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# How CD147-specific nanomedicines end: from target engagement in 2D towards validation using a novel vascularized *in vitro* glioblastoma model

**C. Pacheco, R. Daware, A. Motta, A. Koikalethu, F. Lorenzi, A.M. Sofias, F. Baltazar, B.M. Costa, T. Lammers, and B. Sarmento**

INSTITUTO DE INVESTIGAÇÃO E INOVAÇÃO EM SAÚDE
UNIVERSIDADE DO PORTO

February 23, 2023

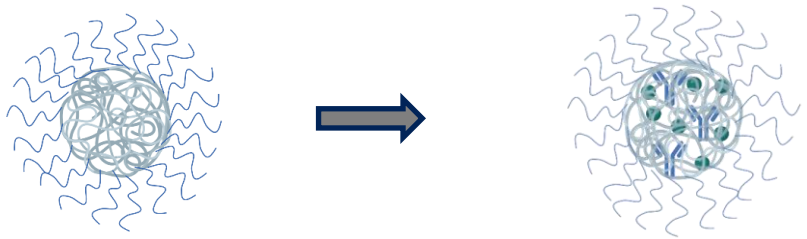
ExMI
EXPERIMENTAL MOLECULAR IMAGING

COST ACTION CA 17140
NANO2CLINIC
CANCER NANOMEDICINE - FROM THE BENCH TO THE BEDSIDE

cost
EUROPEAN COOPERATION IN SCIENCE & TECHNOLOGY

# Cancer Nanomedicine

## Polymeric Nanoparticles



Drug Encapsulation and Delivery

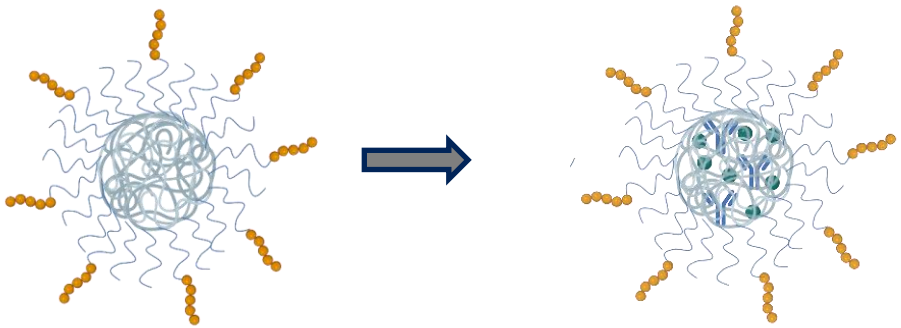
**Refine anticancer drugs' pharmacokinetics:**

Solubility

*In vivo* Stability

Tumor Permeability and Retention

## *Version 2.0 – Surface-decorated* Polymeric Nanoparticles



Drug Encapsulation and Delivery

Solubility

*In vivo* Stability

Tumor Permeability and Retention

Specific Cells/Tissues/Subcellular Compartment

Ø

**Clinically Approved**

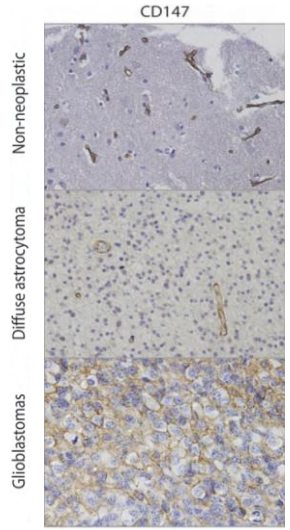
- Ligand decoration procedure?
- Surface decoration density?
- In vitro validation?

ACS Nano. 2020;14:7832–46

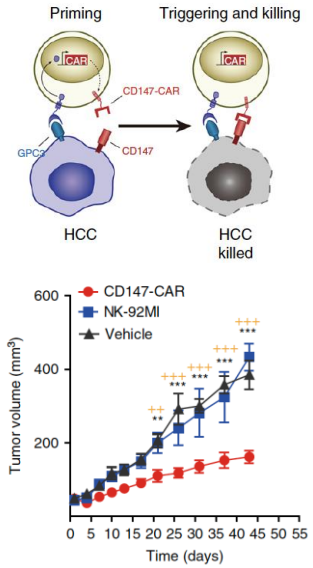
# Cancer Nanomedicine

**Tumor Targeting**

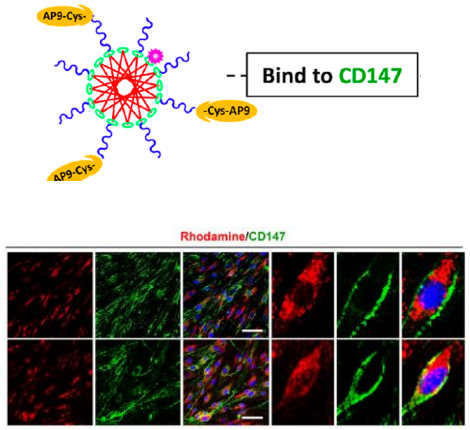
"**CD147** expression is upregulated in GBM patient samples and cell lines"



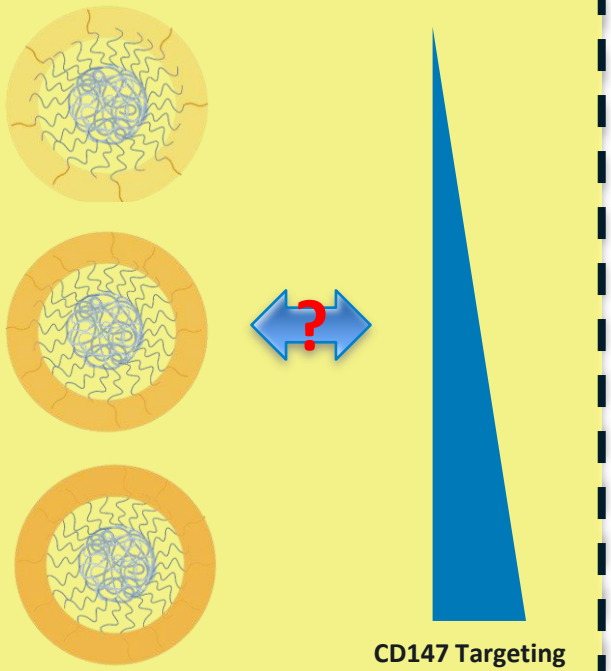

"**CD147** molecule can be used as an effective and valid target for immunotherapy *in vitro* and *in vivo*."




"**AP-9**-NPs bound specifically to endogenous **CD147**."




***AP-9 decorated* Nanoparticles**




Nat. Commun. 2020, 11: 4810 and ACS Appl. Bio Mater. 2020, 3:1976-1985



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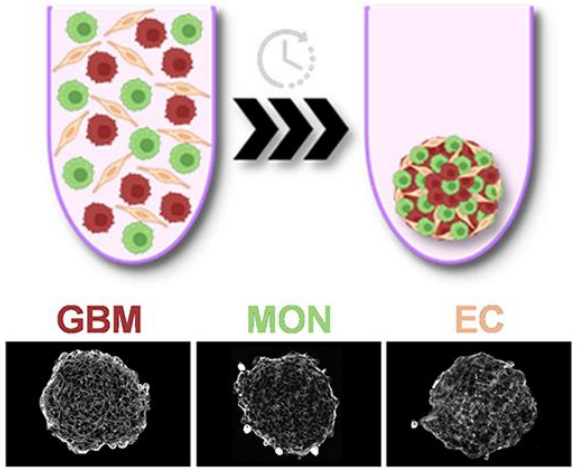
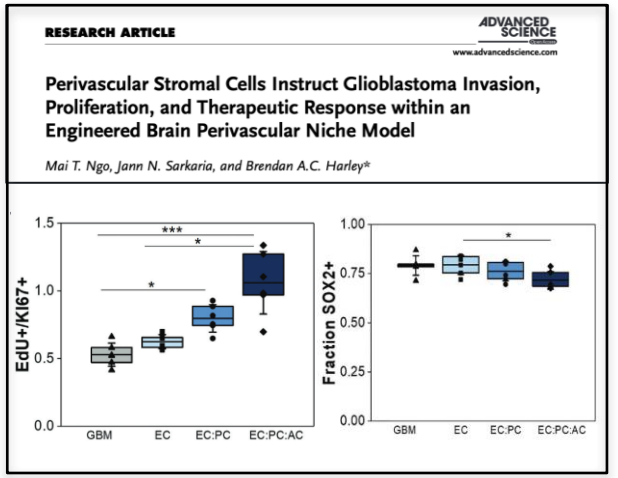
# Cancer Nanomedicine

***In Vitro* Validation**




Cell Uptake
Anti-proliferative Effects
Immune Cells Polarization

Angiogenesis?
ECM-cell Interaction?
Invasion and Migration?


RESEARCH ARTICLE

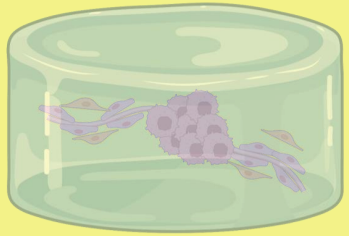
ADVANCED SCIENCE
www.advancedscience.com

**Perivascular Stromal Cells Instruct Glioblastoma Invasion, Proliferation, and Therapeutic Response within an Engineered Brain Perivascular Niche Model**

*Mai T. Ngo, Jann N. Sarkaria, and Brendan A.C. Harley**



**Glioblastoma-in-the-Perivascular niche**



**3D Matrix and Stromal cells to mimic TME?**

JCR 2023, 353: 77-95 and Adv. Sci. 2020, 9:202201888



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# Main Goals:

EXPERIMENTAL MOLECULAR IMAGING

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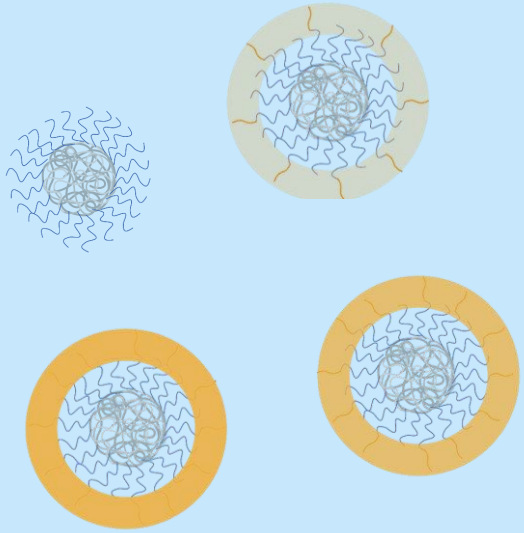
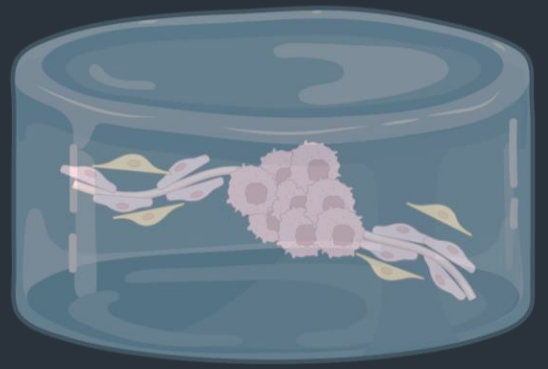
## CD147-targeted Nanoparticles

- Assess Targetability





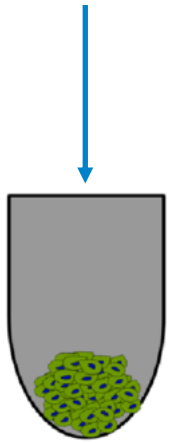
## Glioblastoma-in-the-Perivascular Niche Model

- Development and Characterization

# GBM-in-the-Perivascular Niche Model

**Microenvironment with a vascular-like structure:**

Cy5-labeled-NHDF: HBMEC : GFP-HUVEC
(10:8:2)



On top of 96-ULA Well Plates
spheroids

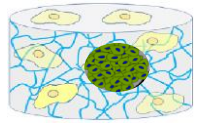
**Without 3D matrix!**

96-ULA Well Plates

Cy5-labeled-NHDF : HBMEC : GFP-HUVEC
(10:8:2)

**Fibrin/Collagen Hydrogel**

20 000 cells/well at
day 5 after seeding



**With 3D matrix!**



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# How CD147-specific nanomedicines end?

- ❖ AP-9 decoration does not increase NPs affinity towards non-tumor cells.
- ❖ Low decoration densities are sufficient to beneficially alter the targeting behavior of the formulations.
- ❖ In vitro, the 3D matrix allows stromal cells preferential distribution of along the matrix and around the spheroids.

## On-going Work:

- Confirm affinity assay through imaging techniques.
- Testing cell viability.
- Evidences of cell/cell and cell/matrix interaction.
- Gel rheologic characterization.



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**NTDD Group**

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Alessandro Motta
Anu Thomas Koikalethu



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