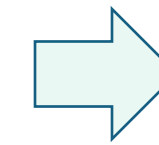
117 staff (12 amm. (13 tecnici)  
 71 TD, Assegni  
 88 associati



**12.000 m<sup>2</sup> 6 Open Access Facilities,  
 Joint Labs with industries & IRCCS, Start ups**

|   |   |   |
|---|---|---|
| <b>NanoChem</b><br>  | <b>Biotech</b><br> | <b>Nanofab</b><br>       |
| <b>Photonics</b><br> | <b>Devices</b><br> | <b>Adv materials</b><br> |

 **TecnoMedPuglia**  
*Traslational Medicine Infrastructure*



From basic research...

...To Clinics

*Bio Engineering  
biotechnology  
Nanotechnology  
Molecular Biology  
Genetics/Epigenetics*

*Oncology  
Neurology  
Ageing diseases  
Neuro degenerative D.*

 **TecnoMedPuglia** Main Partners:



CNR Nanotec @ Lecce

- **Joint lab**  OSPEDALE SAN RAFFAELE
- **Joint lab**  STMicroelectronics
- **Joint lab** 

*Research Inf.*



*Oncology*

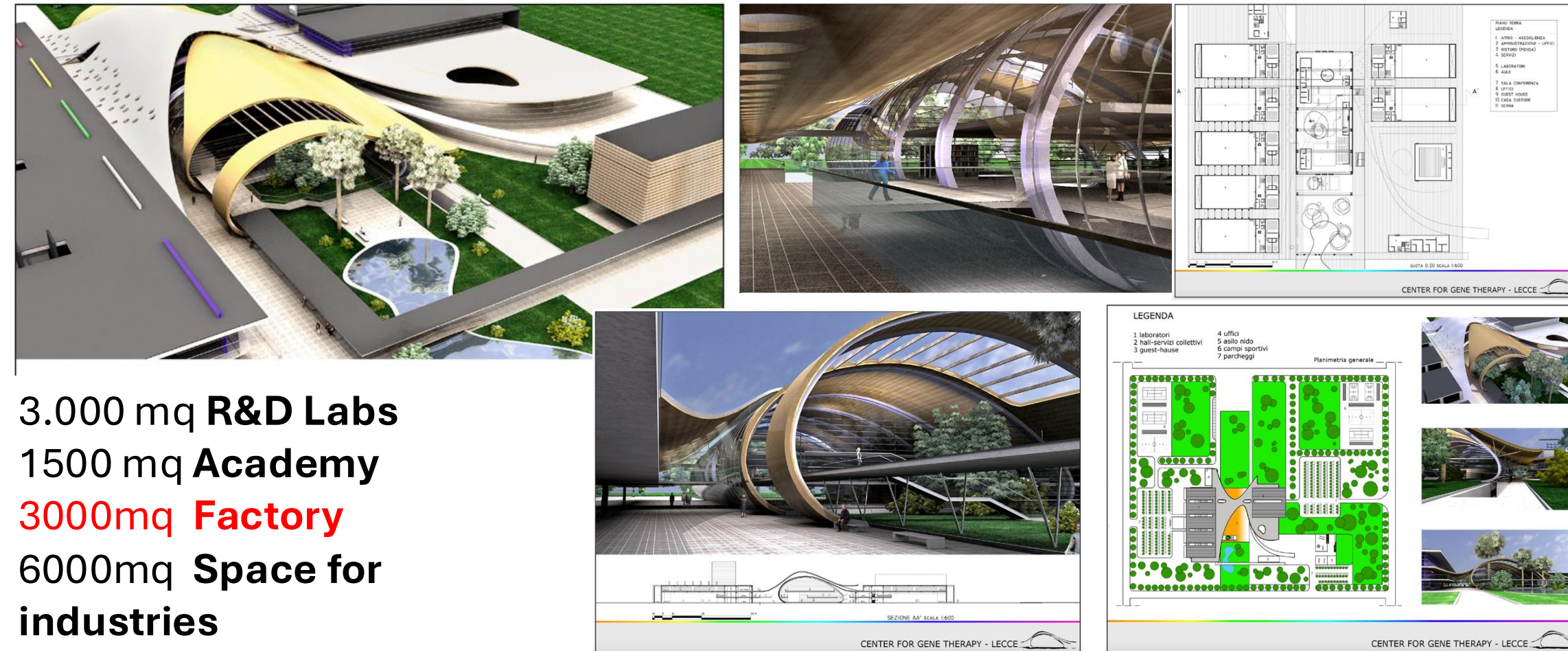


*Neurology*

- **Joint lab**  FONDAZIONE EBBI  
"Rita Levi-Montalcini"

*Clinics*

**Puglia Life Science HUB: CART cells factory**



**3.000 mq R&D Labs**  
**1500 mq Academy**  
**3000mq Factory**  
**6000mq Space for industries**

Polo high tech per lo sviluppo di ATMP e tecnologie diagnostiche e terapeutiche avanzate.

# TecnoMedPuglia

## Precision Medicine Technopole



3000mq Open Access Infrastructure

### Center for translational Nanomedicine

- Liquid biopsy\_
- Tecnologie per Drug & Gene delivery
- 3D models on chips
- Microscopia multimodale di correlazione assistita da intelligenza artificiale

### Programma di formazione

joint lab NANOTEC- ITS x la formazione di nuove professionalità nell'ambito delle ATMP

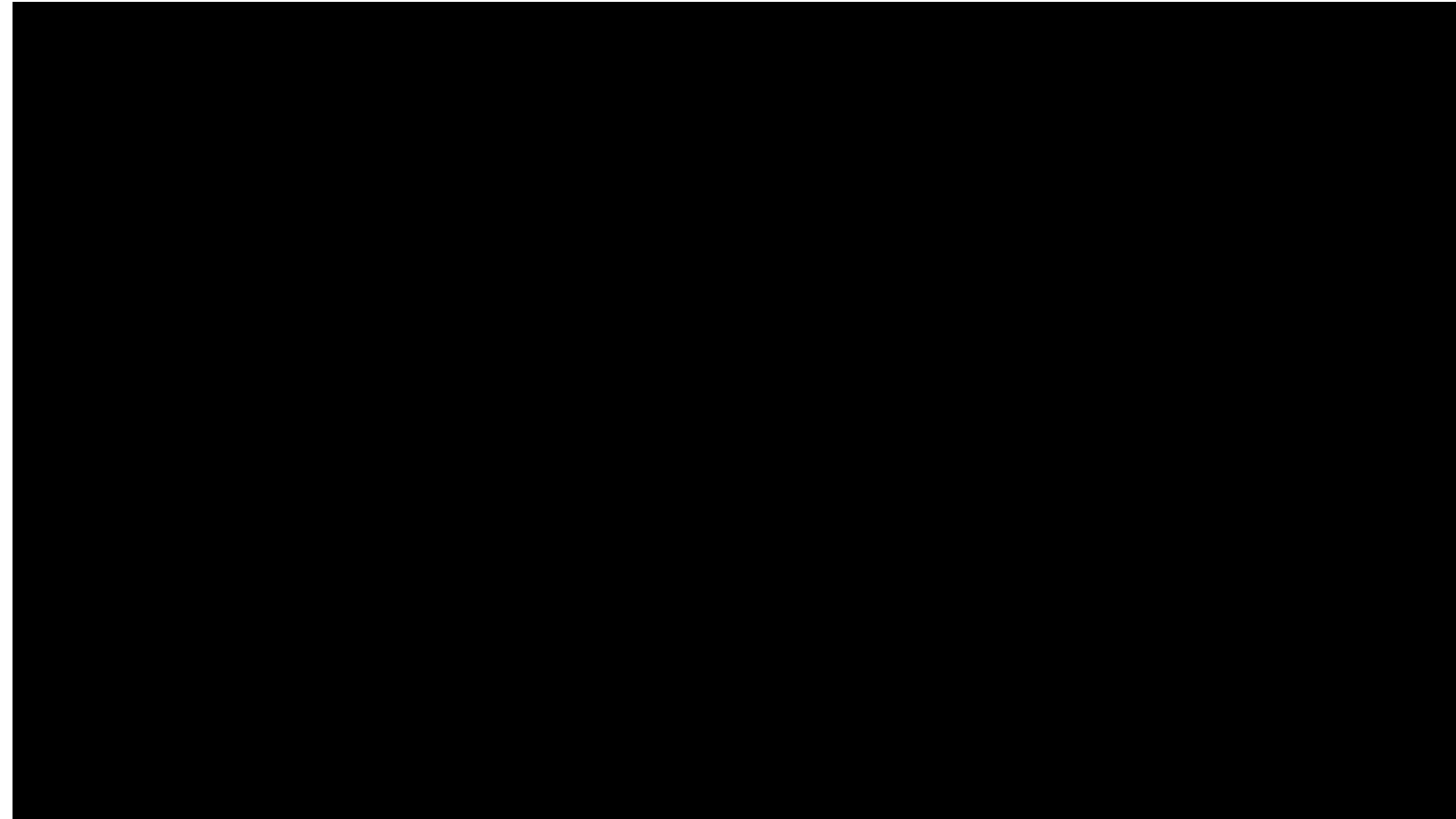
### Programma di comunicazione & divulgazione

(Nanoclip formative, inserti scientifici, caffè scientifici, etc)



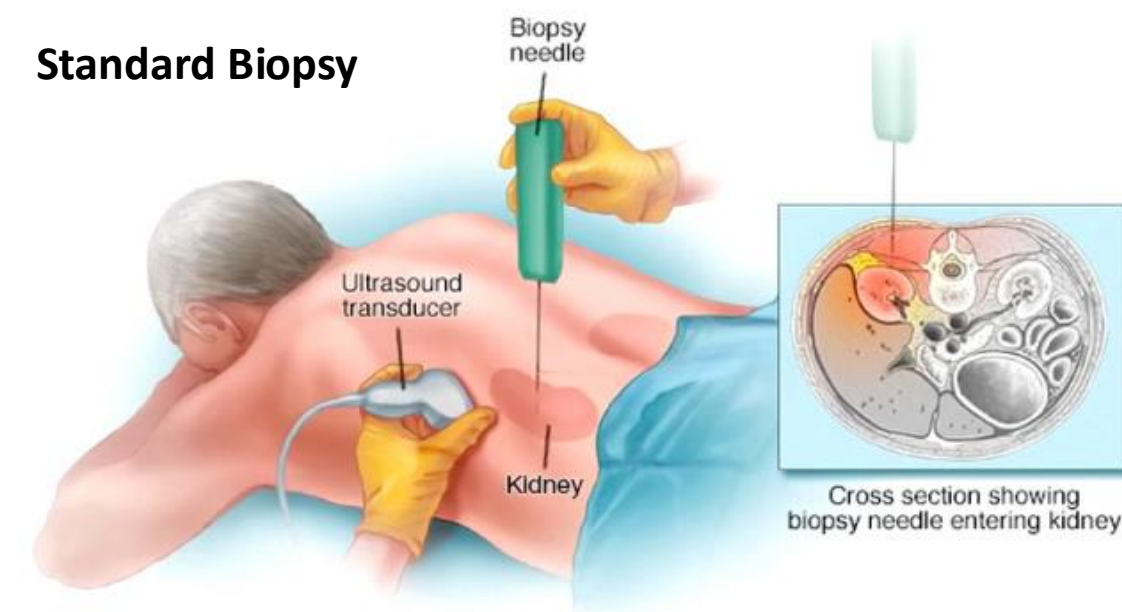
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**18-19-20 SETTEMBRE 2024**  
**BARI | VILLA ROMANAZZI CARDUCCI**





## LIQUID BIOPSY



**Standard Biopsy**

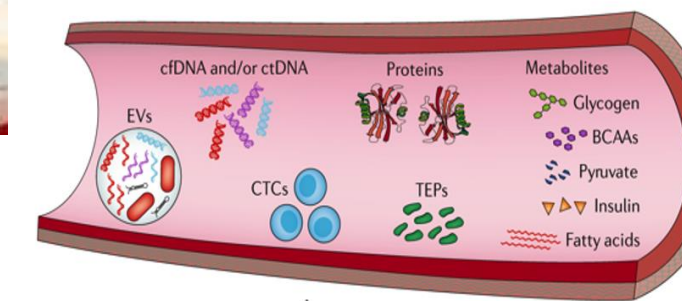
- Tissue Extracted by surgery
- Time intensive procedure
- Invasive, painful, some Risks
- No repeatable
- Localised sampling of tissue (FN)

### Liquid Biopsy



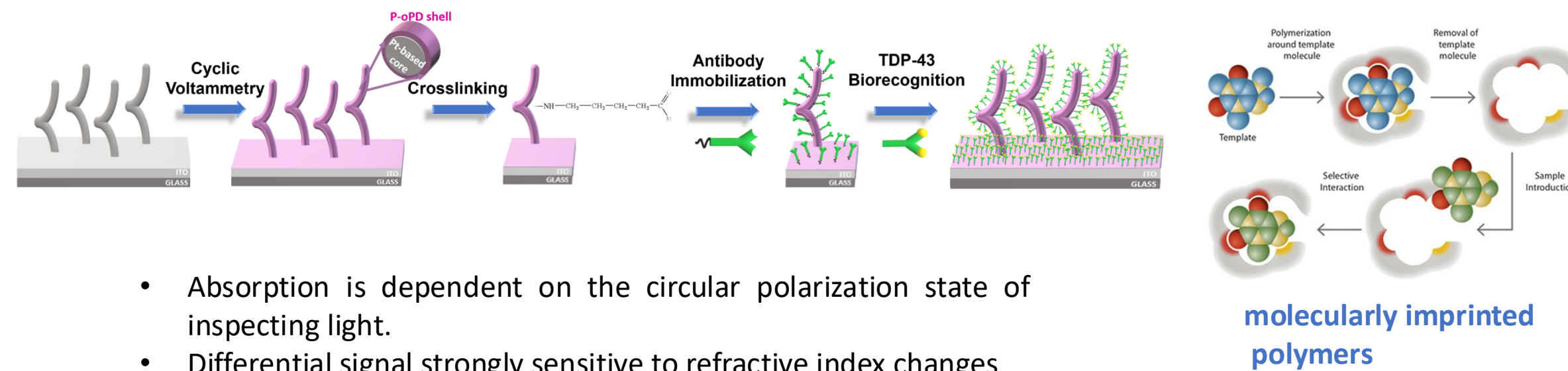
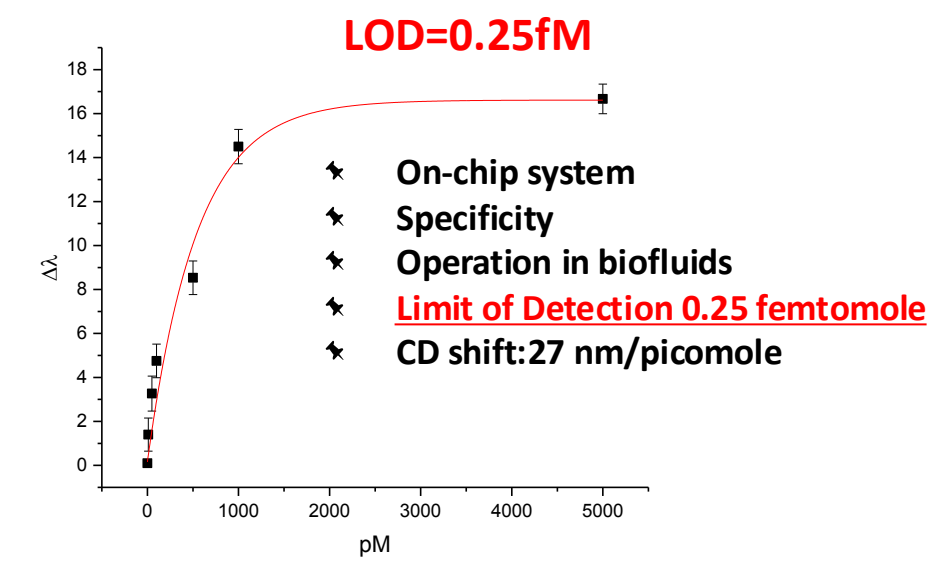
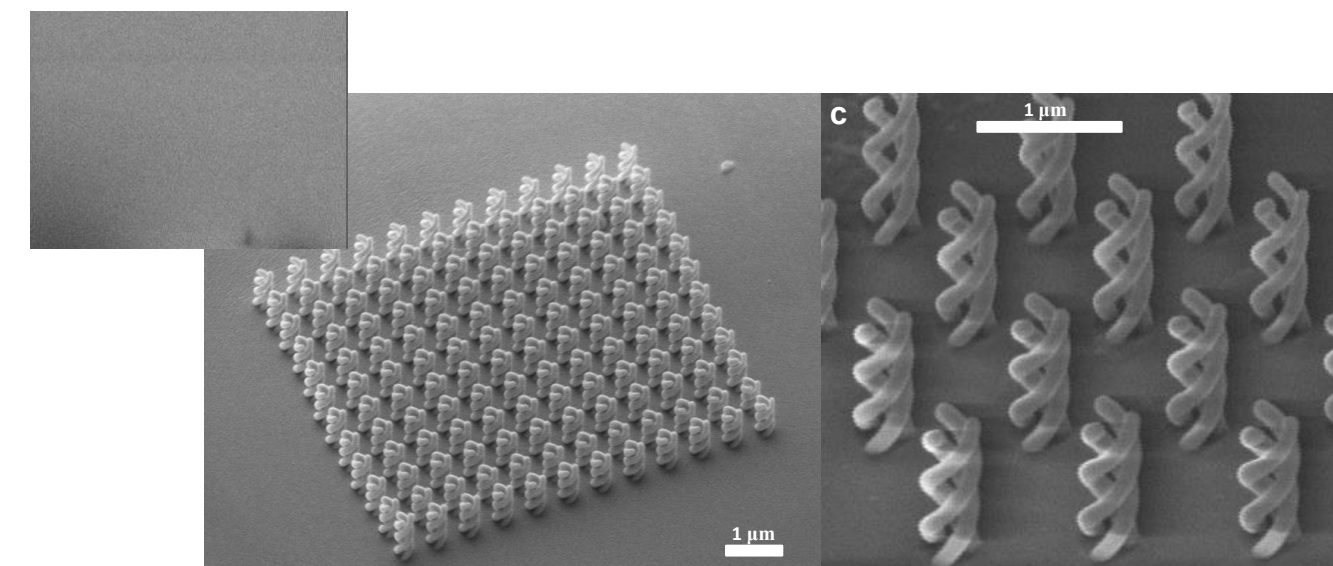
**Detecting biomarkers in bio fluids**  
Not invasive,  
Quick, Minimal pain \risk  
Full Tissue profile

**Open issue:**  
Standard techniques sensitivity ( Elisa, PCR, NGS, WGA, IHC,..) is low

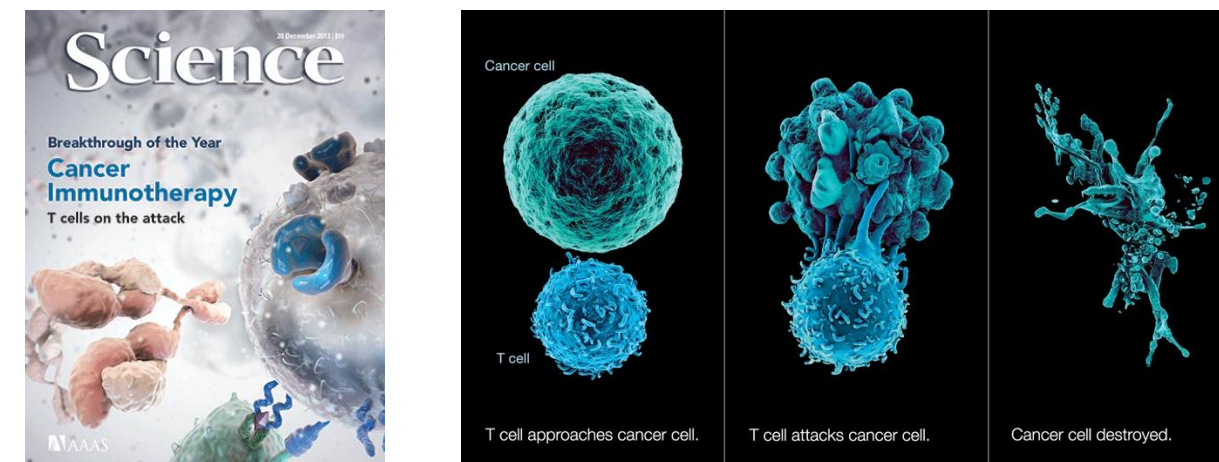


Biomarkers

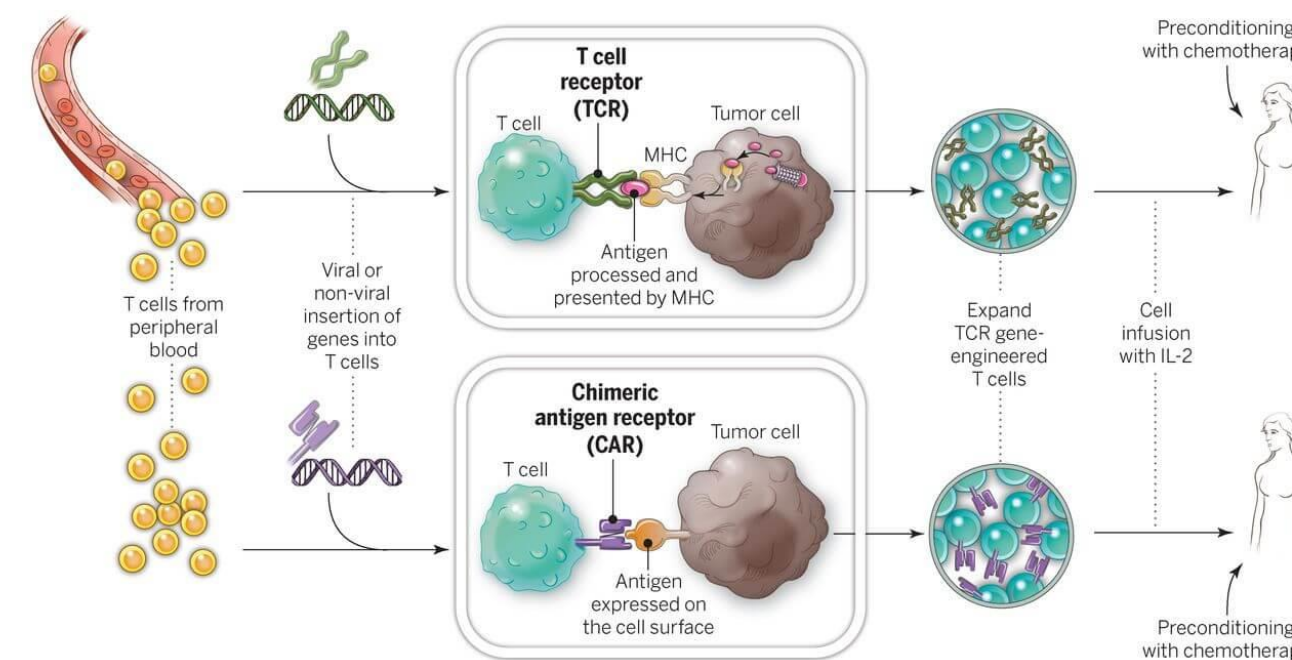
**Chiro-Optical Sensors for Specific Femtomolar Detection of TDP-43**



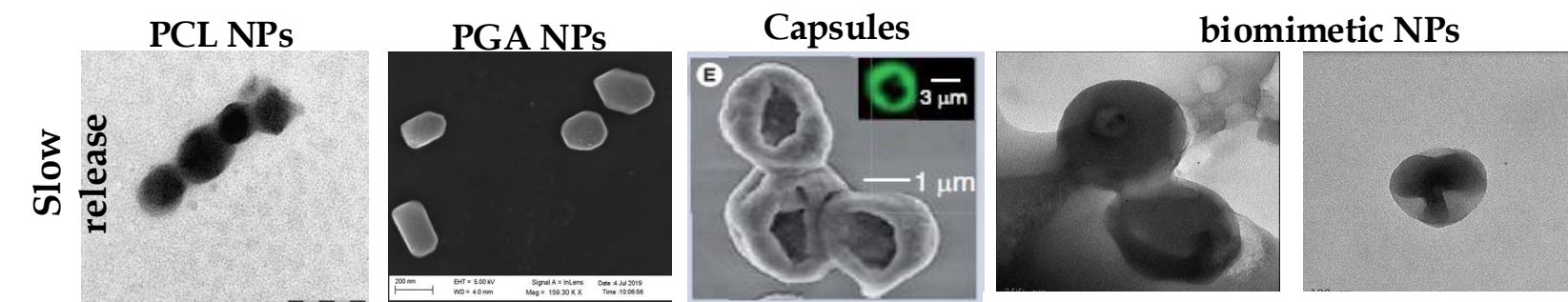
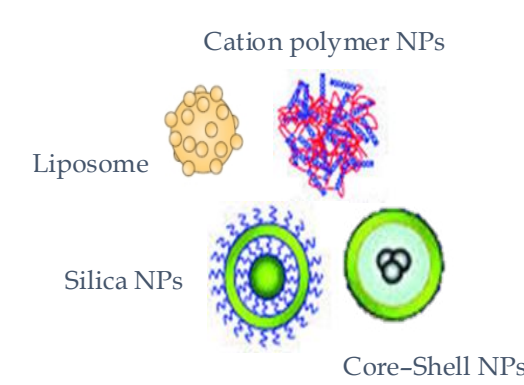
## IMMUNOTHERAPY: CAR-T cells approach



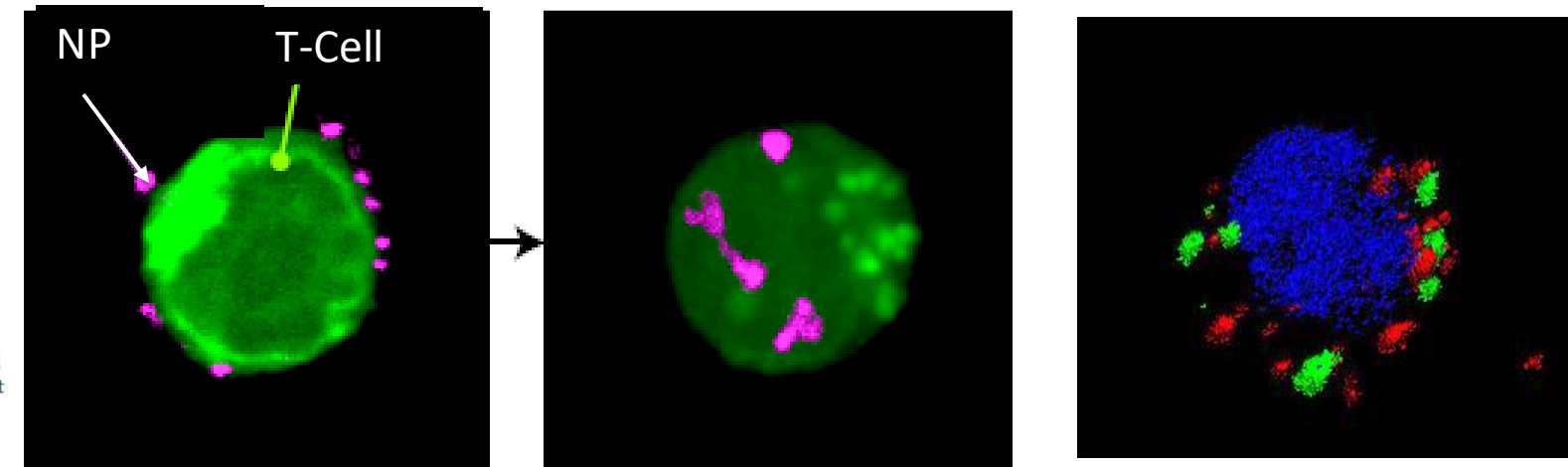
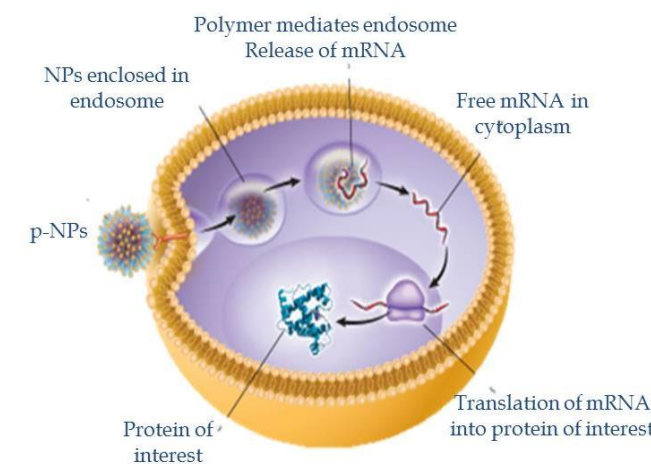
Boosting body's natural defences (IS) to treat cancer



## Cancer immunotherapy by exploiting nanotechnology



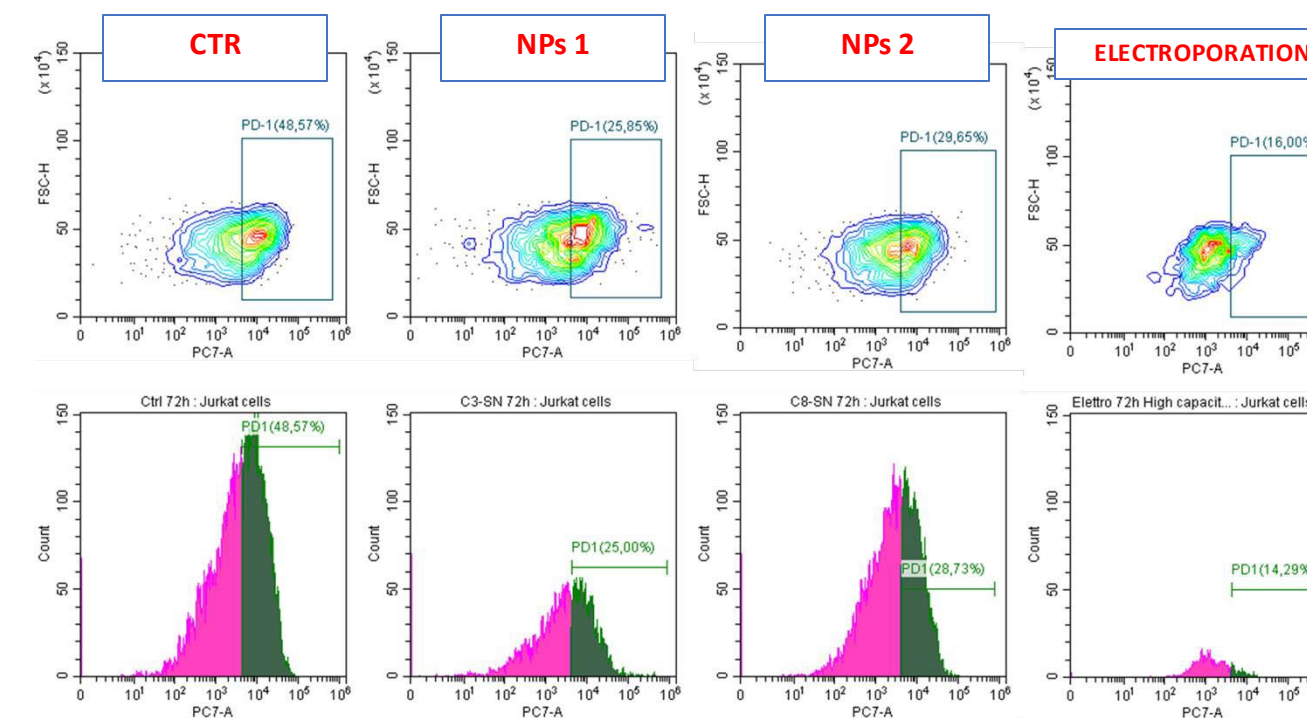
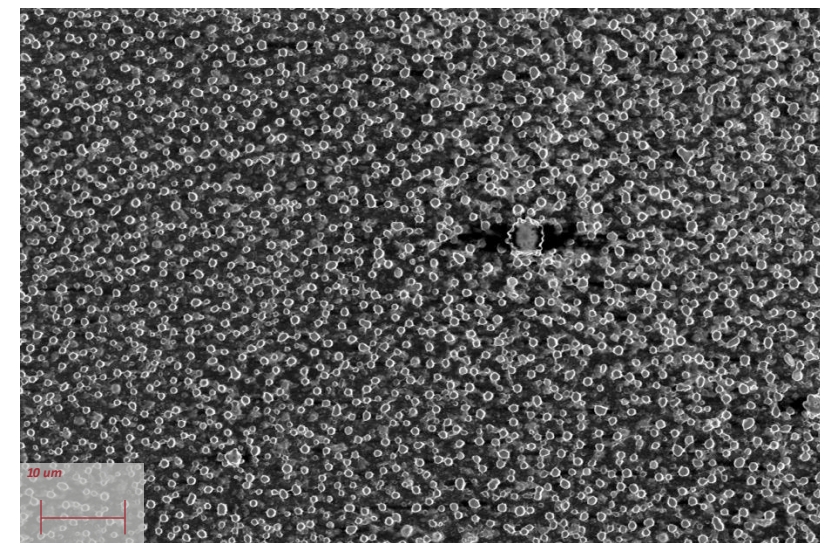
Tool box of safe (bio)organic NPs with tunable physico-chemical properties





### Nanoparticles for delivery of CRISPR/Cas9 for Genome Editing of T-cells

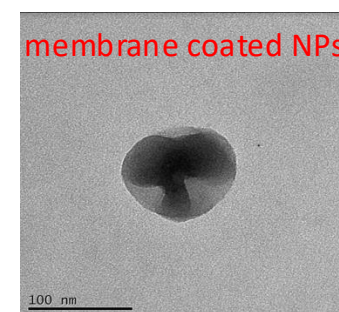
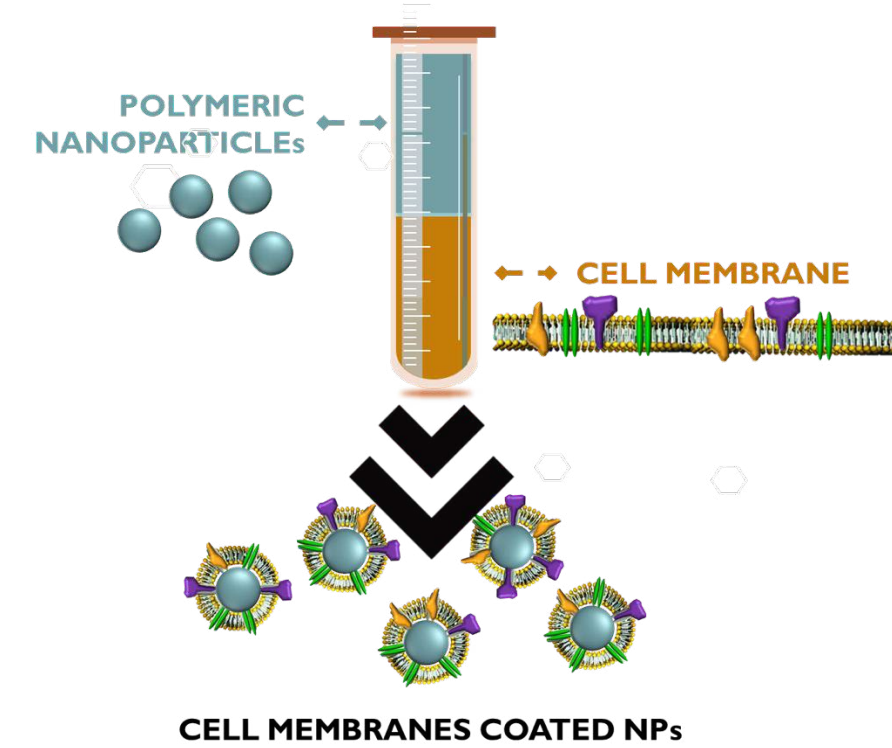
Knockout of PD-1 in T-cells to increase CAR-T cell activity in solid tumours



G. Maiorano, A. Galeone, I.E. Palamà, et al., in preparation

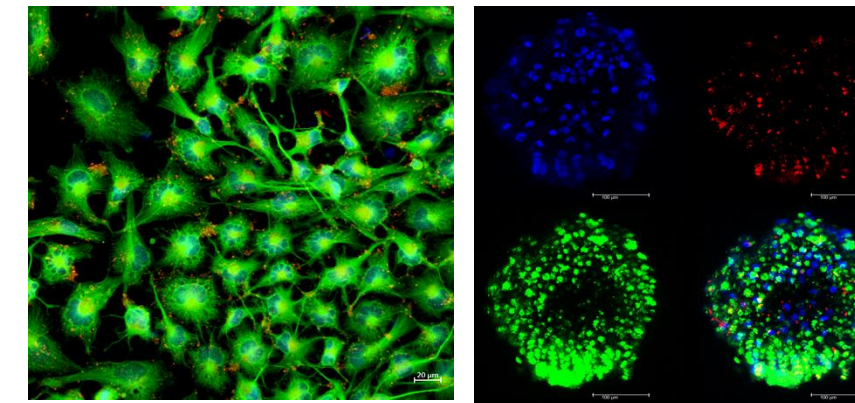


**Biomimetic Nanoparticles for homotypical targeting**

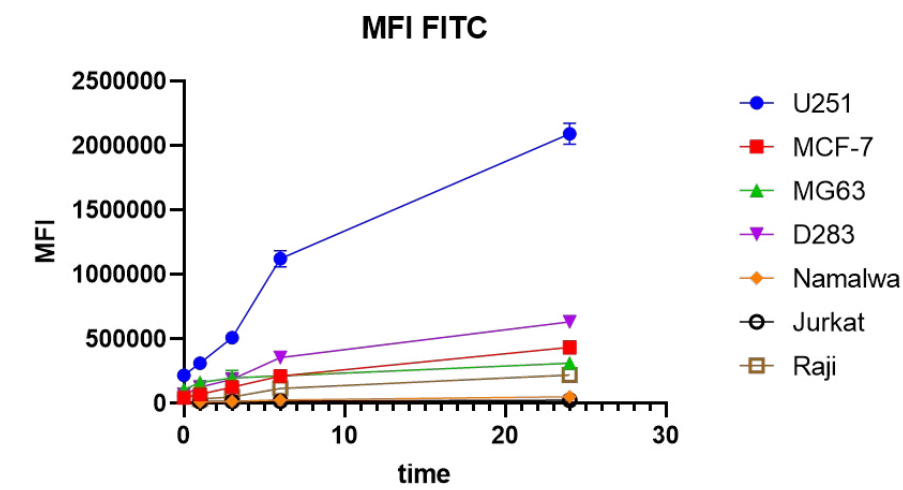


- Targeting capabilities
- Immune system evasion/stimulation
- Camouflaging
- Evading clearance

Glioblastoma membrane-coated biomimetic NPs target 2D and 3D GBM models and show homotypical targeting properties



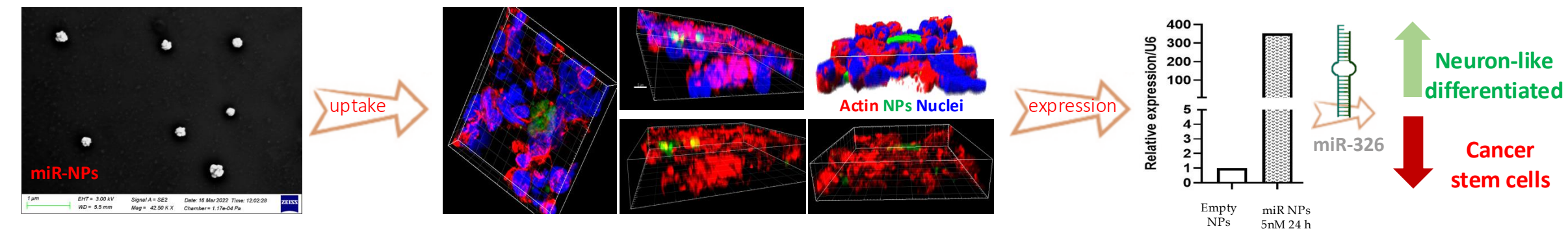
DAPI- nuclei FITC- beta-tubulin DiD- NPs



C. Baldari, G. Maiorano, I.E. Palamà, et al., under submission

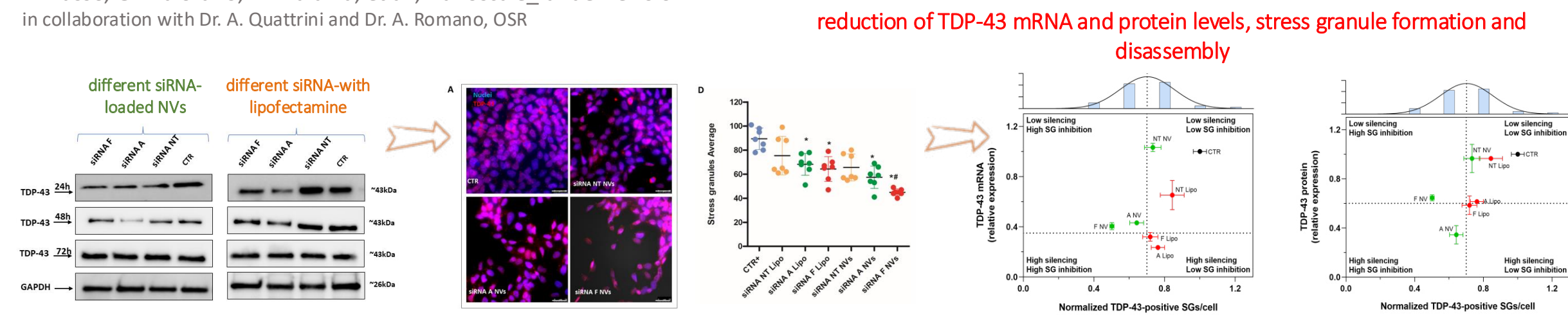
**Nanoparticle-mediated delivery of oncosuppressor miRNAs in pediatric medulloblastoma**

G. Maiorano, I.E. Palamà, et al., under submission  
 in collaboration with Prof. Ferretti, La Sapienza University

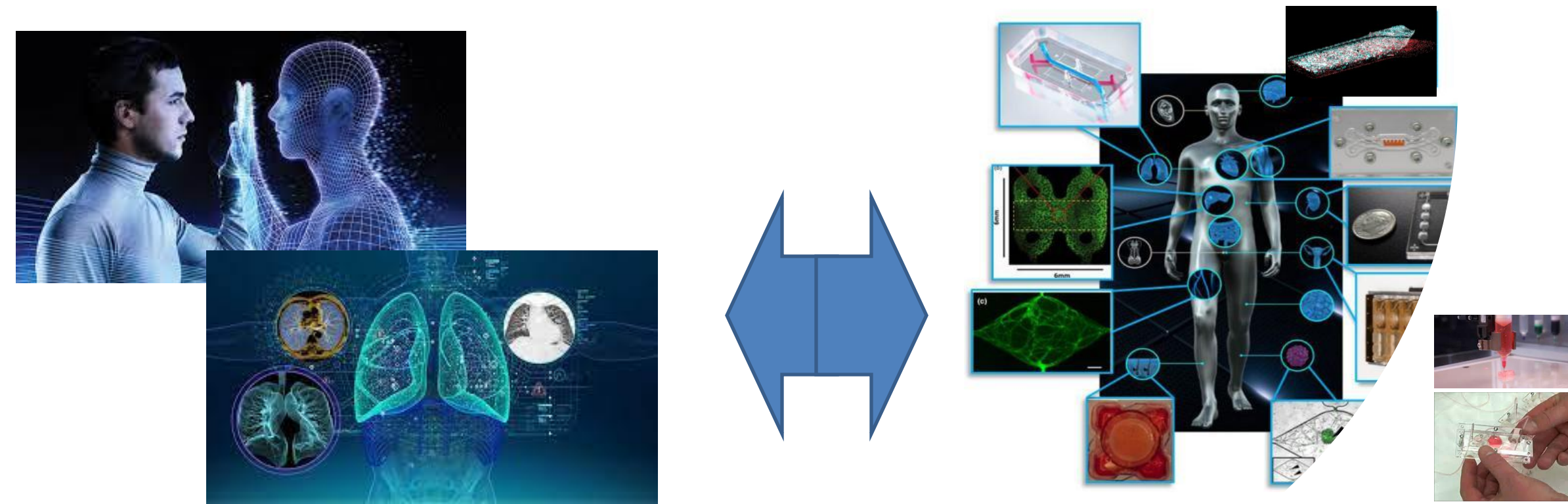


**Optimizing TDP-43 silencing with siRNA-loaded polymeric nanovectors in neuronal cells**

A. Russo, G. Maiorano, I.E. Palamà, et al., Nanoscale\_ under revision  
 in collaboration with Dr. A. Quattrini and Dr. A. Romano, OSR



## Digital Patient vs the body on chip



- Dynamic virtual representation continuously fed with data from integrated sensors and software.
  - Use machine learning (**AI**) and big data technology
  - monitor status, diagnose and predict diseases and test solutions remotely
- *In vitro* model able to recapitulate the patho-/physiological complexity of the human organs
  - Allow to test drug, and study biological mechanisms



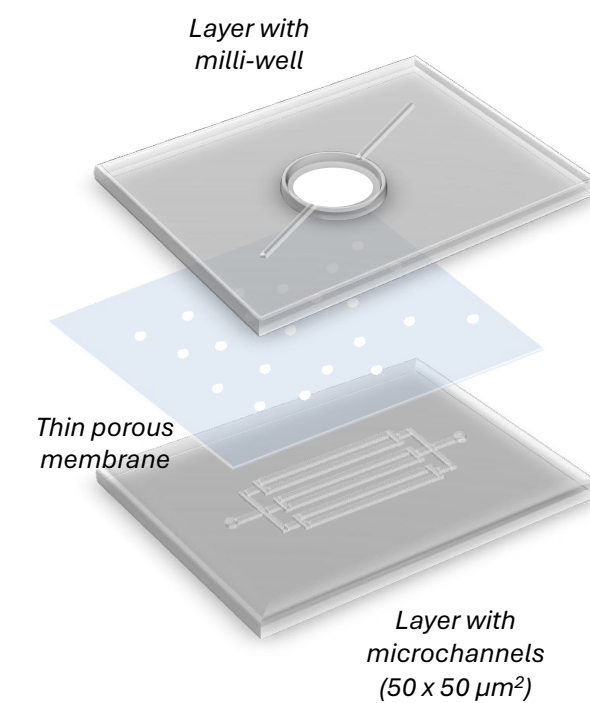
## Development of a Human BBB on chip model

Human BBB-on-chip models provide powerful platforms for studying **neurovascular interactions** and hold great potential for **drug screening** and **therapeutic research** related to central nervous system diseases.

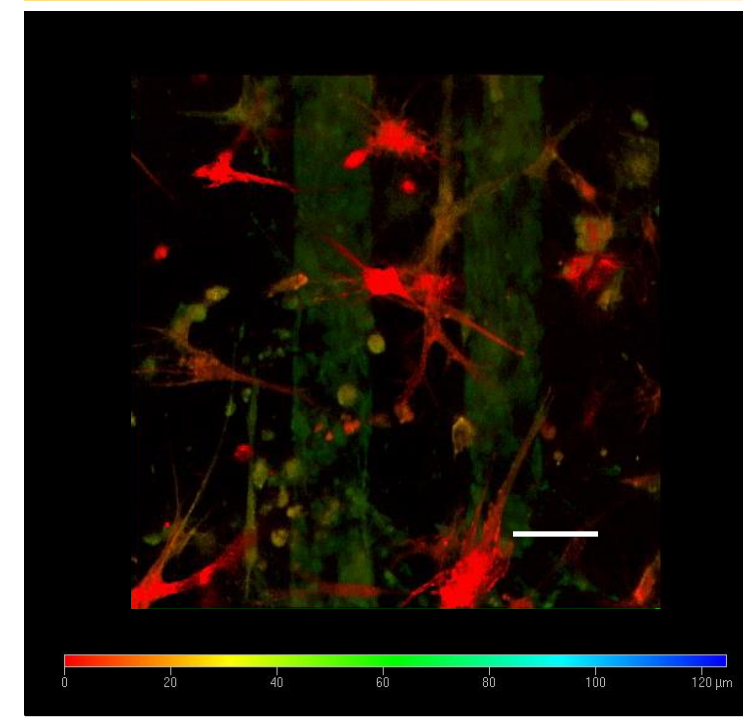
**Our model** distinguishes itself with its small, square microchannels that support **vascular lumen formation** and replicate the **in vivo hemodynamic environment**. By simulating cerebral blood flow, we gained key insights into the **alignment** and organization of **actin filaments** in **brain endothelial cells (ECs)**. Additionally, we investigated the **roles of pericytes** and **astrocytes** in maintaining vascular lumen structure and stability.

This work is currently under review in *Advanced Healthcare Materials* (Guarino et al.)

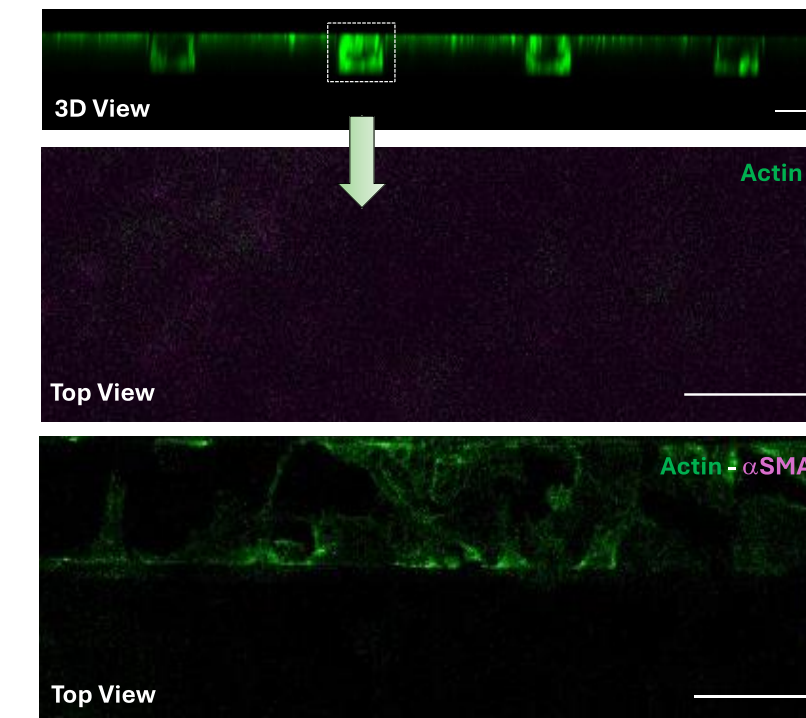
Exploded view of the microfluidic device illustrating the three constituent layers



Depth map of the chip showing cell 3D distribution (astrocytes-pericytes-ECs)

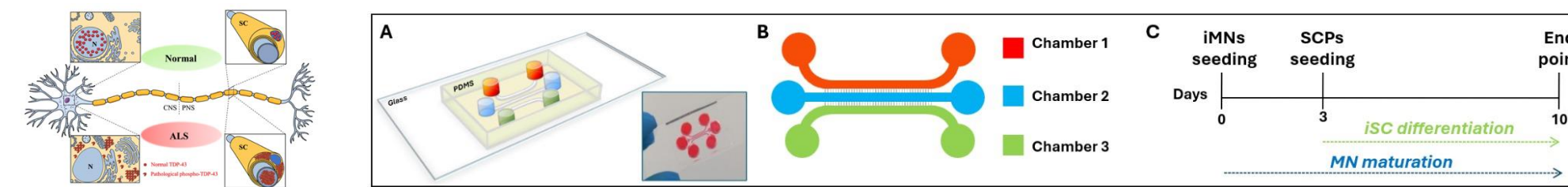


Microchannels lined by ECs (green) and Pericytes (magenta) forming a lumen



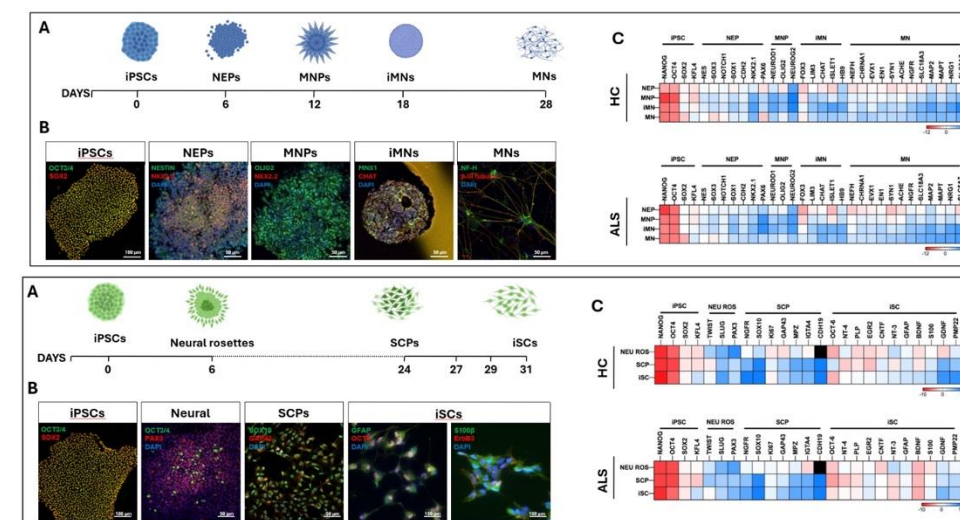
## Organ-on-Chip systems for ALS study: neuro-motor unit

We fabricated a multi-compartment microfluidic device that allows up to three cell populations to be cultured into fluidically independent circuits<sup>3</sup> (Fig.3). Our device allows the spatial separation between MN soma, axons and SCs, and therefore the investigation of the axon-SC interactions and their mutual effects on differentiation and function. The final steps of MN and SC differentiations were performed on chip



### iPSCs differentiation

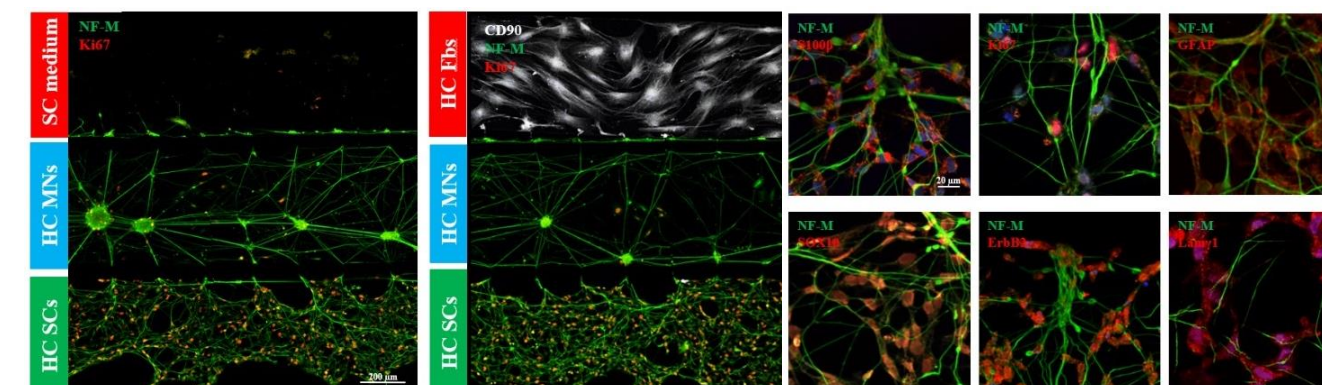
Human iPSCs, derived from human fibroblasts belonging to healthy control and p.A382T TARDBP patients, were differentiated into a nearly pure MN population and a highly pure population of immature SCs (iSCs) respectively.



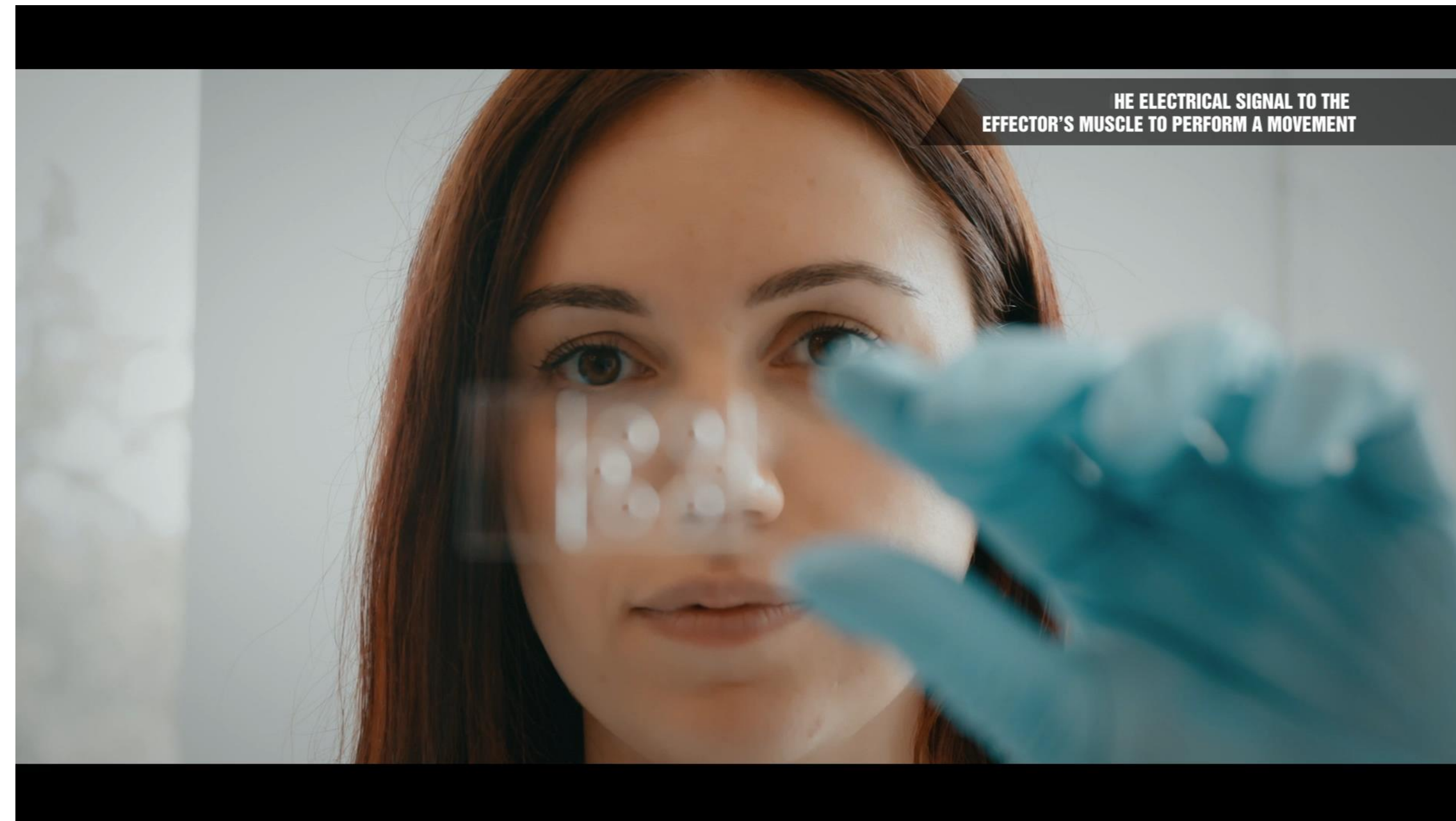
The progression of differentiation processes was assayed at the gene and protein expression level by real-time PCR techniques and immunofluorescence, respectively.

### Physiological conditions mimicked on chip

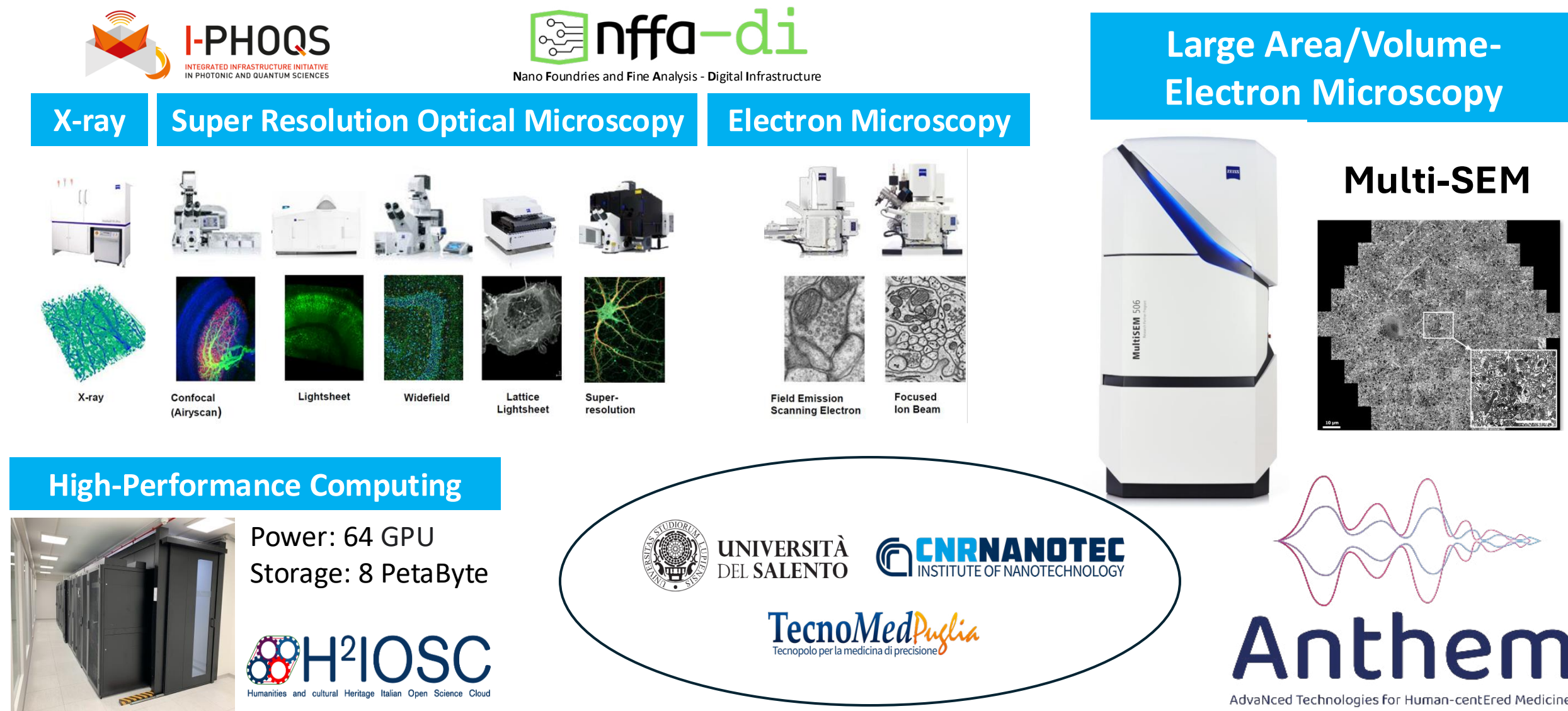
In physiological conditions, HC SCs had an attractive effect on HC axons which protruded into chambers that contained only SCs while they did not expand into chambers that contained only medium or another cell type, as in the case of human HC Fbs.



Immunofluorescence was performed to study axon/iSC interaction, using specific markers of MNS, as neurofilament-M (NF-M), and of SCs, as S100 $\beta$ , Ki67, GFAP, SOX10, ErbB2 and



## MULTIMODAL CORRELATIVE MICROSCOPY PLATFORM



**I-PHOQS**  
INTEGRATED INFRASTRUCTURE INITIATIVE  
IN PHOTONIC AND QUANTUM SCIENCES

**nffa-di**  
Nano Foundries and Fine Analysis - Digital Infrastructure

**X-ray** | **Super Resolution Optical Microscopy** | **Electron Microscopy** | **Large Area/Volume-Electron Microscopy**

**Multi-SEM**

**High-Performance Computing**

Power: 64 GPU  
Storage: 8 PetaByte

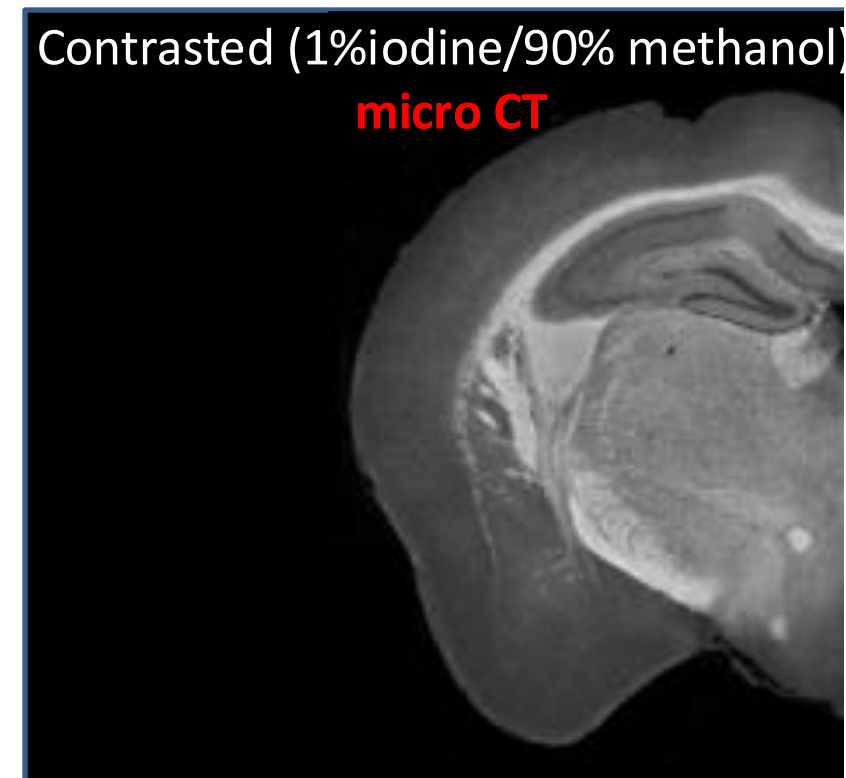
**H<sup>2</sup>IOSC**  
Humanities and cultural Heritage Italian Open Science Cloud

**UNIVERSITÀ DEL SALENTO** | **CNR NANOTEC**  
INSTITUTE OF NANOTECHNOLOGY

**TecnoMedPuglia**  
Tecnopolo per la medicina di precisione

**Anthem**  
Advanced Technologies For Human-centered Medicine

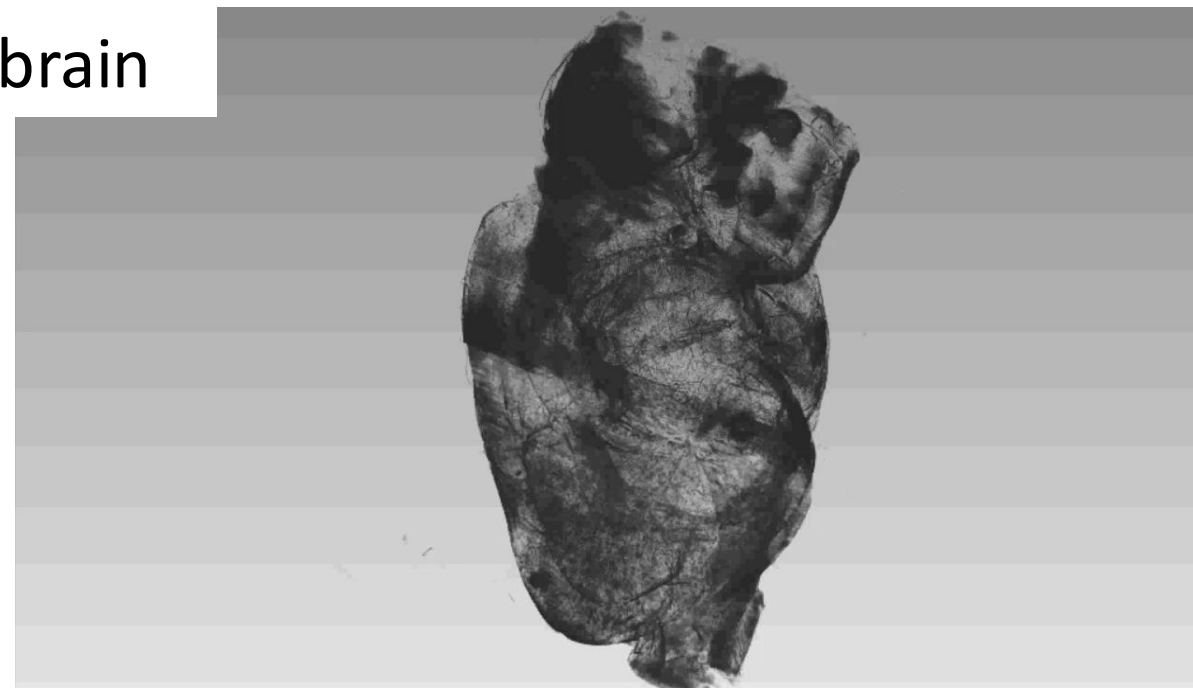
**3D IMAGING:** X-Ray Phase Contrast tomography XPCT



Enables the detection of  
**features classically considered**  
**“X-ray invisible”** without processing of the tissue

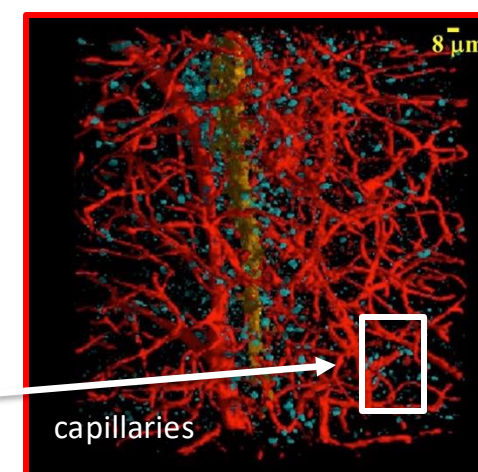
### XPCT- Multi-scale 3D Imaging technique

Mouse brain

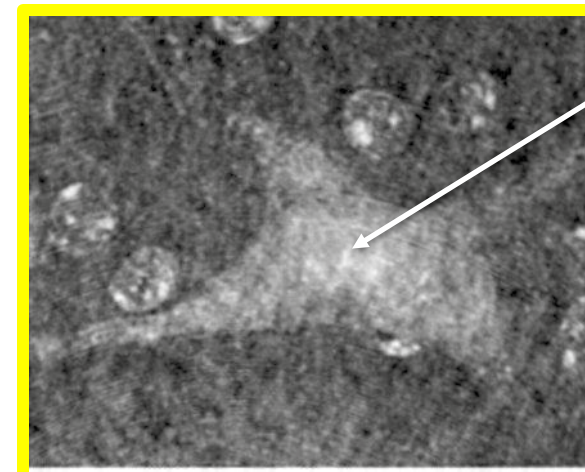


Wide dynamic range,  
from the organ as a  
whole down to single  
cells and capillary

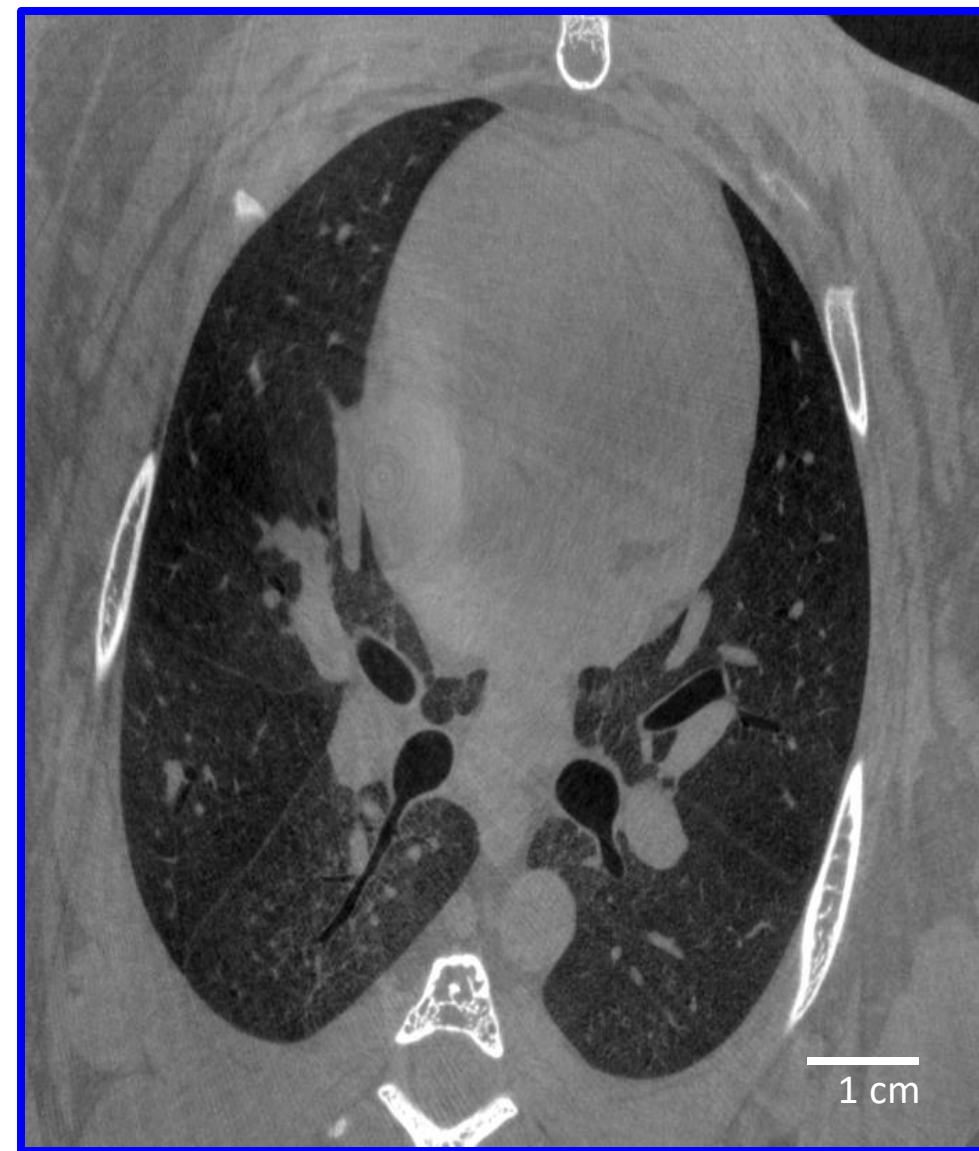
Single capillary



Single neuron



**XPCT: Healty living Rabbit**



**Rabbit Model**

**Healthy Lung**

pixel size: 20 microns

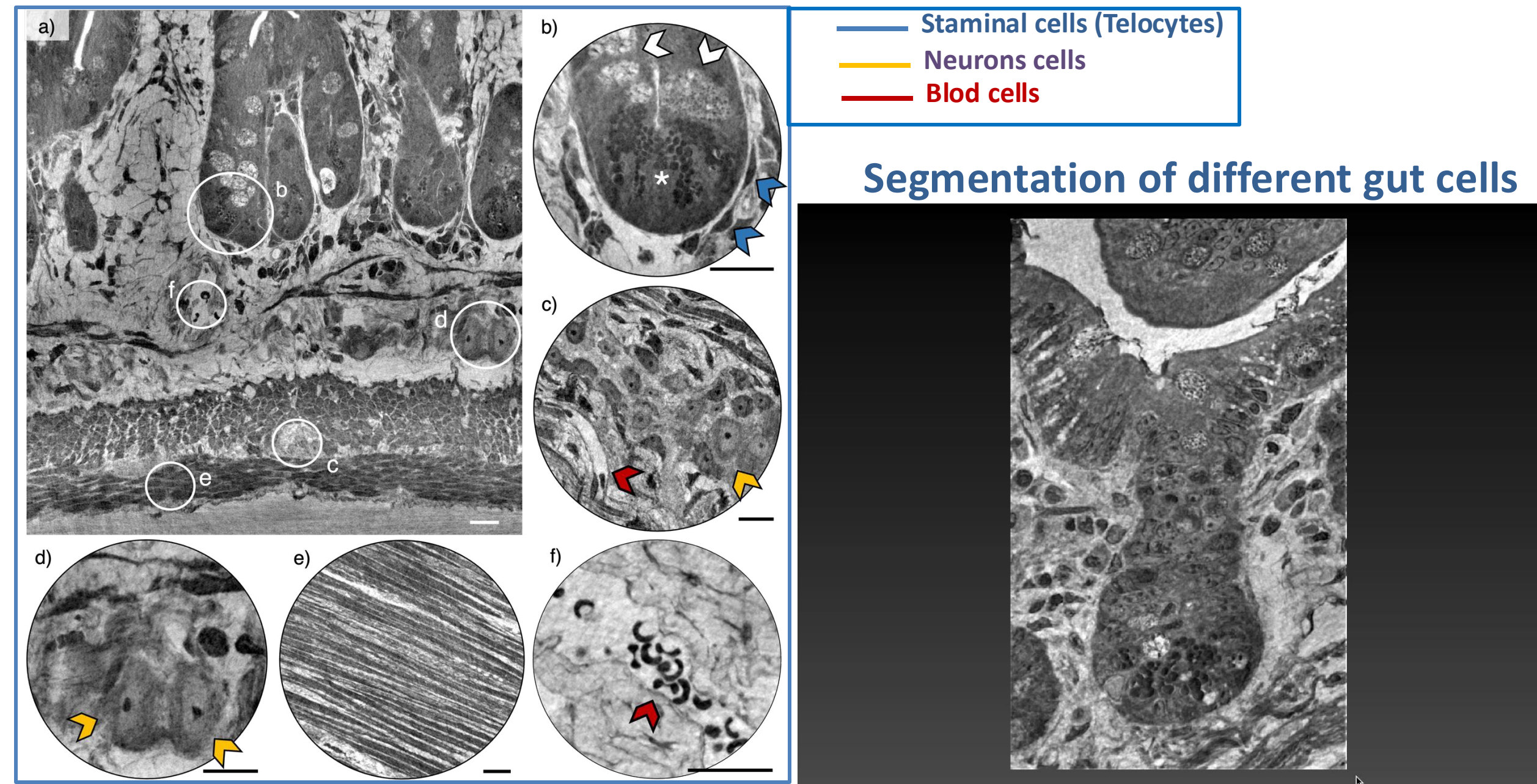
Dynamic scan:

Mechanical ventilation

L. Fardin, A. Bravin, S. Bayat, ESRF,

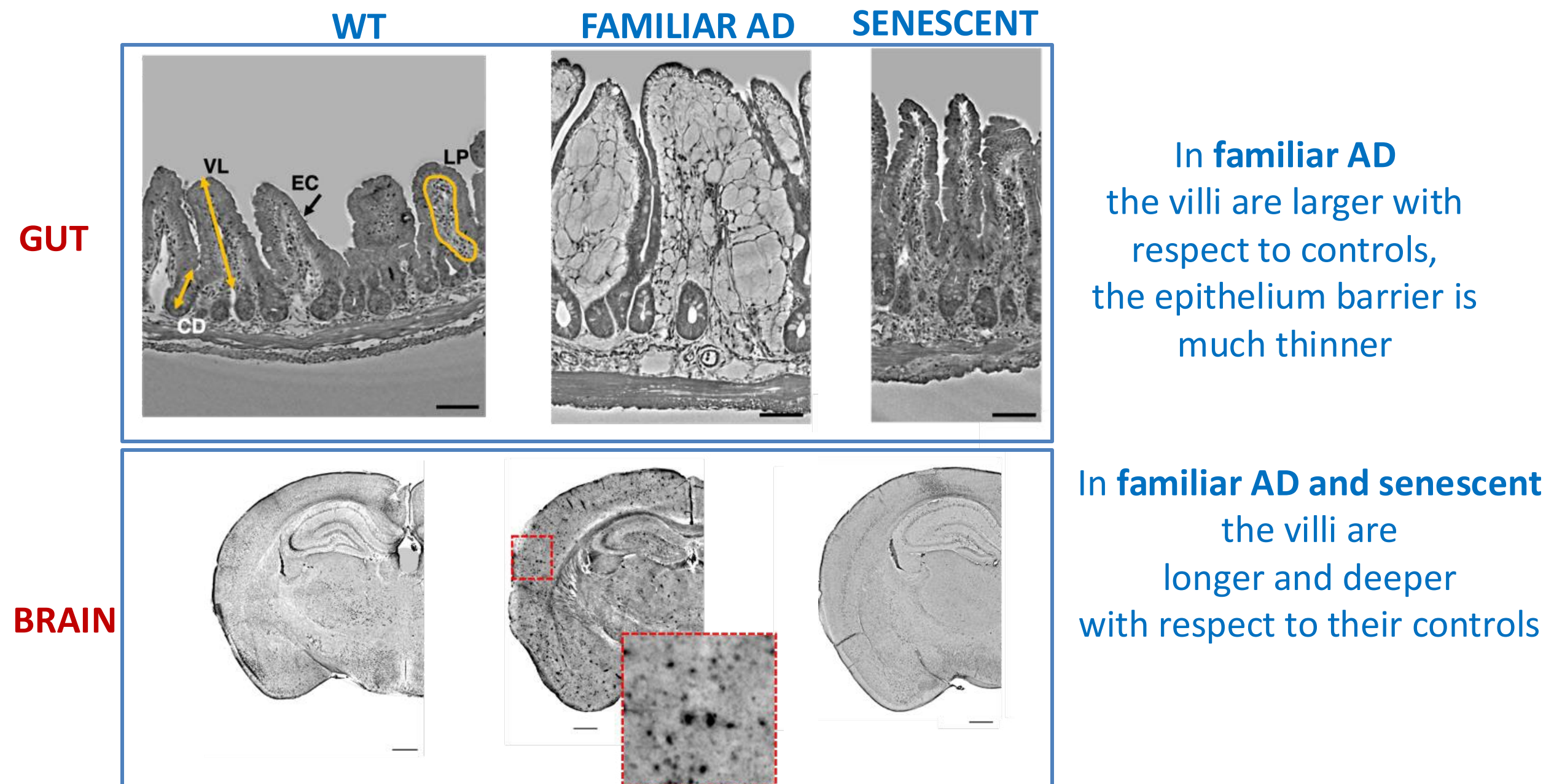


### Mouse GUT

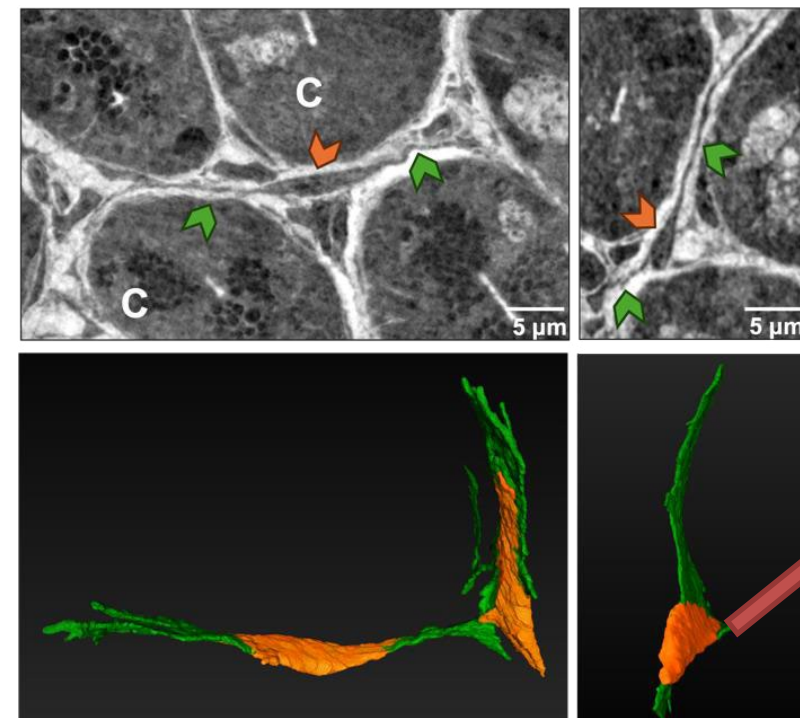




**GUT – BRAIN AXIS IN AD mice**



## GUT – BRAIN AXIS IN AD mice



### TELOCYTES CELLS

Unique mesenchymal cells featured by numerous long cytoplasmic extensions, called telopodes.

Almost impossible to detect.

Telocytes can act as **immune cells**

Are normally quiescent state cells and do not divide until environment perturbations occur, which they react to rapidly expanding in the attempt to restore a physiological condition



**Puglia Life Science HUB: Lecce Pole**



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DEL SALENTO**



*Thanks for your attention!*

### **Delitti in materia di violazione del diritto d'autore (Art. 25-novies, D.Lgs. n. 231/2001) [articolo aggiunto dalla L. n. 99/2009]**

- Messa a disposizione del pubblico, in un sistema di reti telematiche, mediante connessioni di qualsiasi genere, di un'opera dell'ingegno protetta, o di parte di essa (art. 171, legge n.633/1941 comma 1 lett. a) bis)
- Reati di cui al punto precedente commessi su opere altrui non destinate alla pubblicazione qualora ne risulti offeso l'onore o la reputazione (art. 171, legge n.633/1941 comma 3)
- Abusiva duplicazione, per trarne profitto, di programmi per elaboratore; importazione, distribuzione, vendita o detenzione a scopo commerciale o imprenditoriale o concessione in locazione di programmi contenuti in supporti non contrassegnati dalla SIAE; predisposizione di mezzi per rimuovere o eludere i dispositivi di protezione di programmi per elaboratori (art. 171-bis legge n.633/1941 comma 1)
- Riproduzione, trasferimento su altro supporto, distribuzione, comunicazione, presentazione o dimostrazione in pubblico, del contenuto di una banca dati; estrazione o reimpiego della banca dati; distribuzione, vendita o concessione in locazione di banche di dati (art. 171-bis legge n.633/1941 comma 2)
- Abusiva duplicazione, riproduzione, trasmissione o diffusione in pubblico con qualsiasi procedimento, in tutto o in parte, di opere dell'ingegno destinate al circuito televisivo, cinematografico, della vendita o del noleggio di dischi, nastri o supporti analoghi o ogni altro supporto contenente fonogrammi o videogrammi di opere musicali, cinematografiche o audiovisive assimilate o sequenze di immagini in movimento; opere letterarie, drammatiche, scientifiche o didattiche, musicali o drammatico musicali, multimediali, anche se inserite in opere collettive o composite o banche dati; riproduzione, duplicazione, trasmissione o diffusione abusiva, vendita o commercio, cessione a qualsiasi titolo o importazione abusiva di oltre cinquanta copie o esemplari di opere tutelate dal diritto d'autore e da diritti connessi; immissione in un sistema di reti telematiche, mediante connessioni di qualsiasi genere, di un'opera dell'ingegno protetta dal diritto d'autore, o parte di essa (art. 171-ter legge n.633/1941)
- Mancata comunicazione alla SIAE dei dati di identificazione dei supporti non soggetti al contrassegno o falsa dichiarazione (art. 171-septies legge n.633/1941)
- Fraudolenta produzione, vendita, importazione, promozione, installazione, modifica, utilizzo per uso pubblico e privato di apparati o parti di apparati atti alla decodificazione di trasmissioni audiovisive ad accesso condizionato effettuate via etere, via satellite, via cavo, in forma sia analogica sia digitale (art. 171-octies legge n.633/1941).

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