Advanced model systems in nanotechnology unravel the impact of mechanical cues.

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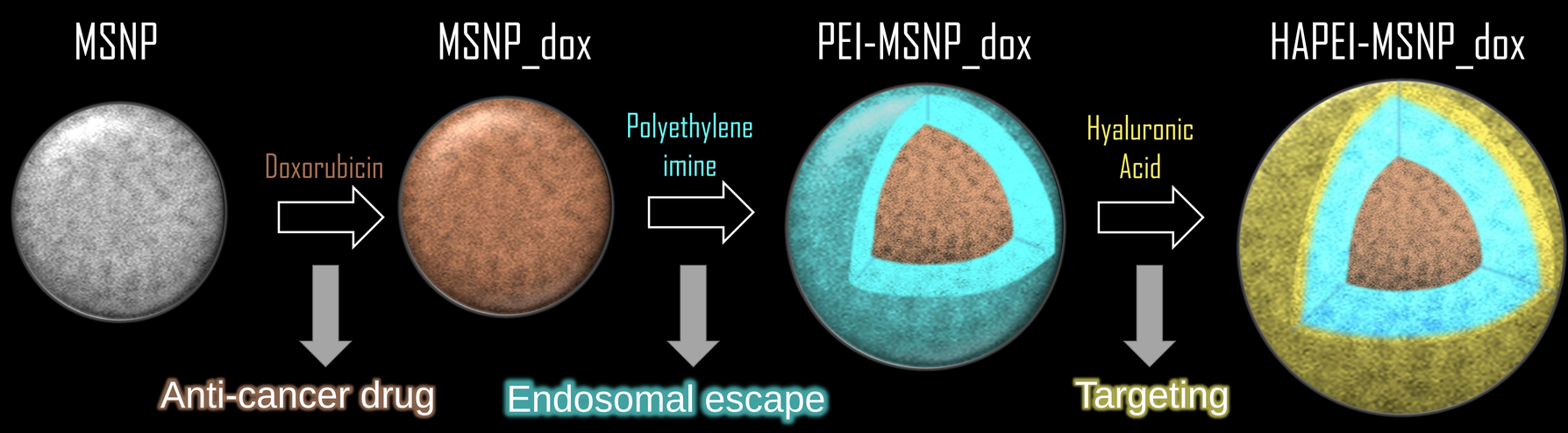
Mesoporous silica nanoparticles

Drug Nano Carrier

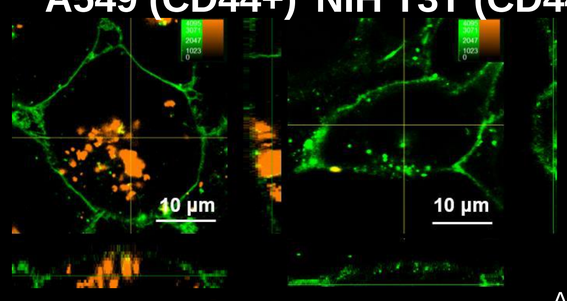


The intracellular pathway

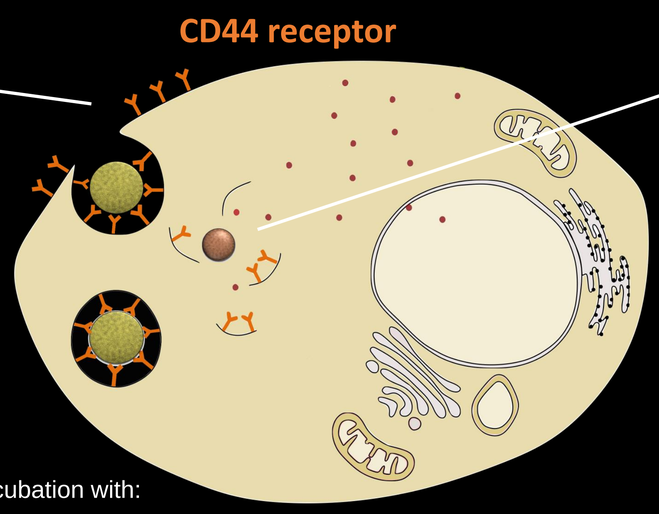
1. Cancer cell targeting

HA binds the CD44 receptor

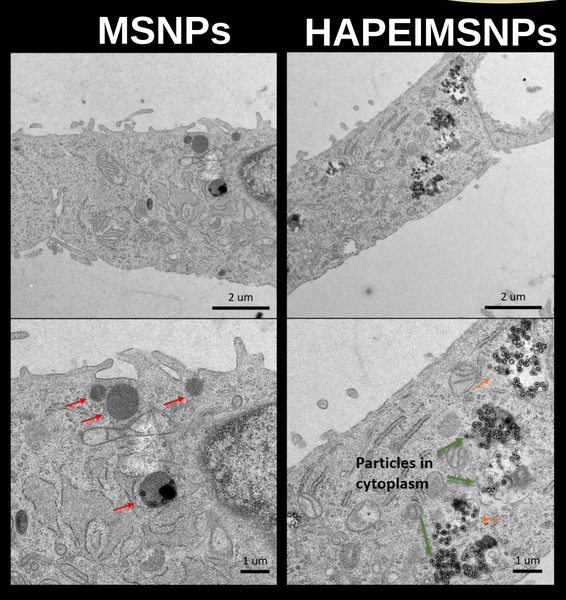
A549 (CD44+) NIH T3T (CD44-)



HA-coated MSNPs
Cell membrane (DiO)



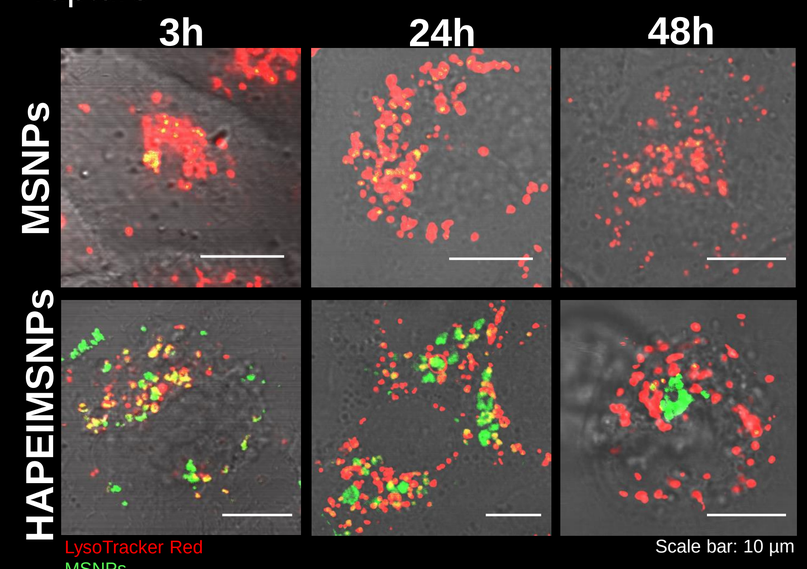
A549 after 24h incubation with:



Start of a detailed study on NP route after endocytosis implementing both SR fluorescence and electron microscopy (CLEM), project ongoing

2. Endosomal escape

PEI is assumed to promote a **proton sponge effect** to induce an endosomal/lysosomal rupture



In more detail

Already after 3h HAPEI MSNPs start to de-colocalize with lysosomes indicating an endosomal escape

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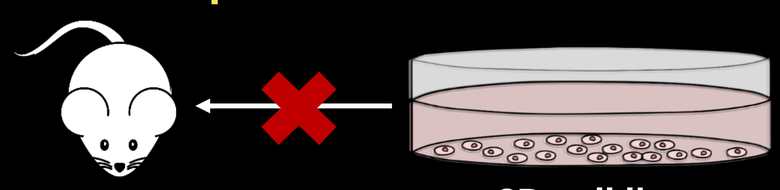
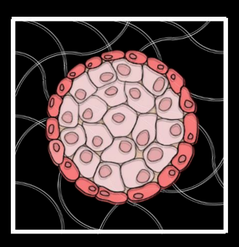
Nanoparticle behavior in advanced model systems

Promising results with nanocarriers *in vitro* do not correspond with the results in *in vivo*

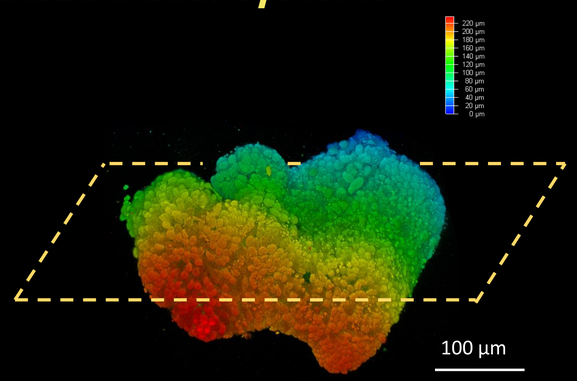


2D cell line
No heterogeneity (-)
No tumor microenvirmonement (-)

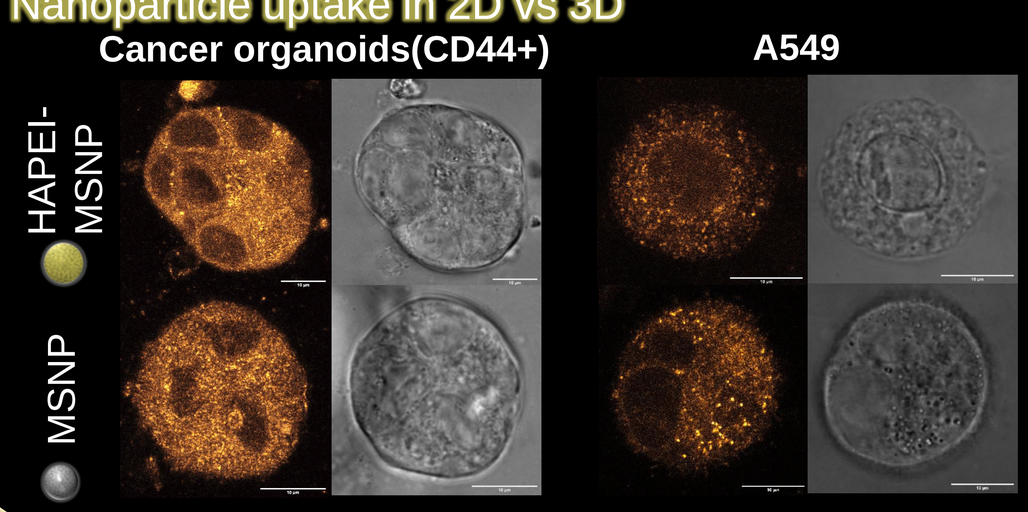
Towards more advanced model systems



Organoid in 3D scaffold
Genetic heterogeneity
Embedded in ECM
Tumor characteristics



Nanoparticle uptake in 2D vs 3D



In gel 3D → **No specific NP uptake**

On glass 2D → **specific NP uptake**

Mechanical properties alter NP uptake!

Fortuni B., Inose, T. & Uji-I, H., Polymeric Engineering of Nanoparticles for Highly Efficient Multifunctional Drug Delivery Systems. *Scientific Reports* 9 (2019)
Boretto, M., Timmerman, D. & Vankelecom, H. Patient derived organoids from endometrial disease capture clinical heterogeneity and are amenable to drug screening. Nature Cell biology (2019) Article accepted