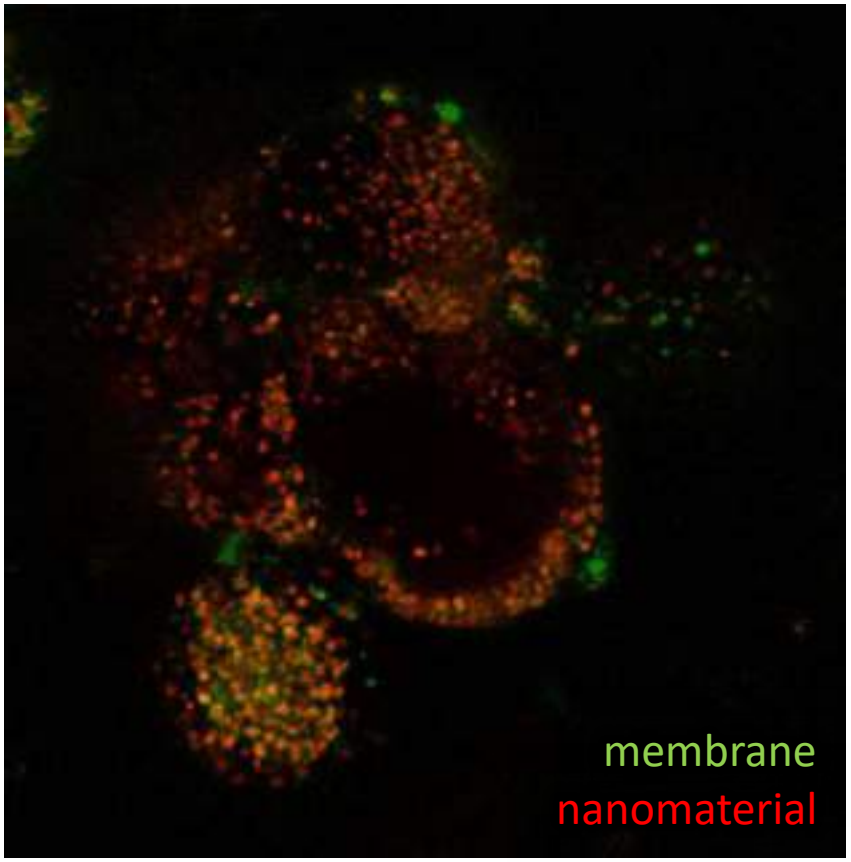
Lipid wrapping:
From bio & nano interfaces to disease prediction



final SNT conference, online, June 2020

*prof. **Janez Štrancar**,*
SNT WP2 leader, Jožef Stefan Institute,
Laboratory of Biophysics,
Condensed matter physics department,

SmartNanoTox (SNT)

The civil war – macrophages attacking alveolar epithelial cell after the exposure to TiO2 nanotubes…

SmartNanoTox
Smart Tools for Gauging Nano Hazards

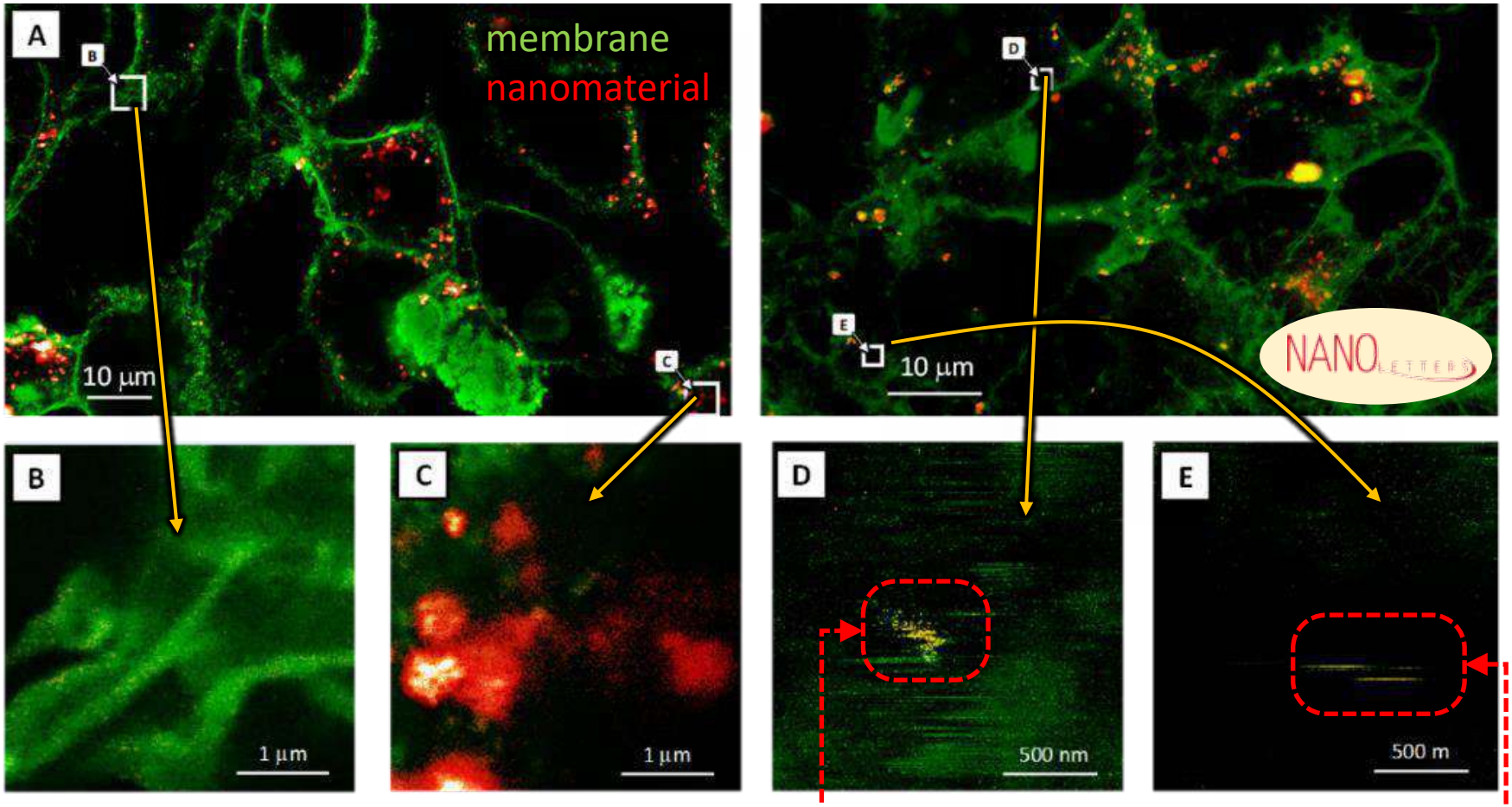
@StrancarLab

Horizon 2020
European Union funding
for Research & Innovation

Why so much of aggression ?

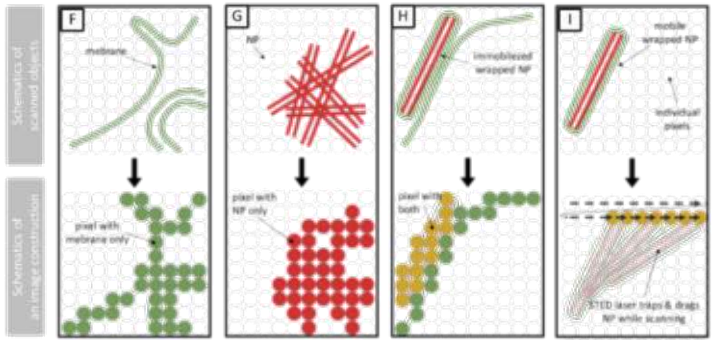
Super-resolved STED image

Representative zoom-in



membranes | NM aggregates | wrapped NM | mobile wrapped NM

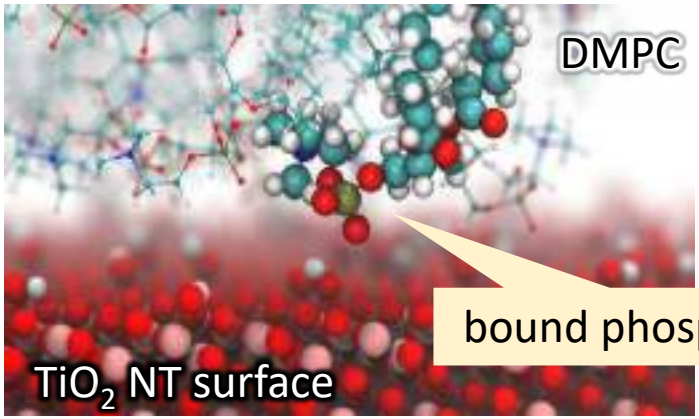
STED

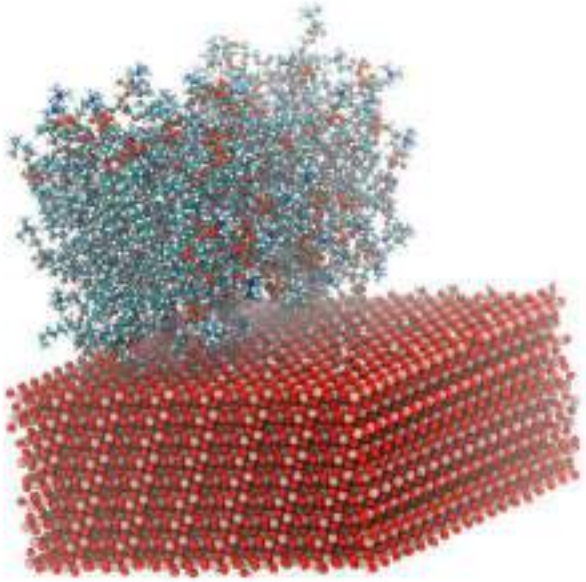


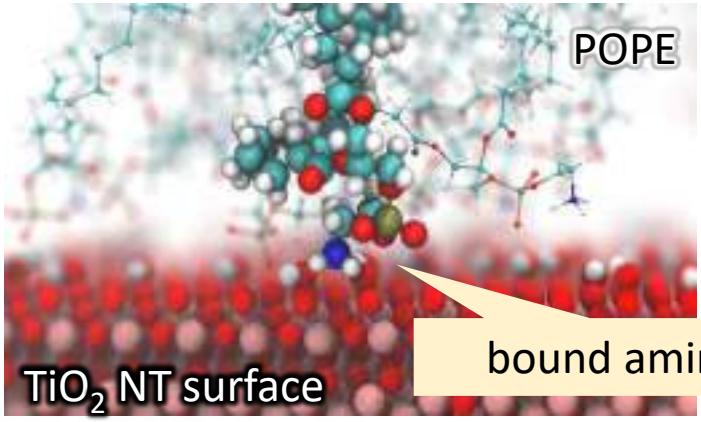
Epithelial cells looks so peaceful 30 min after the exposure to TiO2 nanotubes ...
In reality, they are loosing lipids due to wrapping and wrapped particle diffusion!

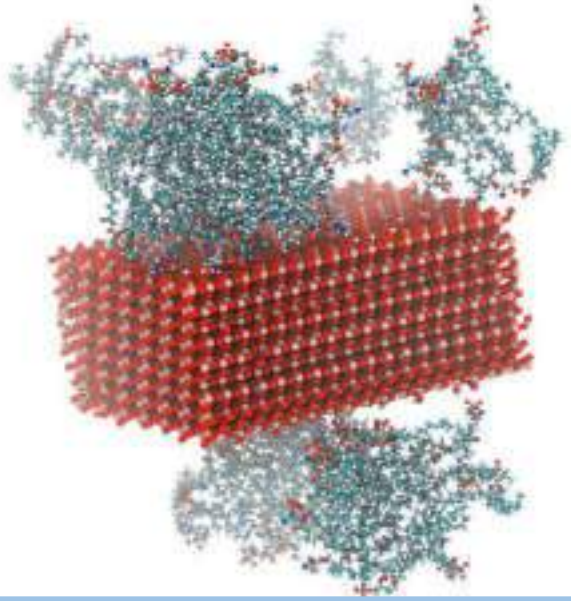
How the wrapping is driven ?

in silico MD modeling of physical interactions





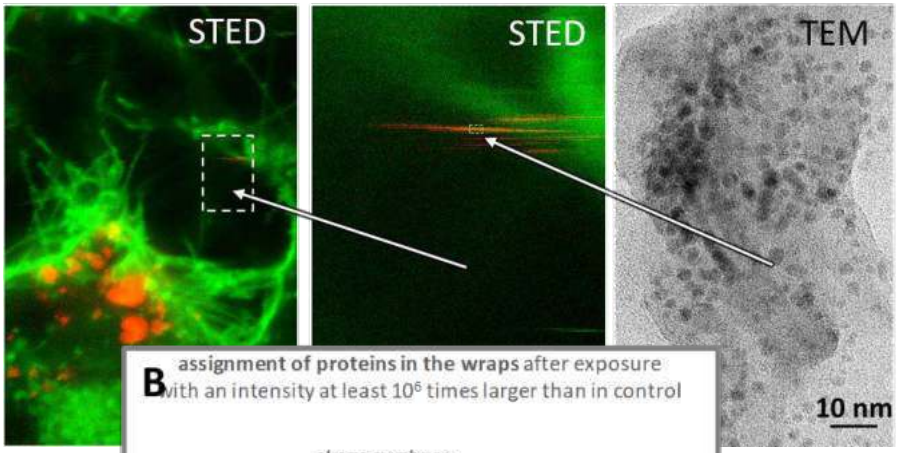


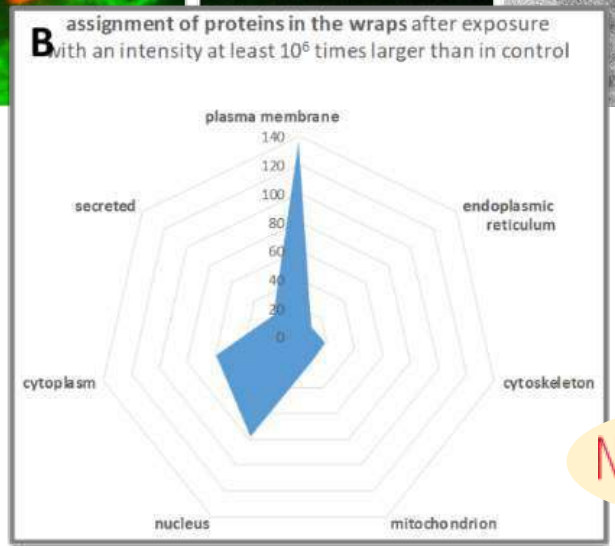


MD

In case of metal-oxides: by binding through amines and phosphates …
Non-standard membrane structures appear …

Is it just lipids that are stolen?



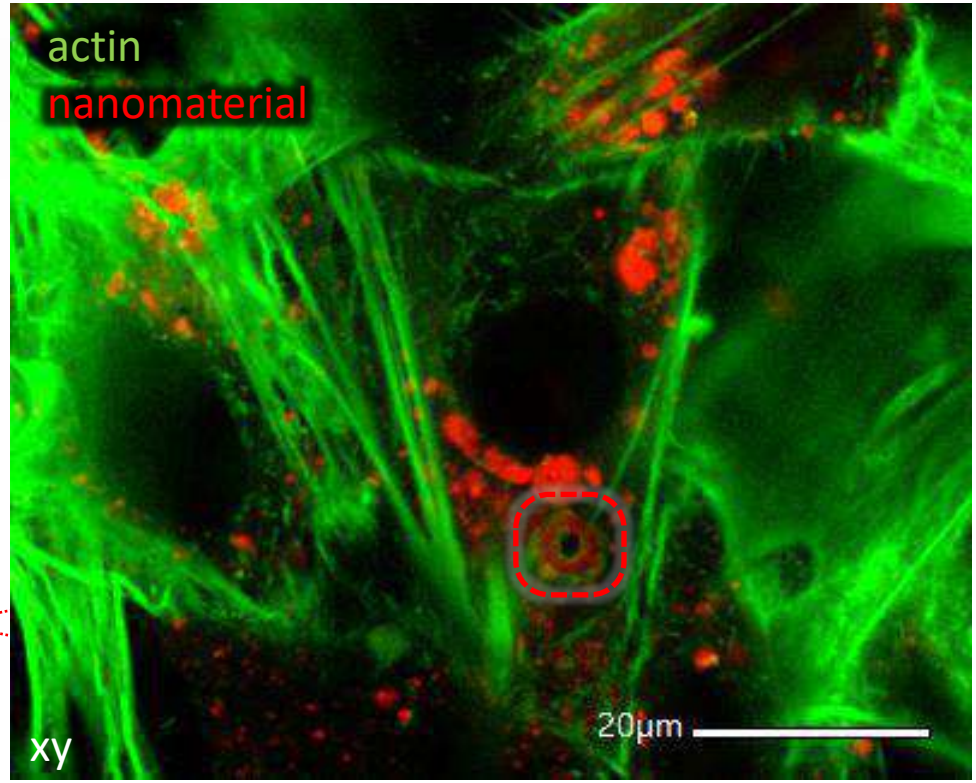


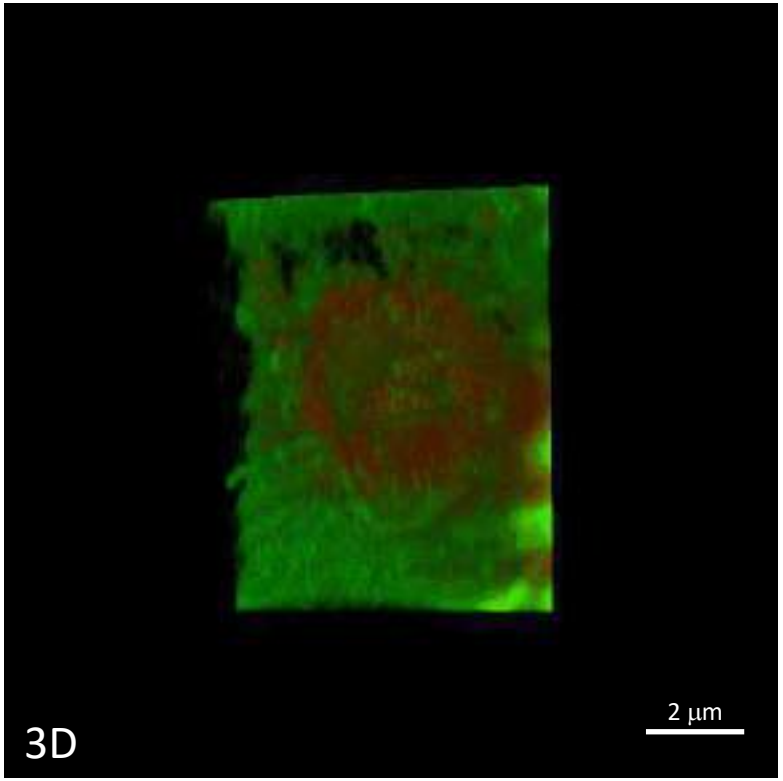
NANO LETTERS

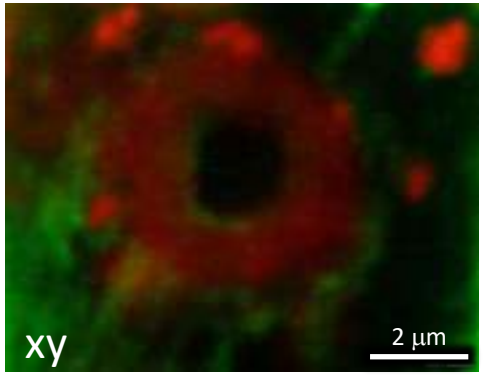
proteomics

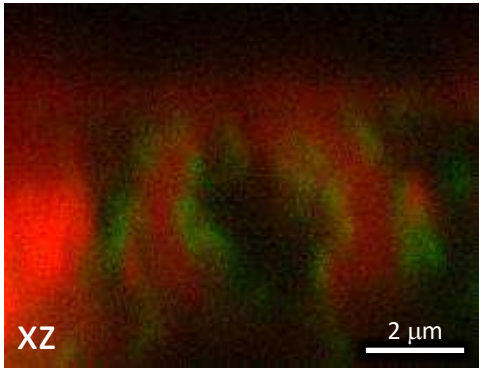
Lots of membrane proteins, but others as well …
Obviously interfering with at least coagulation cascade…

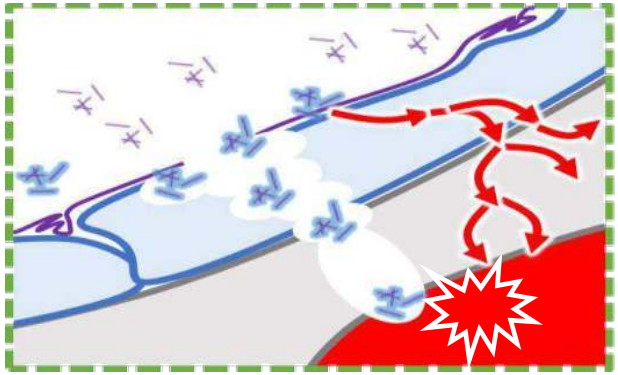
How do they get relocated across the epithelium ?







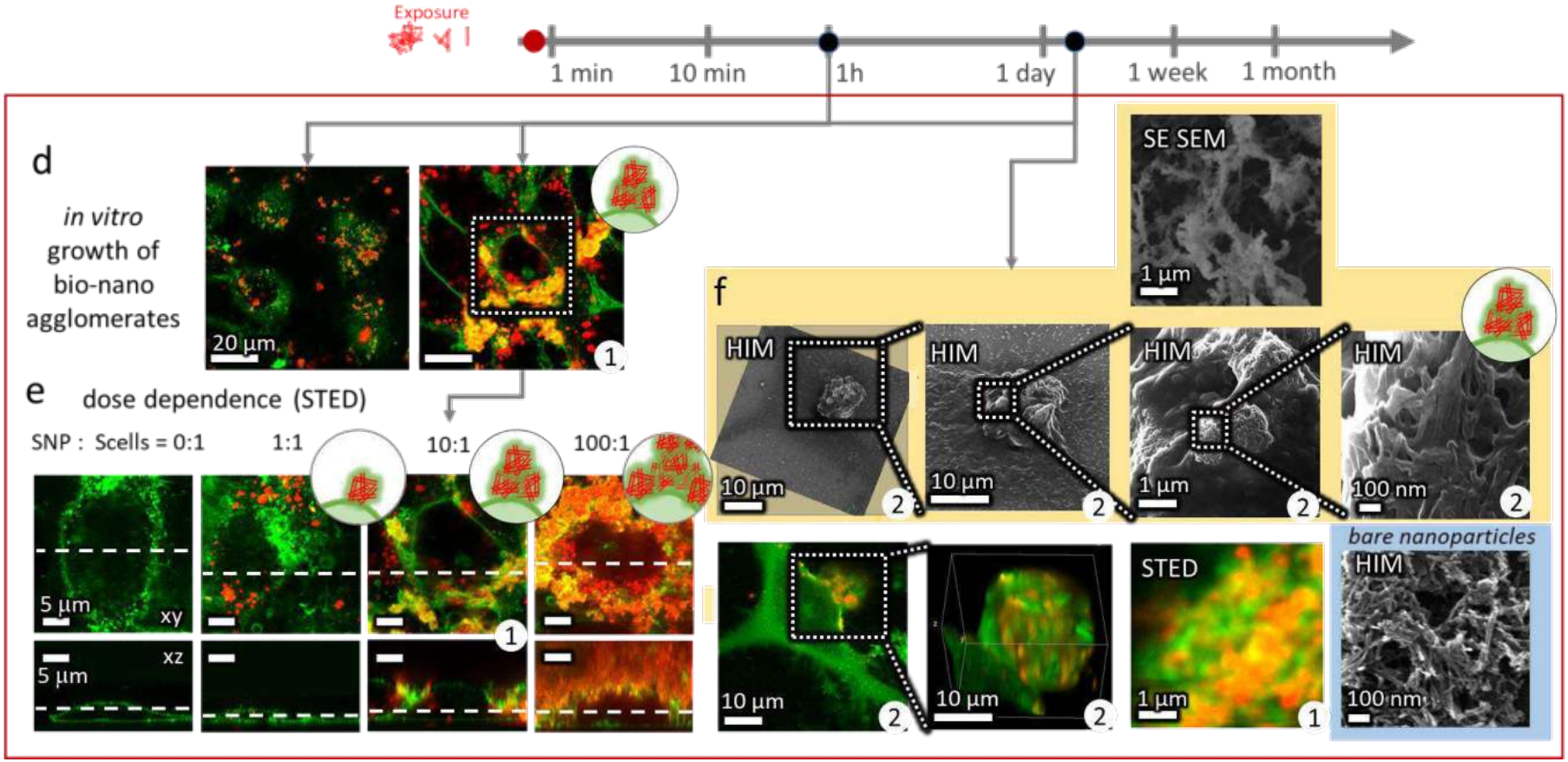




STED

Wrapping makes epithelium porous.
Even some self-assembled wormholes can be seen …

What happens at higher doses?



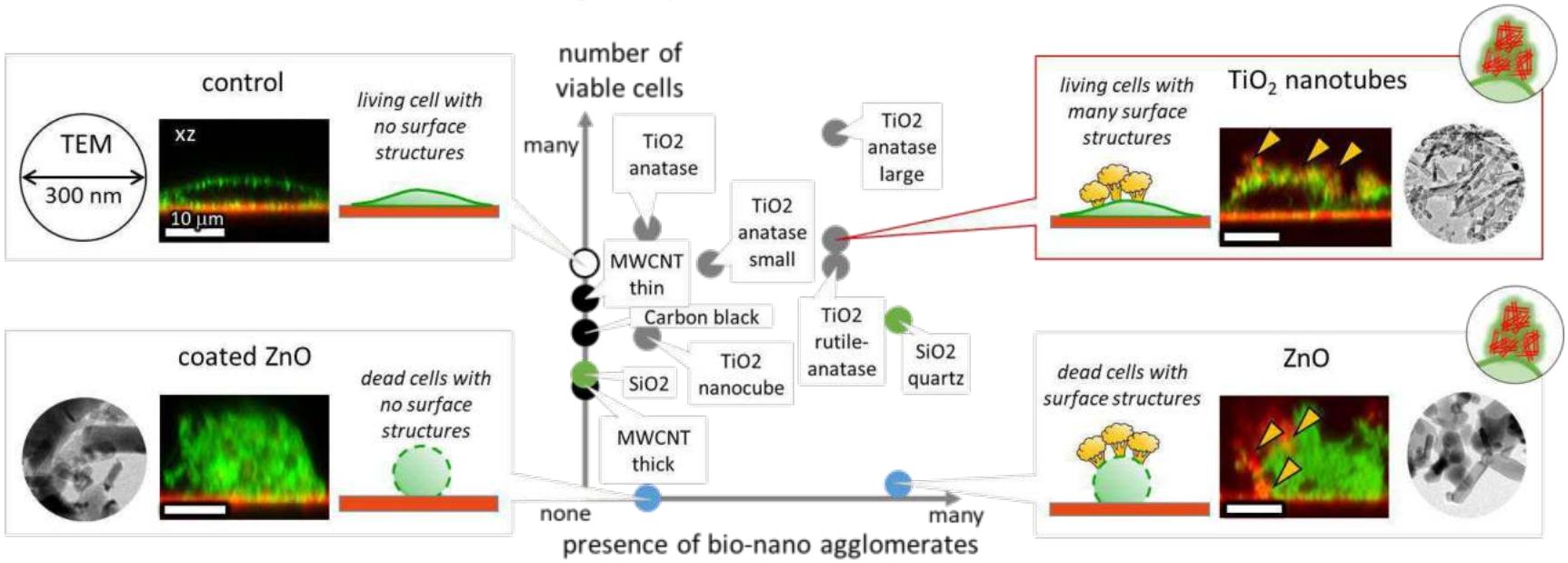
under review in ADVANCED MATERIALS & reposited on bioRxiv

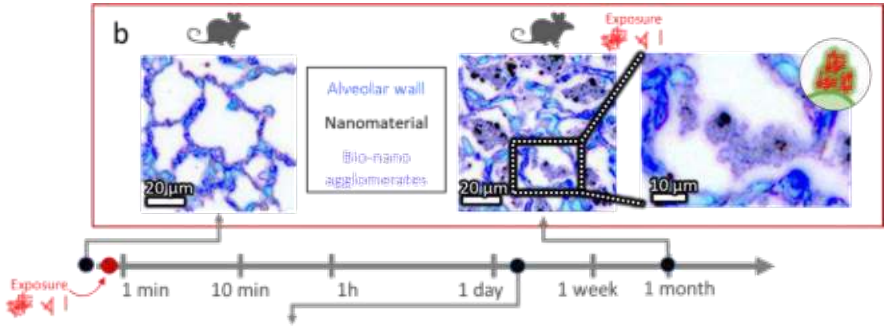
CFM, STED, SEM, HIM

Large bio-nano-composite structures start to form on the surface of epithelial cells.

It seems like a defence mechanism…

surface structures and cell survival following a 2 day incubation with various nanomaterial





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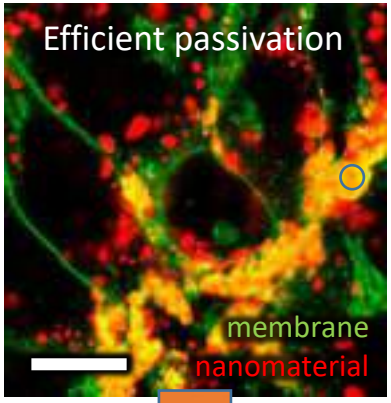
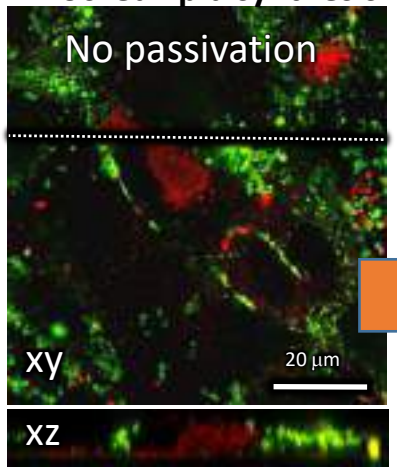
XZ CFM, TEM, dark-field scattering microscopy

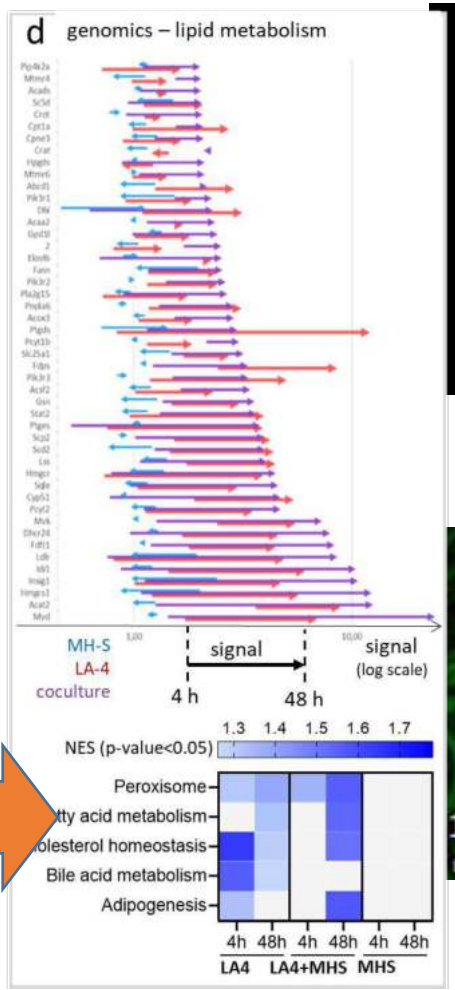
Different nanomaterials harm epithelial cells differently.
Unfortunately, some nanomaterials triggers strong chronic inflammation in vivo.

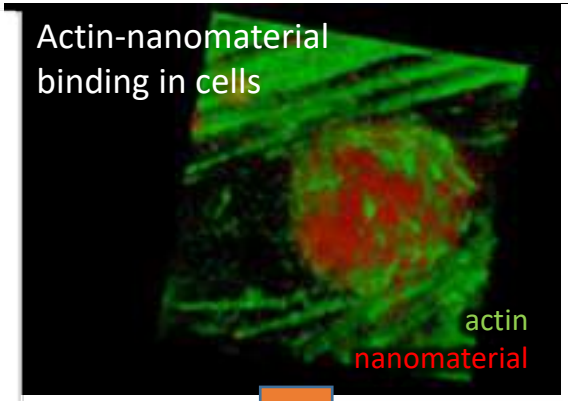
What are the mode of action?



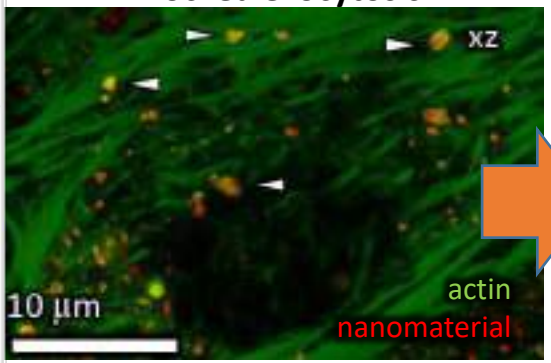
Blocked lipid synthesis

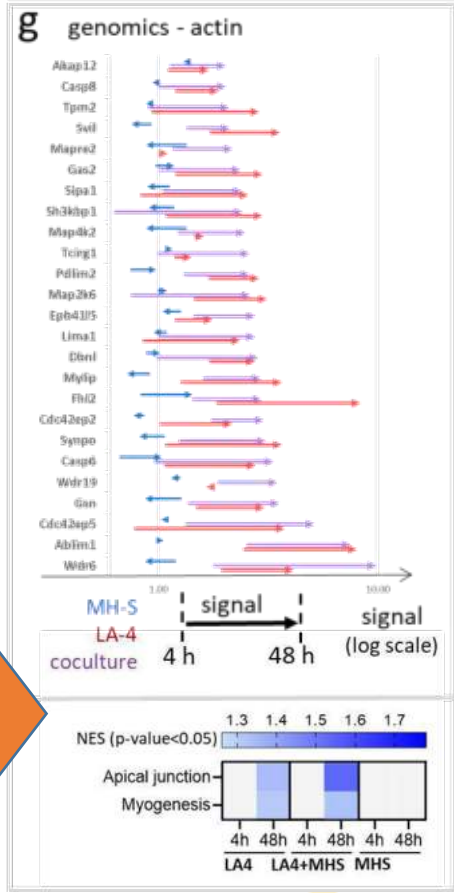






Blocked exocytosis





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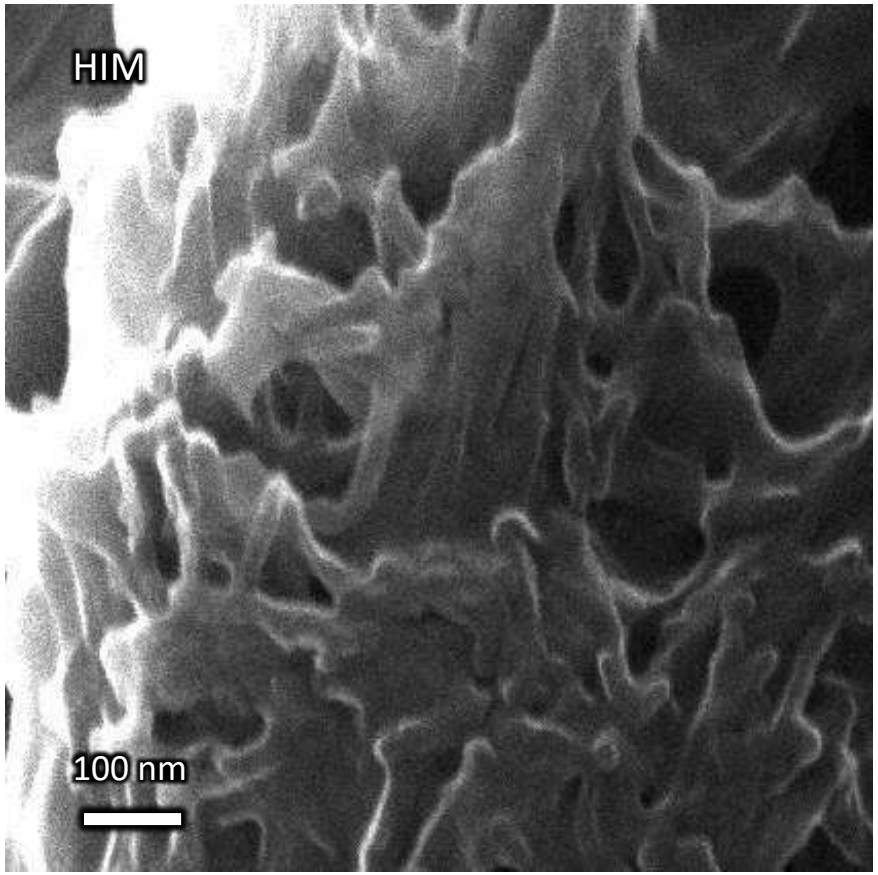
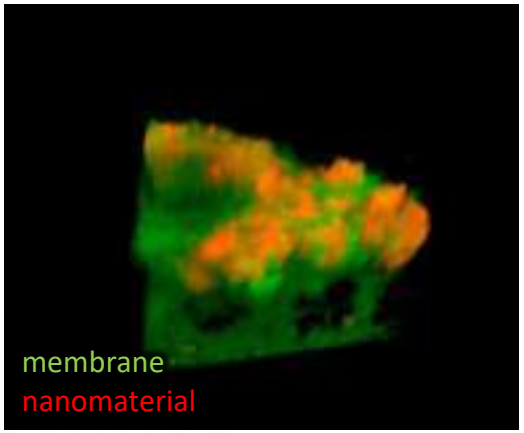
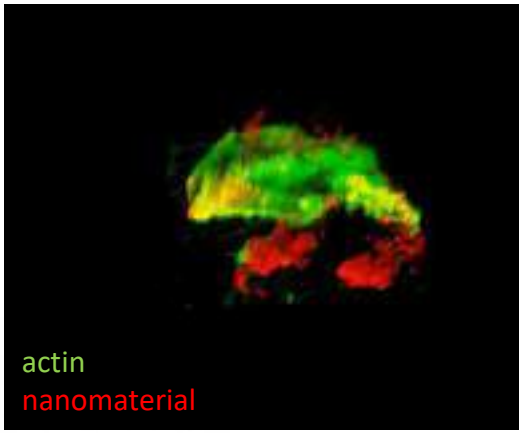
3D STED, transcriptomics

Nanomaterial is uptaken. Lipid synthesis is triggered.
Actin is rearranged. Nanomaterial is excreted.







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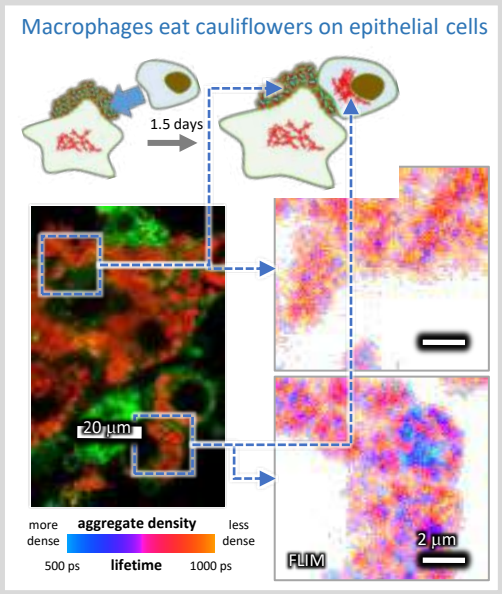
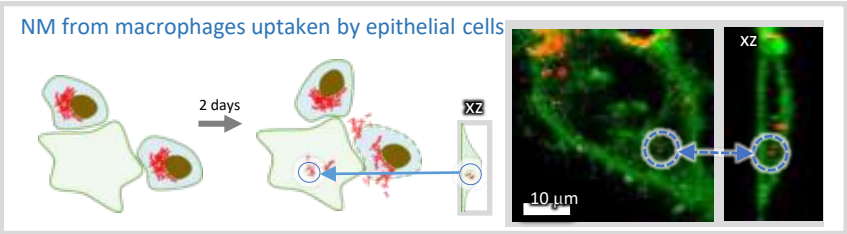
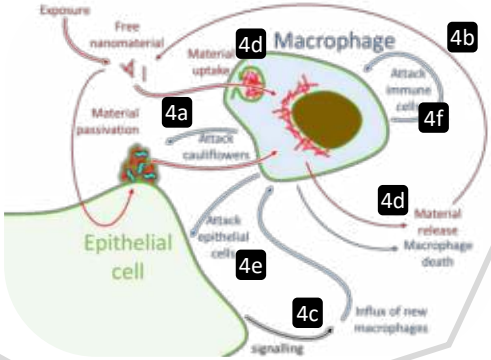
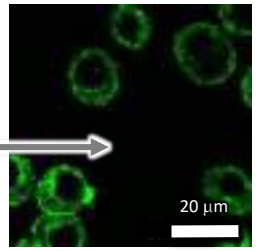
3D STED, HIM

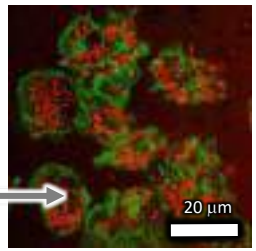
Nano-bio-composites contain lots of lipids, actin and other proteins…

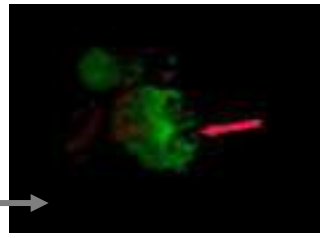


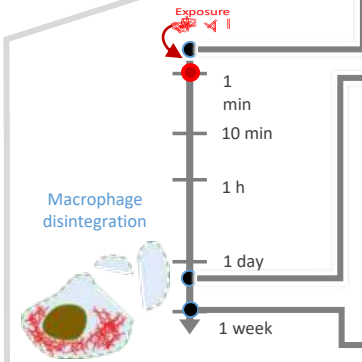


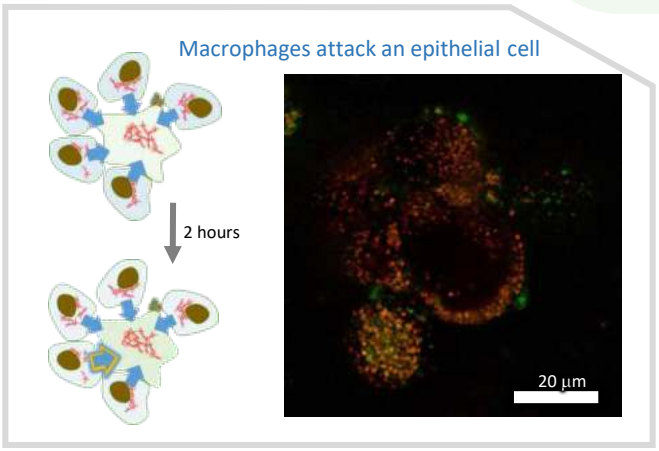


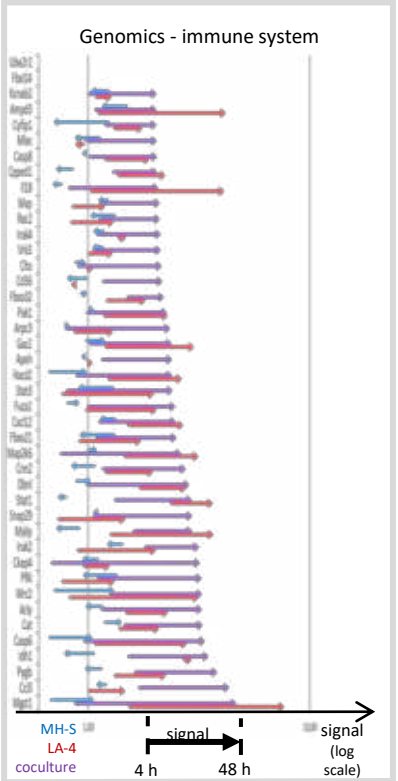


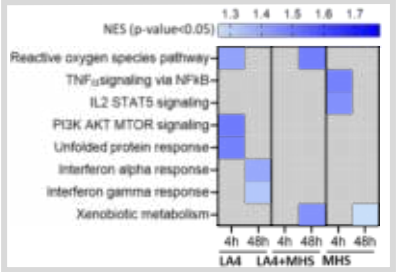










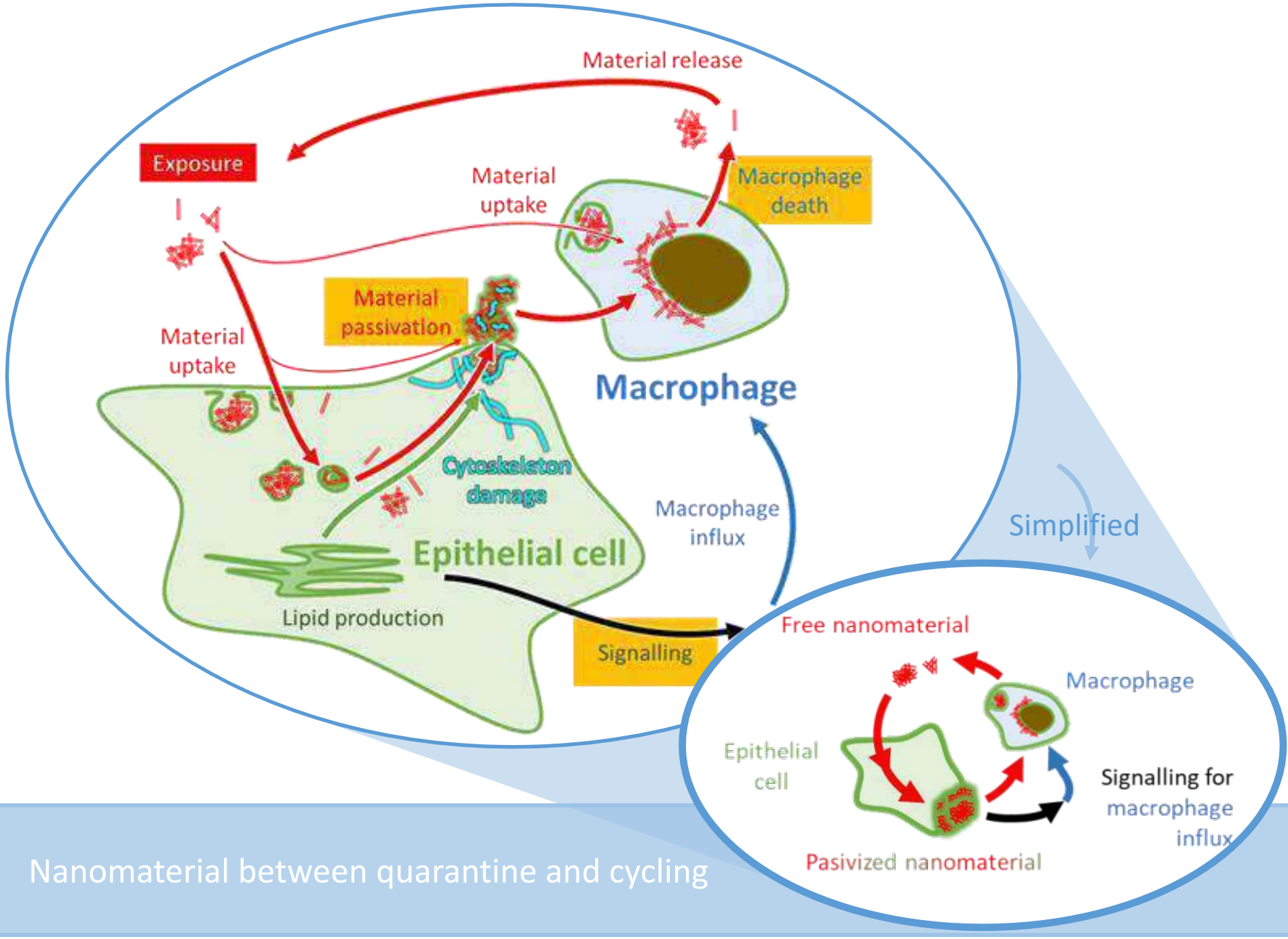


Time-lapse / 3D STED, transcriptomics

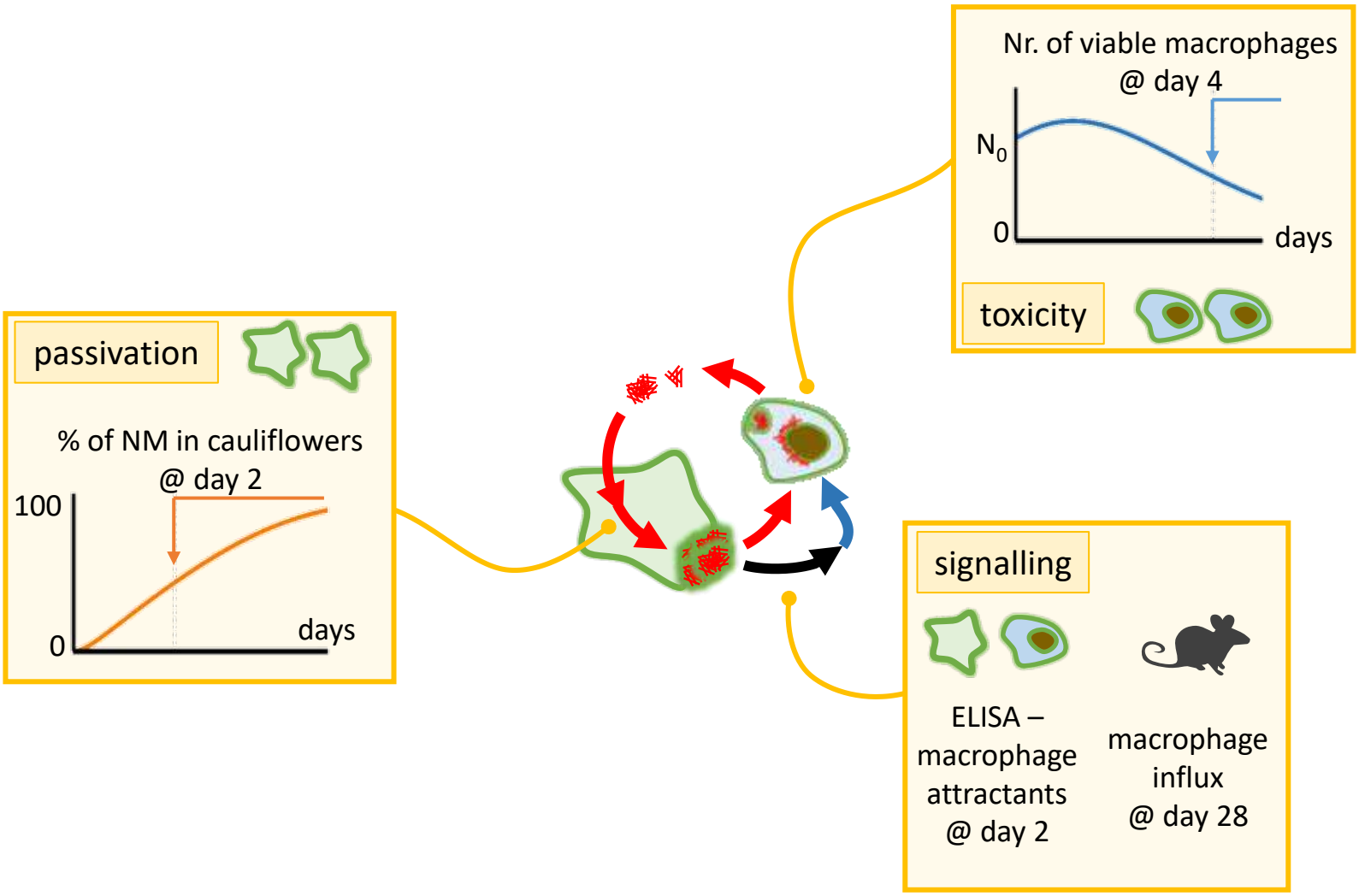
under review in ADVANCED MATERIALS & reposited on bioRxiv

Nanomaterial cycles between different type of lung cells …

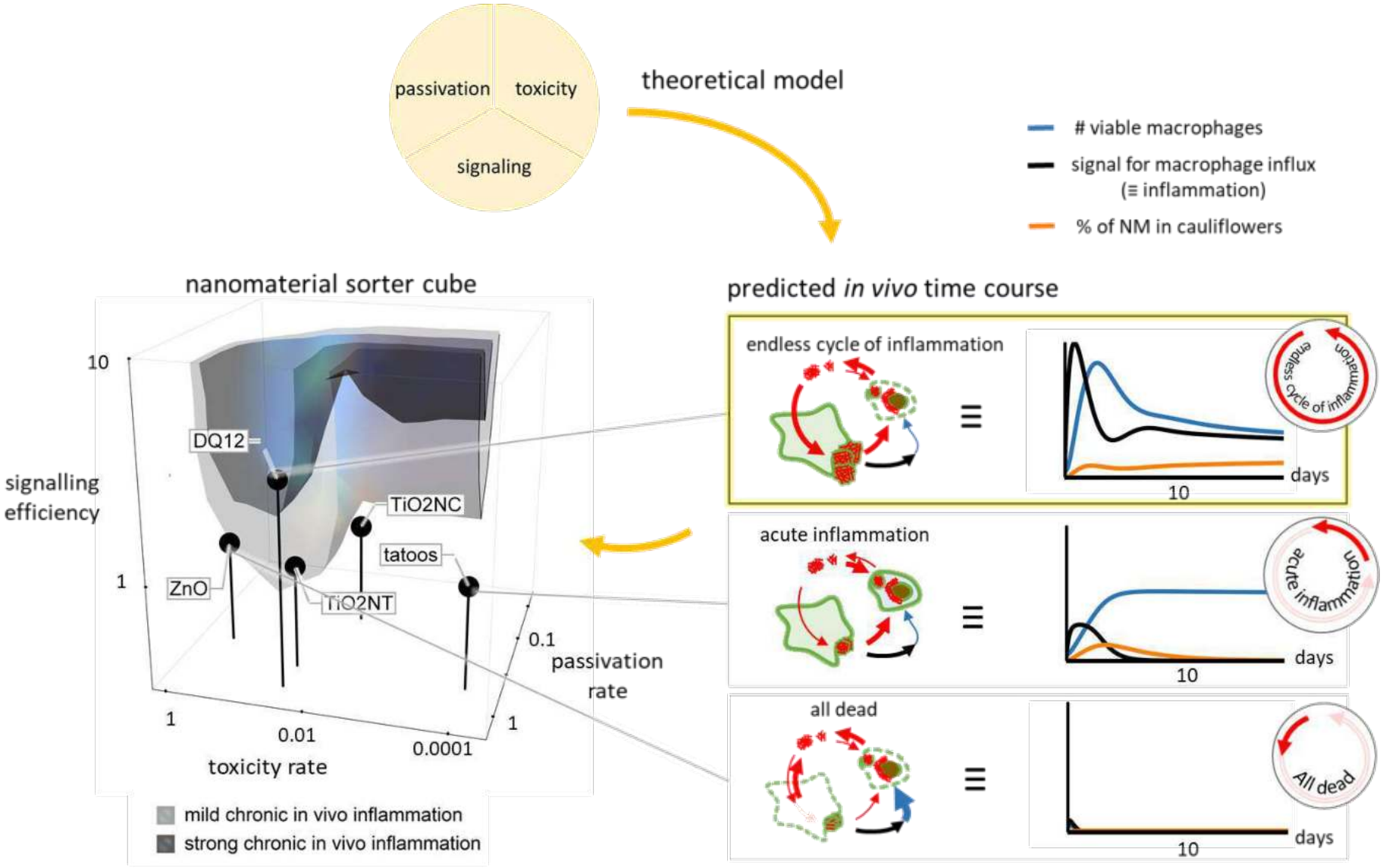
Can we employ new knowledge to predict diseases?



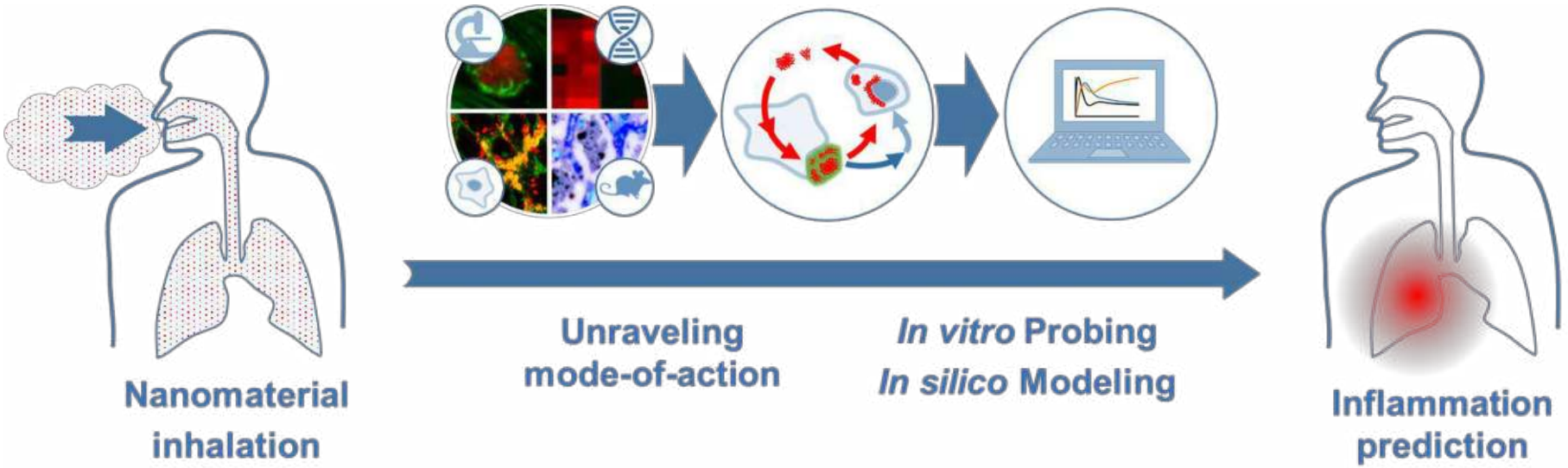
Nanomaterial between quarantine and cycling



Simplified model is converted into an assay with measurable rates in vitro



The measured rates are used to model in vivo time courses and to estimate the type of inflammation by positioning the nanomaterial in a sorter cube.



By identifying complex mode of action, *in vitro* probing and time evolution prediction type of inflammation is predicted (at least) for metal-oxide nanomaterial.

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SmartNanoTox
Smart Tools for Gauging Nano Hazards

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