# Comprehensive Whole-Body Cellular Mapping Technologies: Integrating Advanced Imaging and AI-Driven Analysis

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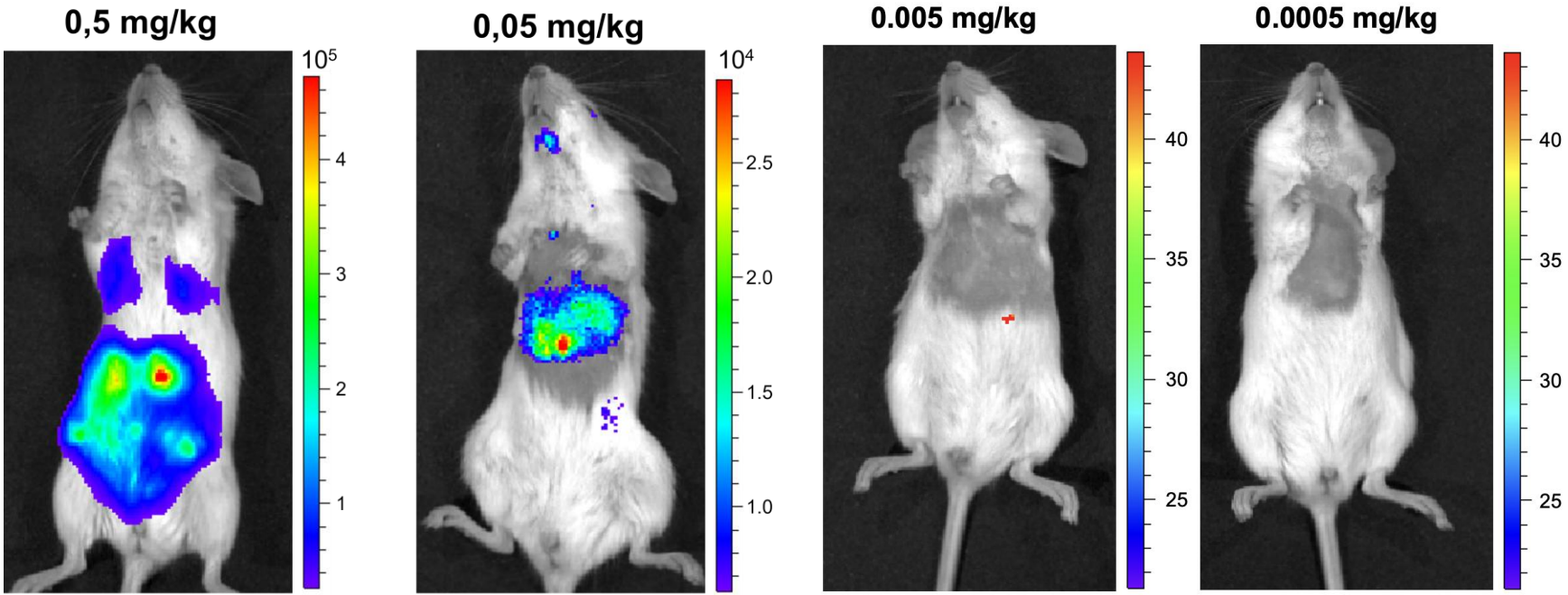
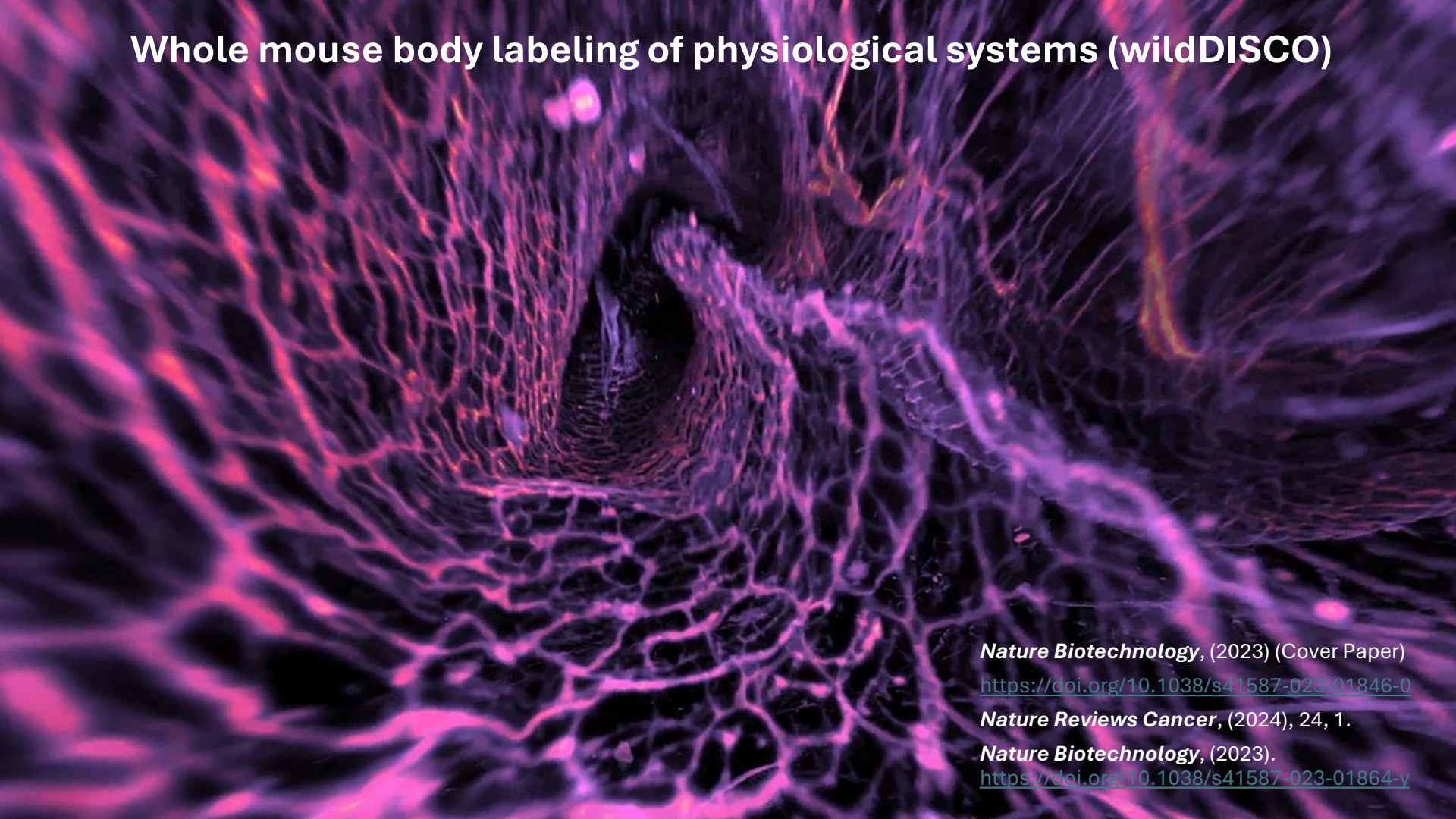
NEXT-GENERATION DELIVERY INNOVATIONS

Lower doses of LNPs are not dateable at by current methods **(sensitivity)**



***Nature Protocols***. 2012
***Nature Neuroscience***. 2019

# Whole mouse body labeling of physiological systems (wildDISCO)

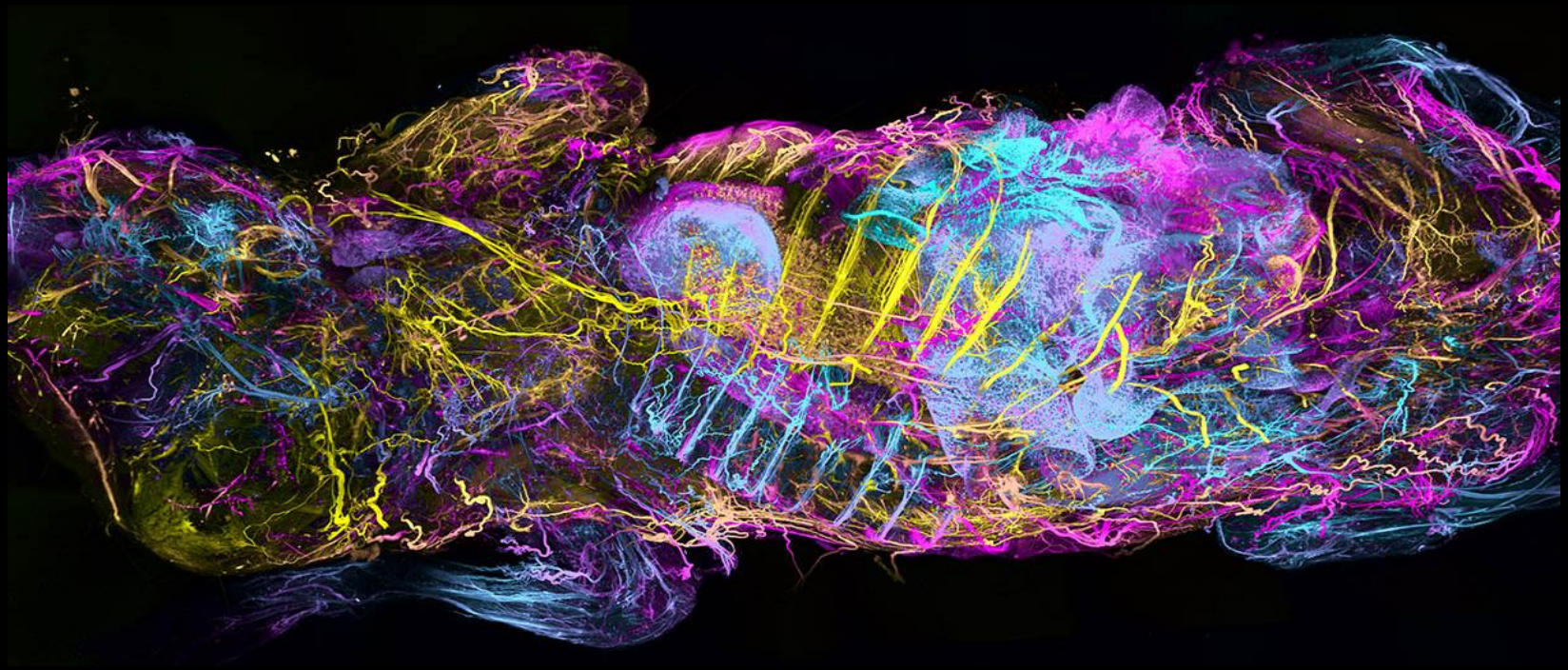


***Nature Biotechnology***, (2023) (Cover Paper)
https://doi.org/10.1038/s41587-023-01846-0

***Nature Reviews Cancer***, (2024), 24, 1.

***Nature Biotechnology***, (2023).
https://doi.org/10.1038/s41587-023-01864-y

# 1. wildDISCO reveals peripheral nerve systems using PGP9.5 Ab

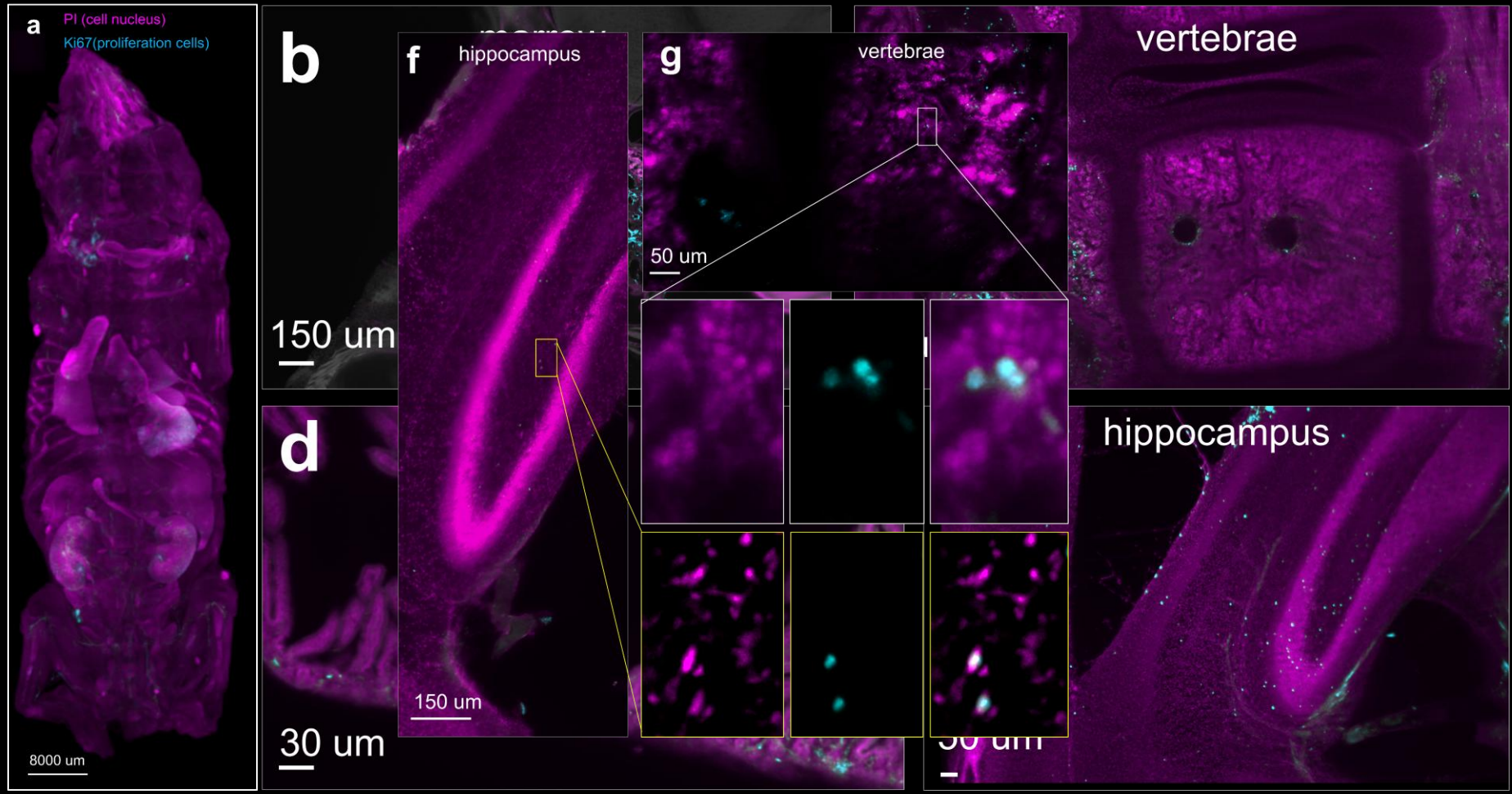


***Science***, (2023). DOI: 10.1126/science.adi4325
***Science***, (2023). DOI: https://www.science.org/content/blog-post/our-favorite-science-photos-2023

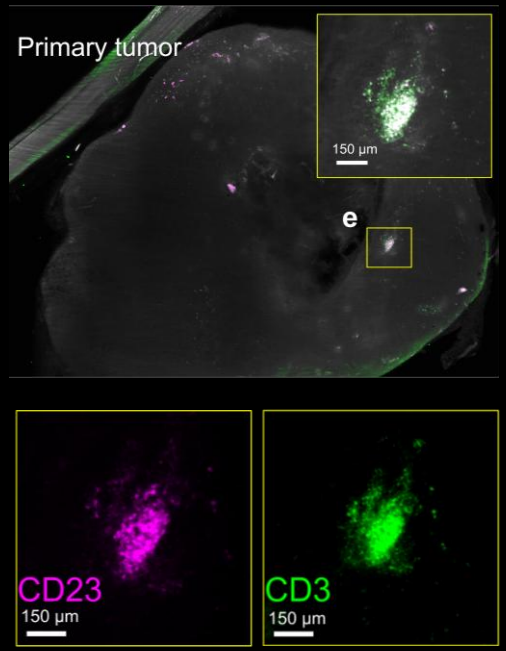
Jie Luo et al, ***Nature Biotechnology***, (2023) (**Cover Paper**)

***BBC News***: https://www.bbc.com/news/science-environment-66119980

# 2. wildDISCO reveals cell proliferation system using Ki67 Ab

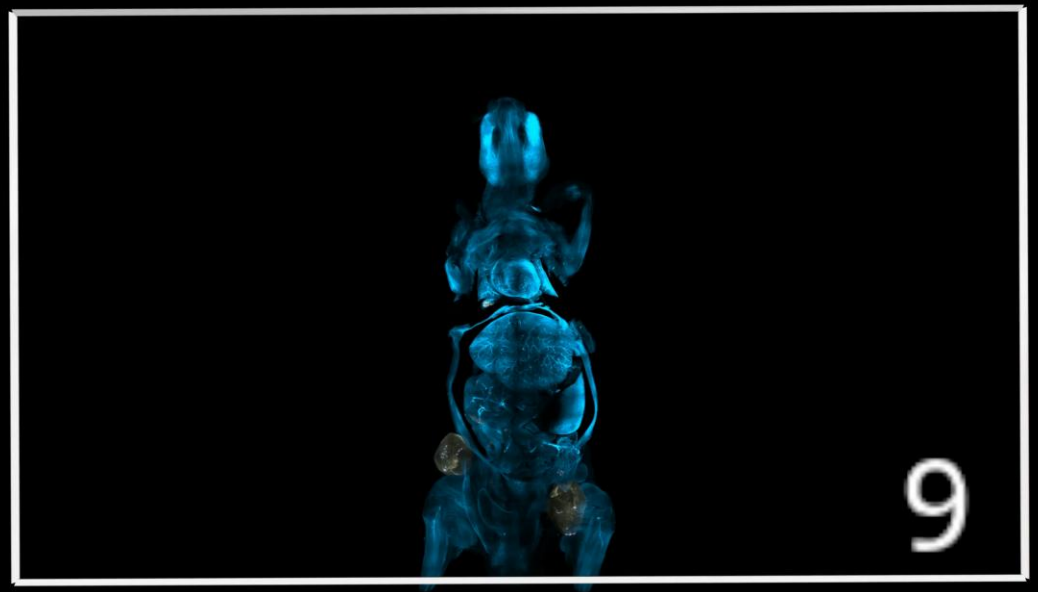


# 3. wildDISCO reveals tertiary lymphoid structure TLS using CD3/CD23

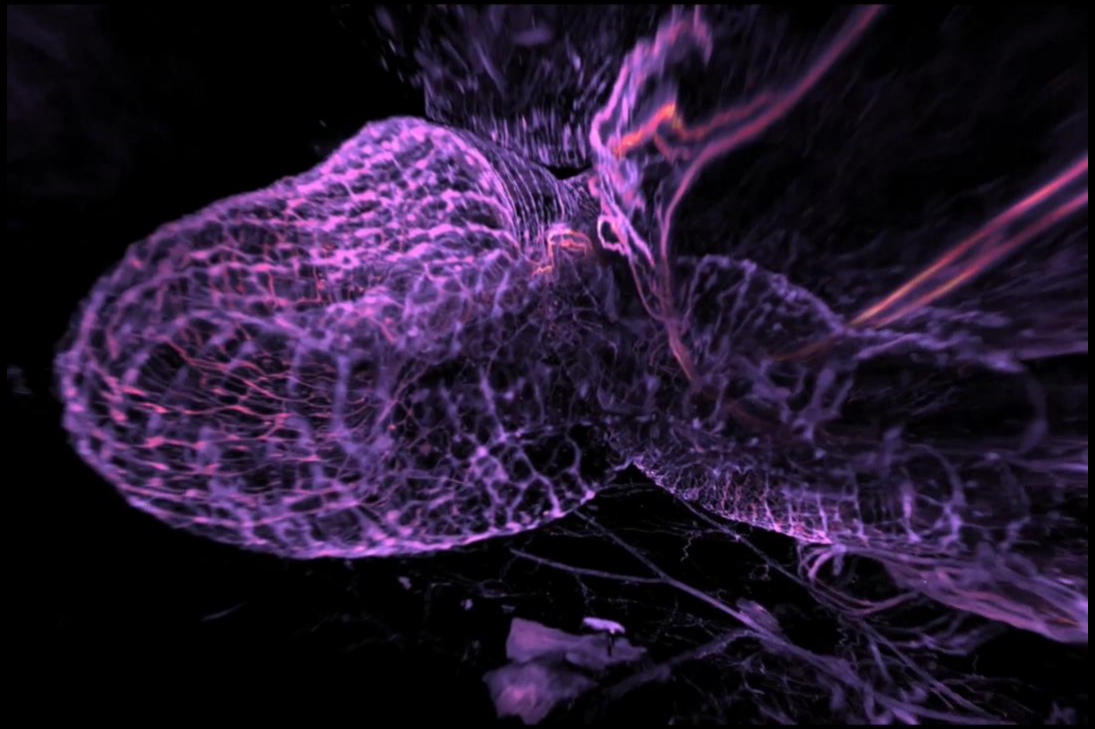


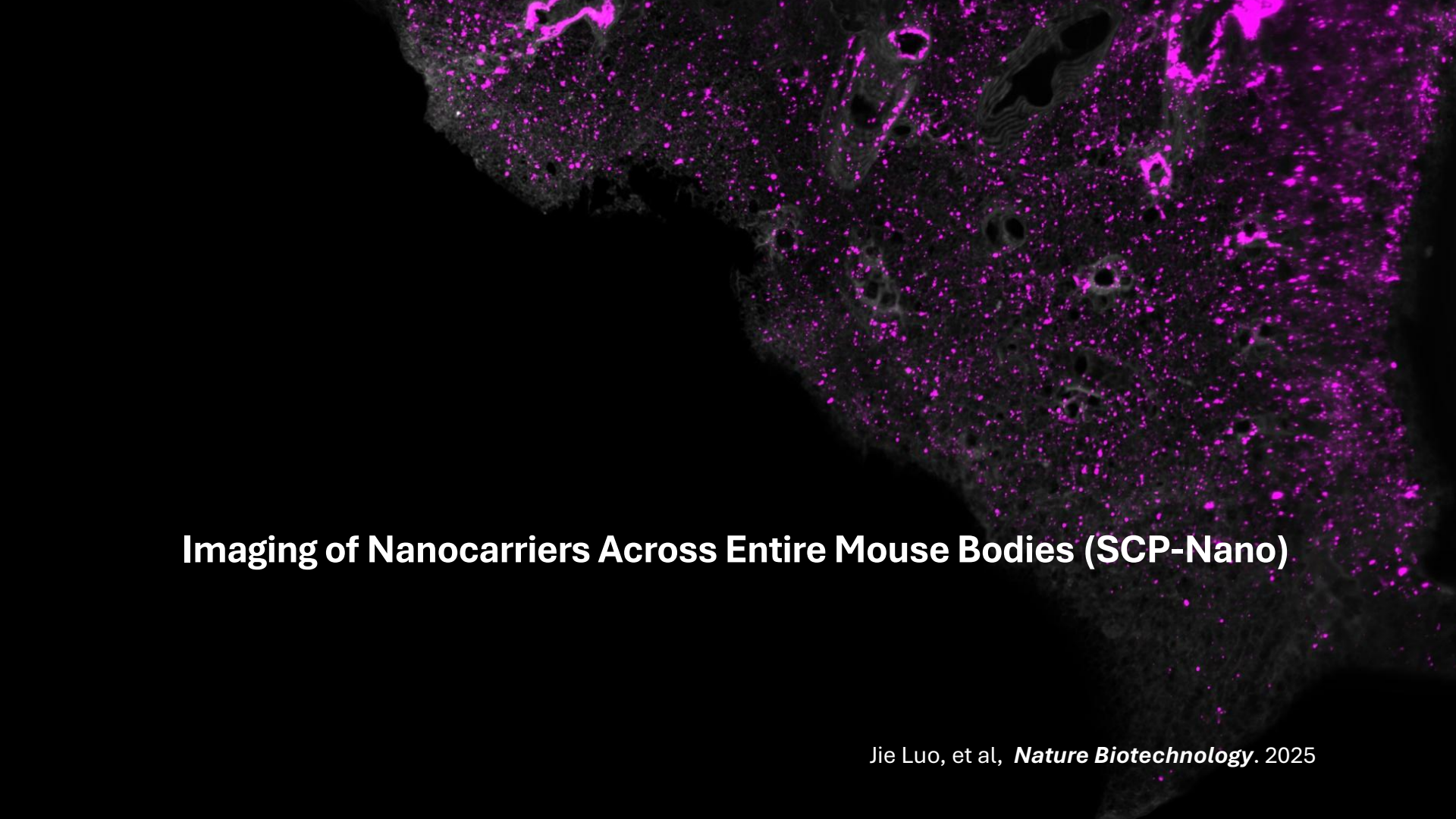

TLS and Metastasis

CD3 and CD23 colocalized TLS




Tertiary lymphoid structures (TLS) surround the primary tumor and are present in tumor metastases in the gut and lung, among others.





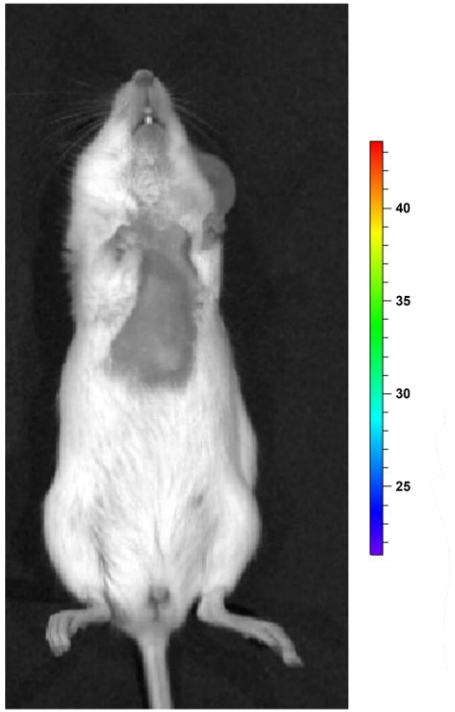
**Imaging of Nanocarriers Across Entire Mouse Bodies (SCP-Nano)**

Jie Luo, et al, ***Nature Biotechnology***. 2025

# Revealing signal in whole body at cellular resolution using very low dosages

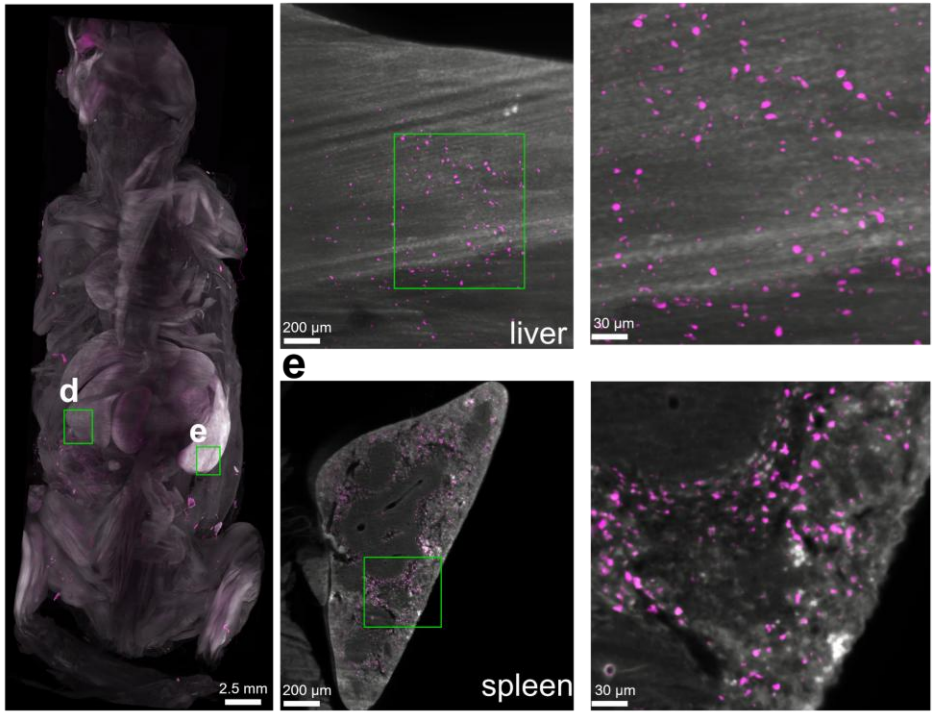
**BLI**

**(0.01µg) i.v.**
**0.0005 mg/kg**



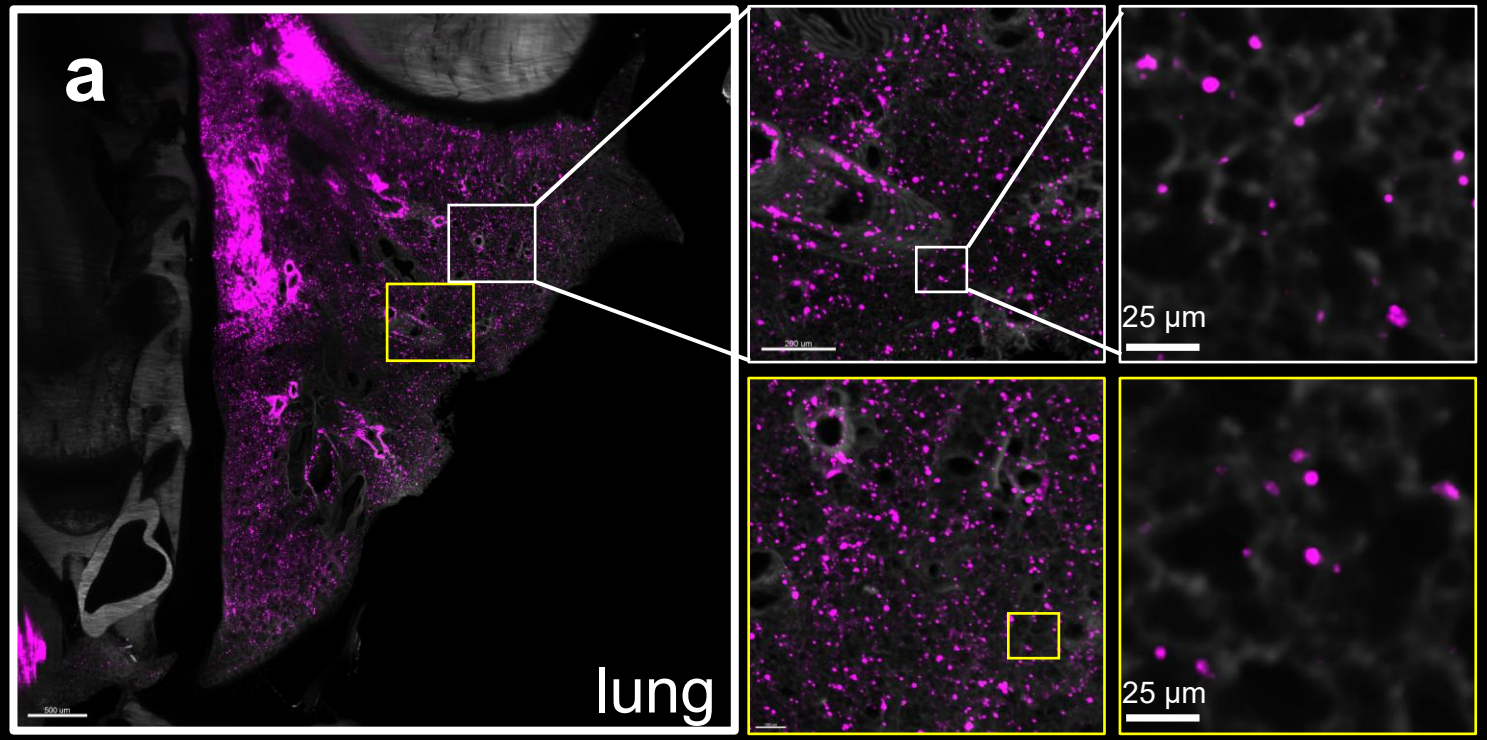

**SCP-Nano**

**(0.01µg) i.v.**
**0.0005 mg/kg**

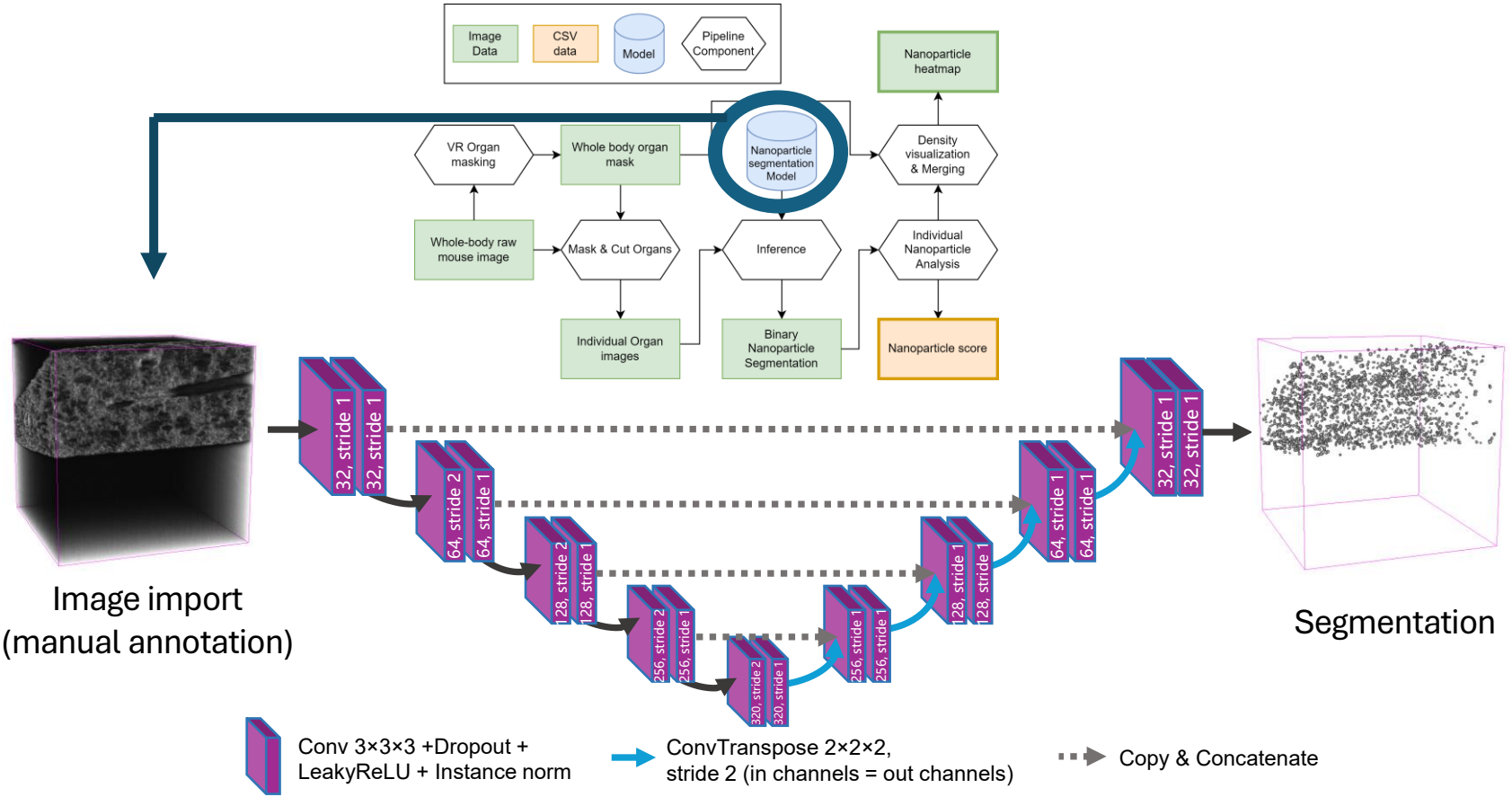



Higher Sensitivity and Cell-Level Resolution

# 2.1. We can image the nanocarriers in 3D in whole mouse at cell level

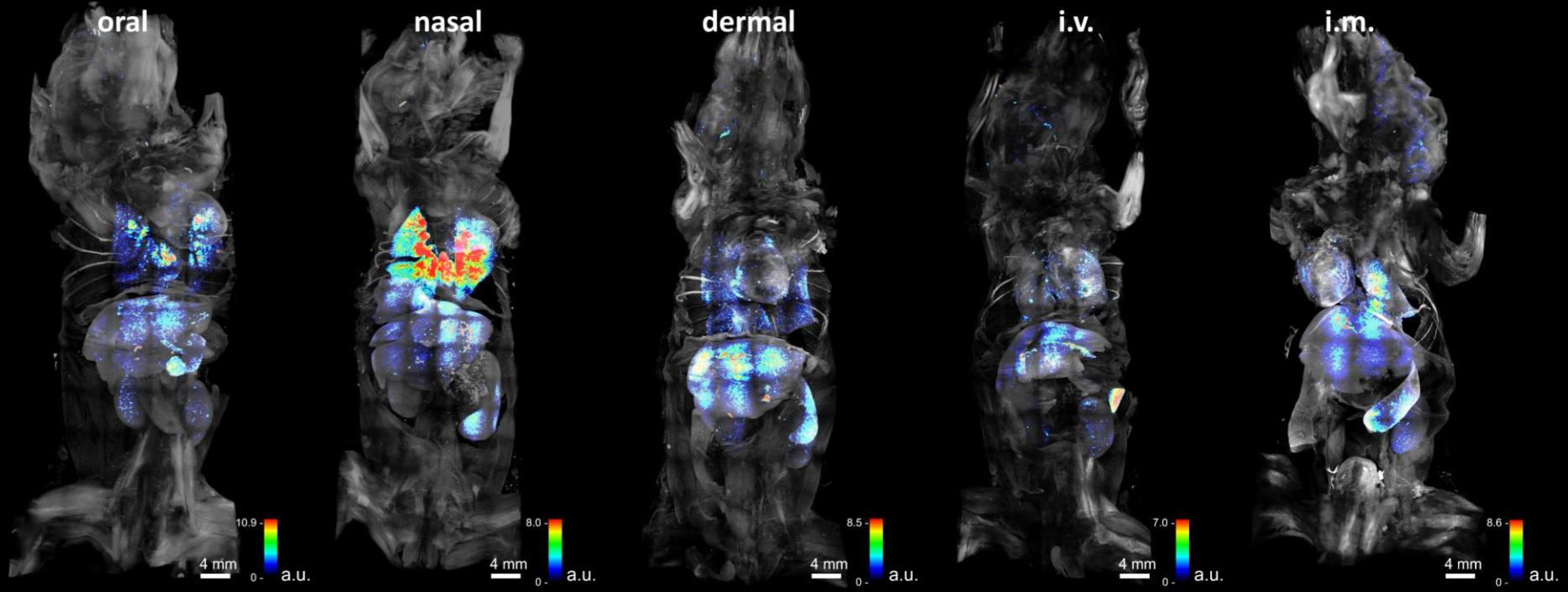


# SCP-Nano: algorithmic pipeline to nanocarrier targeted cell quantification




SCP-Nano can quantify tens of millions of cell-level nanoparticles.

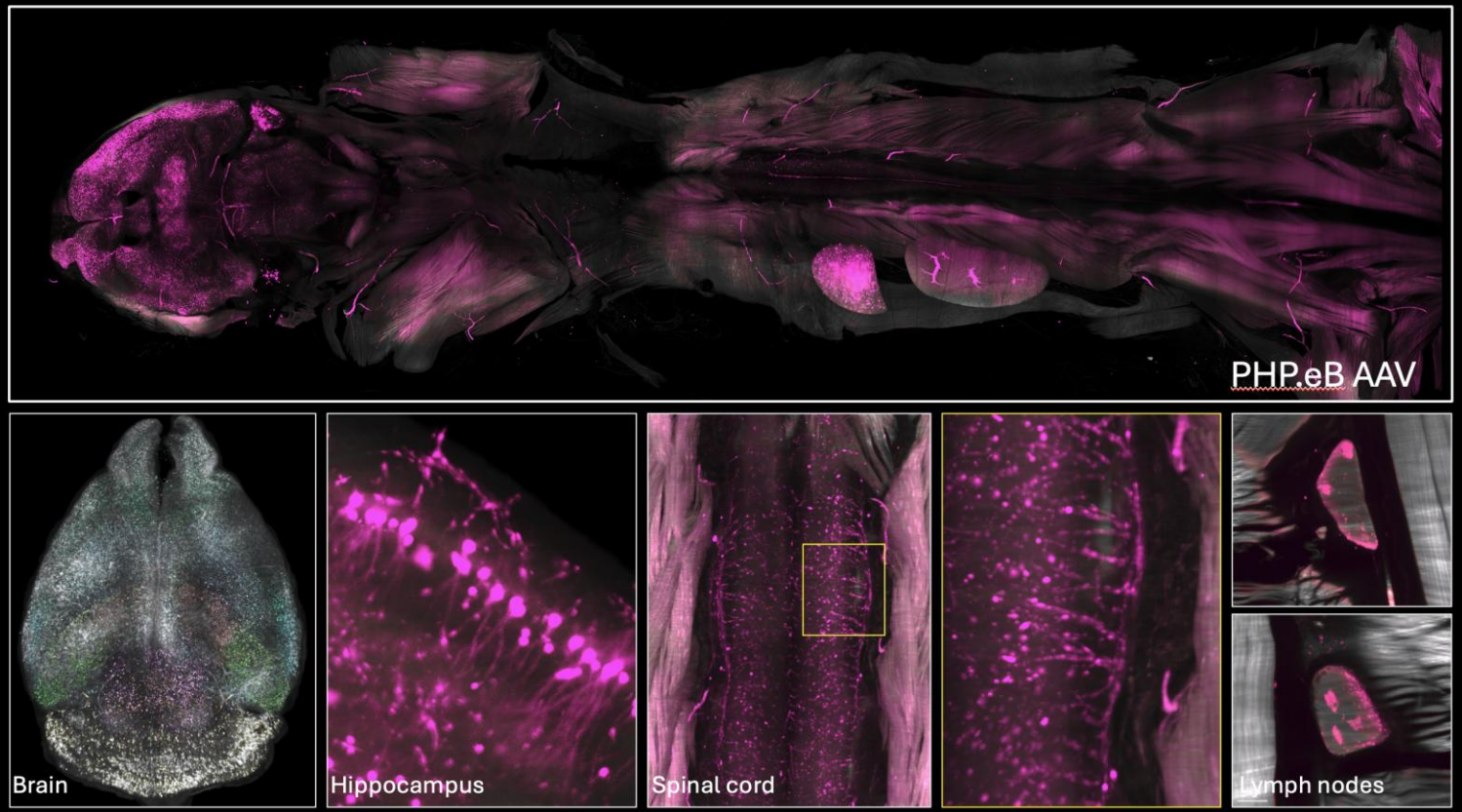
# 2.4 SCP-Nano generates whole body cell-level density maps




SCP-Nano enables assessment of nanocarrier tropism

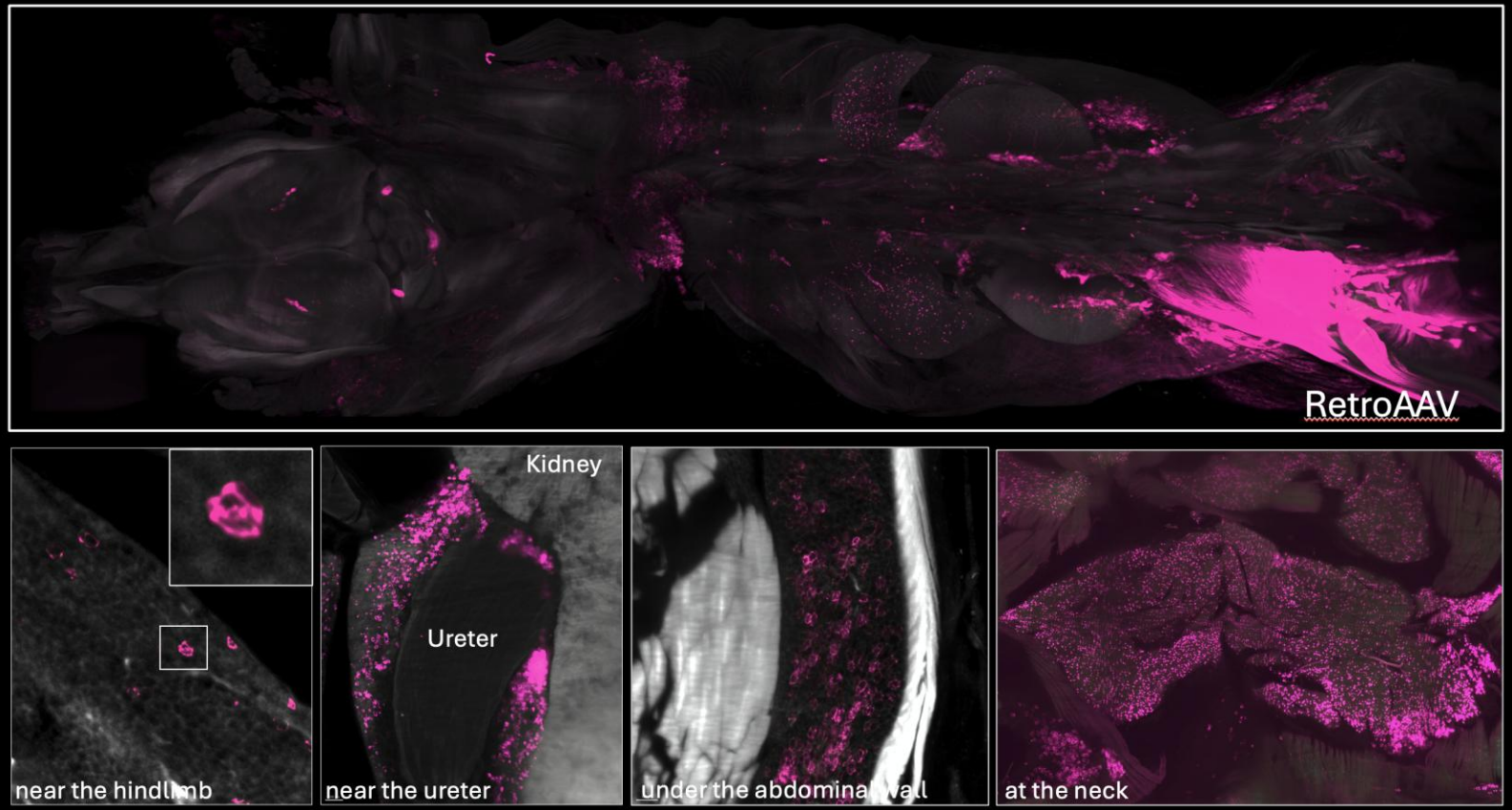
The injection dose of mRNA is 0.0005 mg/kg, perfused 6 hours post-injection.

# 3.1 Visualization of AAV bio-distribution
# PHP.eB AAV: CNS targeting




Besides the CNS targeting, we found that PHP.eB accumulates in some lymph nodes (inguinal and lumbar).

# 3.2. Visualization of AAV bio-distribution
## Retro AAV




Retro AAV (intramuscular injection) targets adipose tissue throughout the entire mouse body.

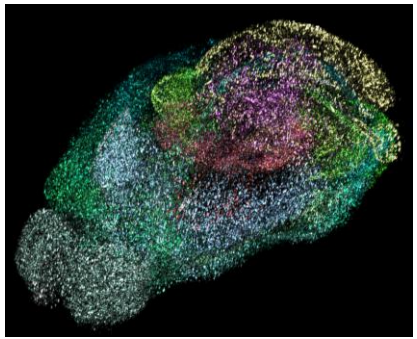
# 3.3. SCP-Nano enables quantification of AAVs' biodistribution

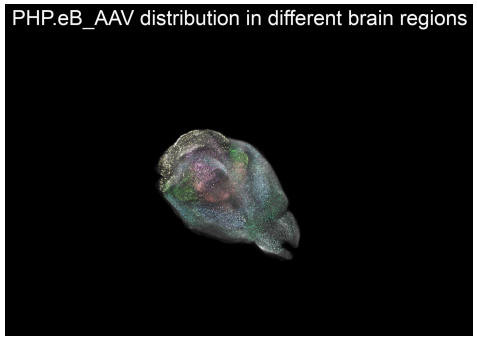
| | SCP-Nano (retrained on AAV traced neuron cell bodies data) | | | |
|---|---|---|---|---|
| | TP | FP | FN | **Instance Dice** |
| **all** | 342 | 132 | 37 | **0.8019** |

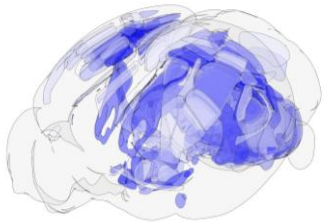
SCP-Nano can achieve a prediction accuracy of 0.8019

| Number of AAV labelled cells | | |
|---|---|---|
| Organ | PHP.eB | Type of RetroAAV |
| brain | 245,229 | 6,300 |
| spinal cord | 5,331 | 1,903 |
| lung | 3,776 | 5,326 |
| liver | 8,844 | 19,588 |
| spleen | 55 | 0 |
| kidney | 571 | 5,337 |
| **all** | **263,806** | **38,454** |

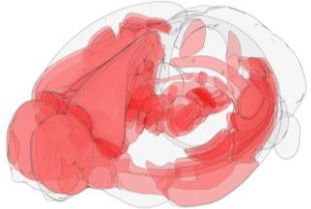
The accumulation of neuronal cell bodies by PHP.eB is 40 times higher.





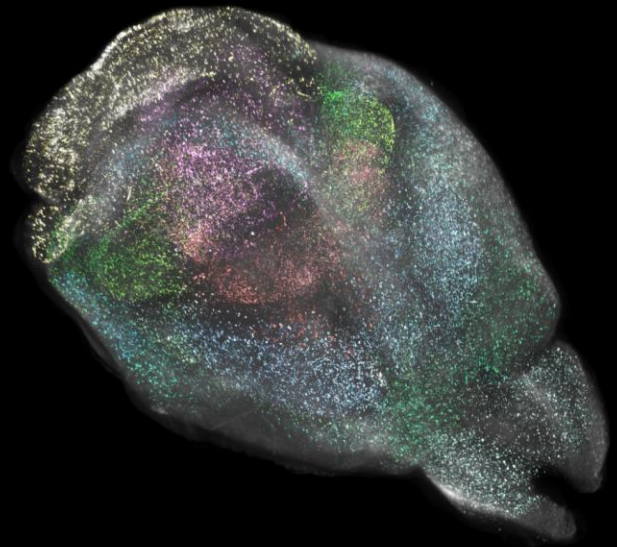
less than 0.5x median density (blue)

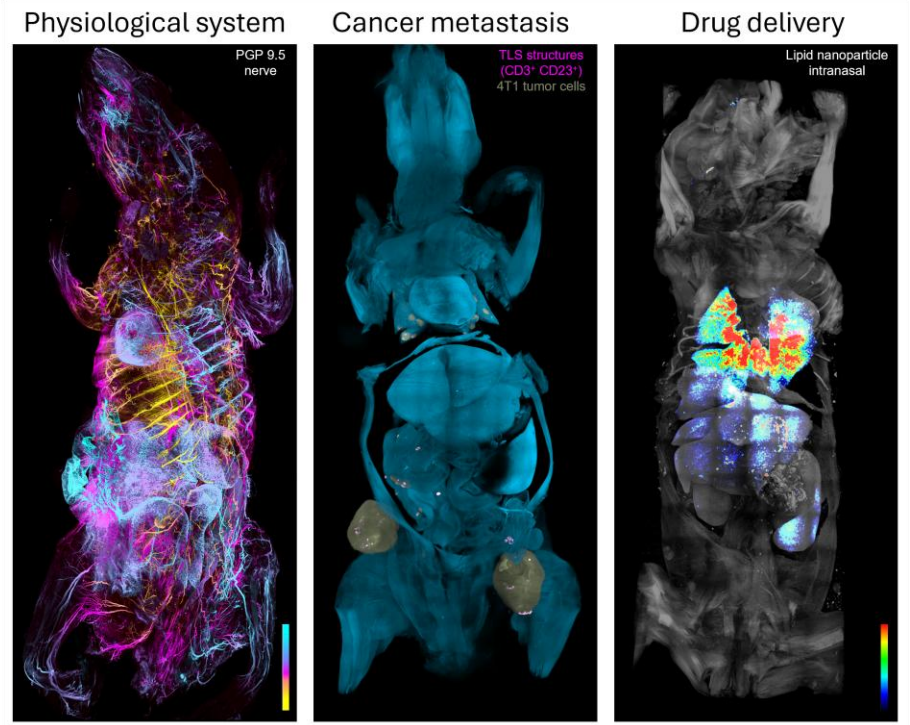


more than 2x median density (red)

Density map showing the distribution of PHP.eB in different brain regions, with the thalamus being the densest region.

# PHP.eB_AAV distribution in different brain regions






SCP-Nano and wildDISCO techniques

**Physiological systems**, **pathological changes** and **drug delivery** throughout the entire mouse body at the cell-level resolution.

***Nature Biotechnology***, (2023)
***Nature Biotechnology***, (2025).