Dendritic Cell-Targeted Nano-Vaccine: A tool for sensitizing cancer to immunotherapies

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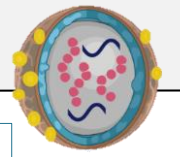
CRS 2022 Annual Meeting & Expo
July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada
Advanced Delivery Science

Current cancer therapies rely mostly on non-specific drugs

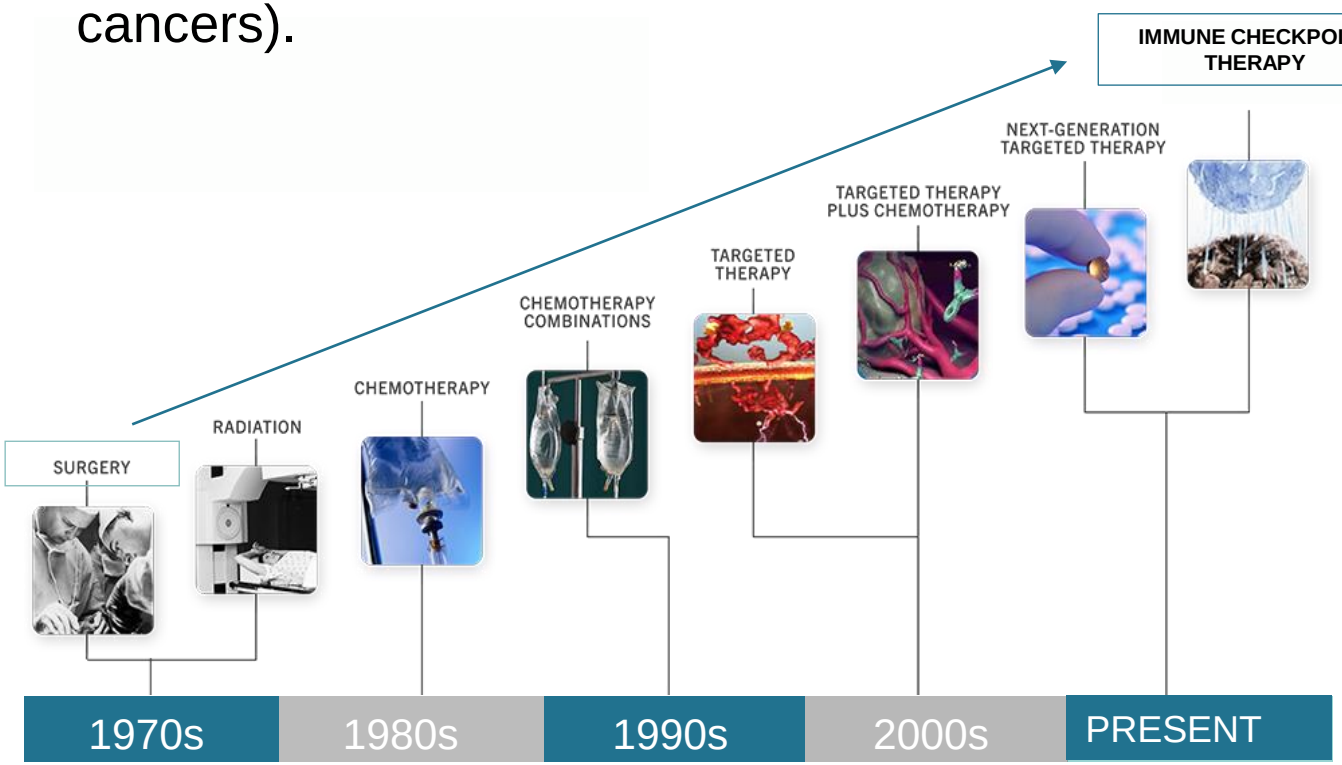


- **Non-specific drugs** for cancer cell destruction.

Severe adverse effects

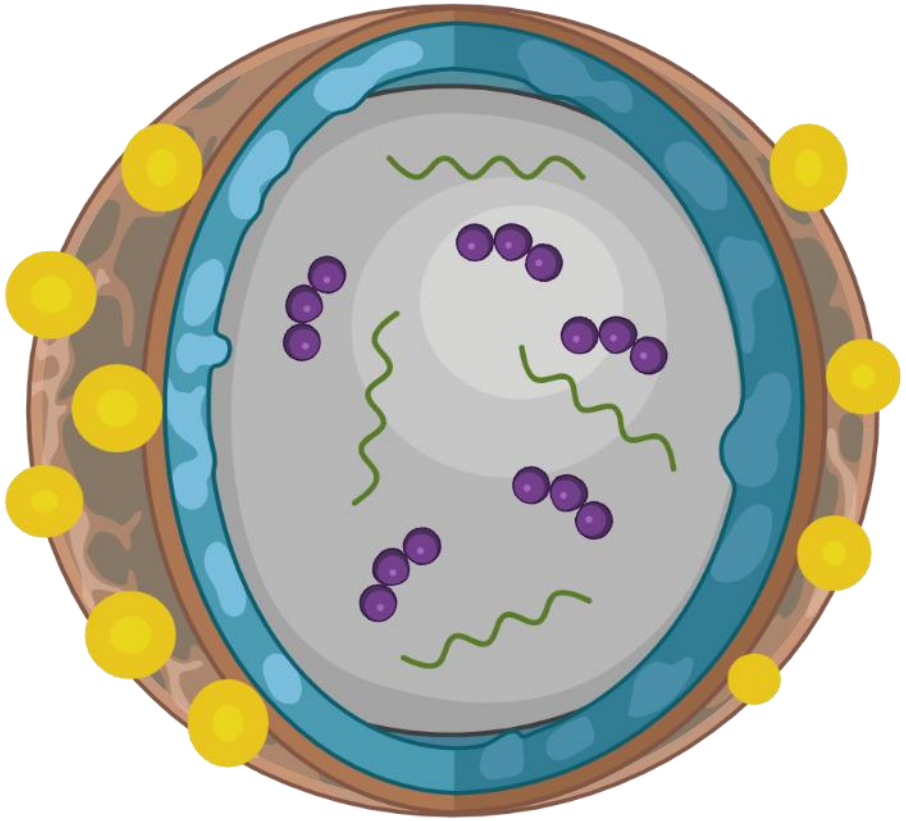
- **Anti-PD-1 approved by the FDA** in 2017 and by **EMA** in 2020 for mismatch-repair-deficient or microsatellite instability-high (dMMR/MSI-H) tumors (5-10% of all GI cancers).

- CRC **dMMR-MSI-H** tumors with **31%** response rate
- **pMMR-MSI-L** with **0% response rate**



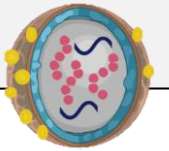
Adapted from Puccini A. Et al. J ImmunoTher Cancer 2020; 8:e000404.

DC- targeted Nano-Vaccine



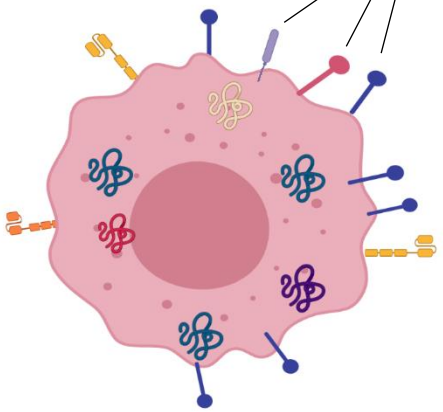
- **Sensitize tumors to immunotherapy.**
- **Increase the number of infiltrating immune cells.**
- **Amplify the effect of immunotherapies.**

DC-Targeted Nano-Vaccine as potential immunotherapy against cancer



Overexpression of antigens / Generation of neoantigens by the cancer cell

Cancer associated antigens



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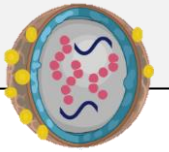
DC-Targeted Nano-Vaccine as potential immunotherapy against cancer



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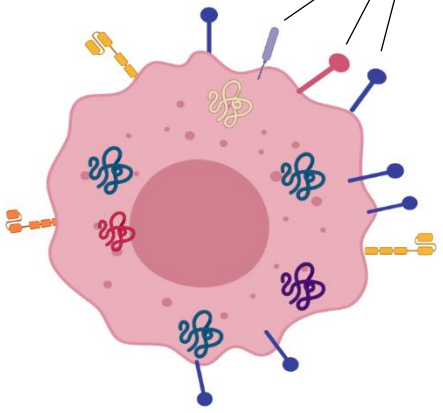
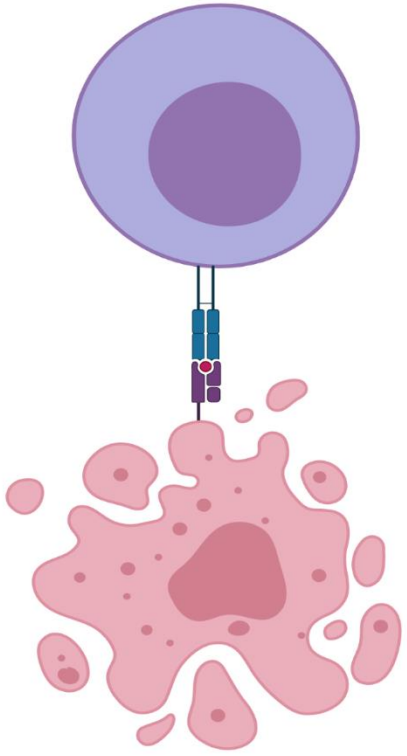


The antigens provide target for immune cells



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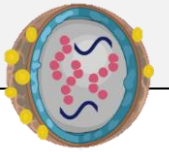
DC-Targeted Nano-Vaccine as potential immunotherapy against cancer



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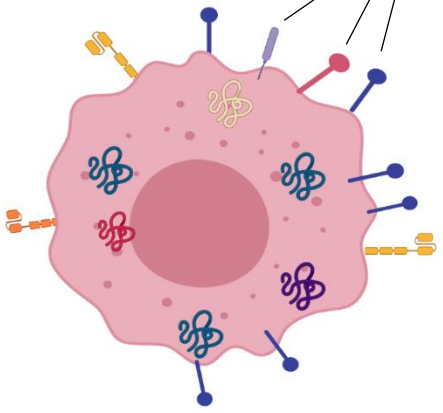

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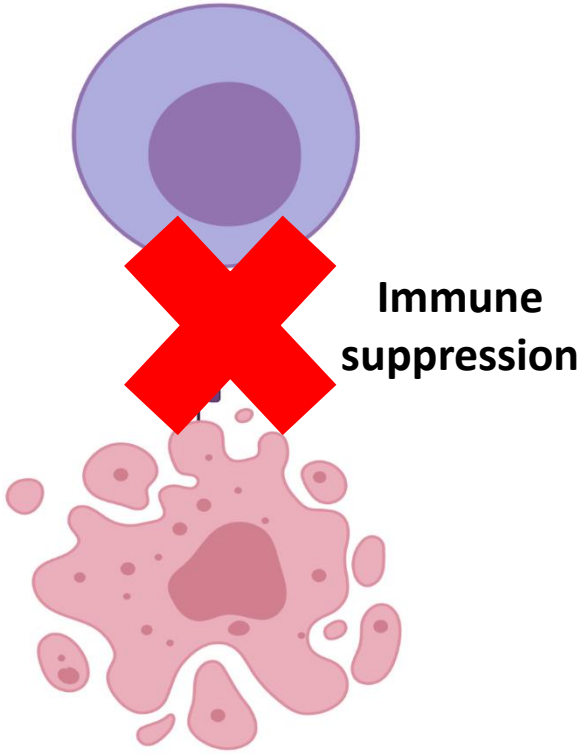
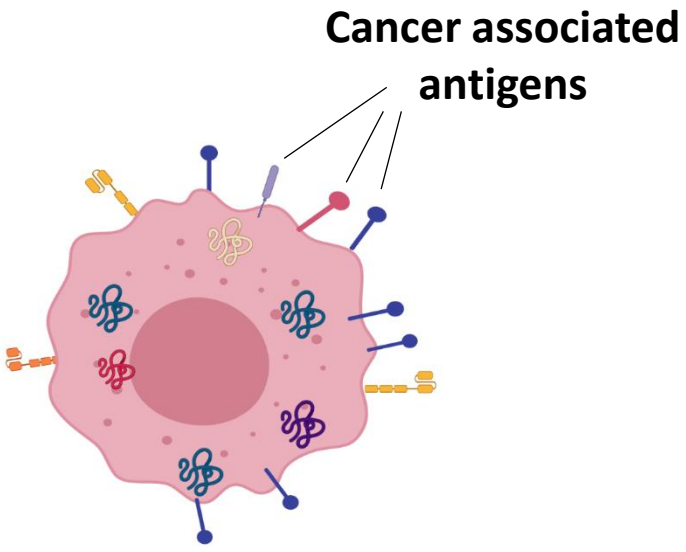


DC-Targeted Nano-Vaccine as potential immunotherapy against cancer

Overexpression of antigens / Generation of neoantigens by the cancer cell



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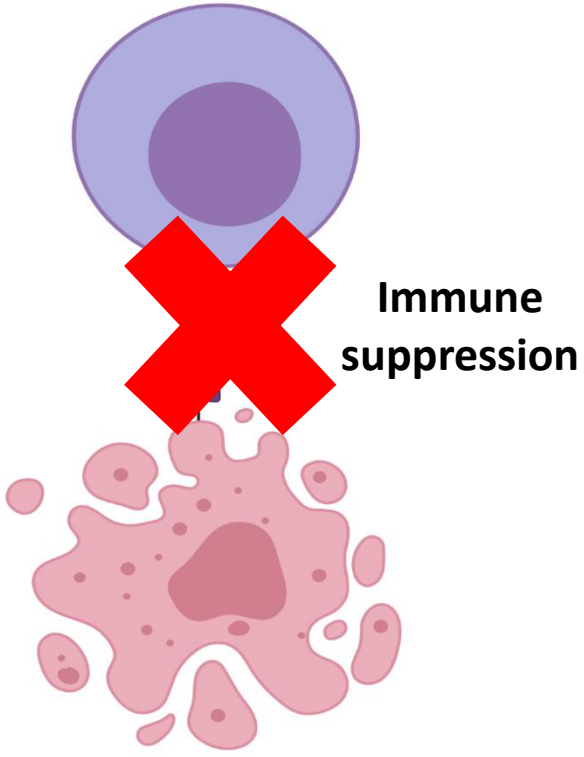
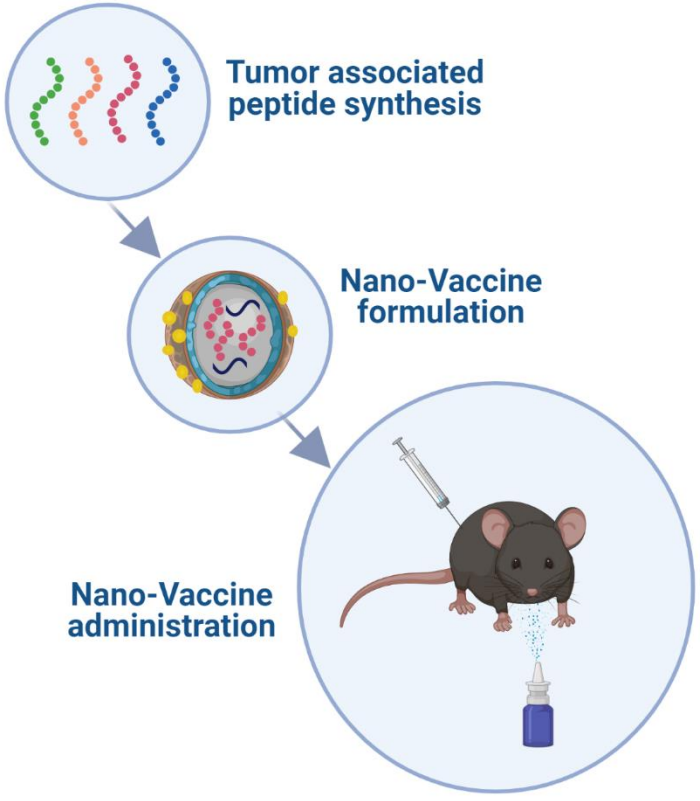


Peptide based Nano-Vaccine for cancer treatment



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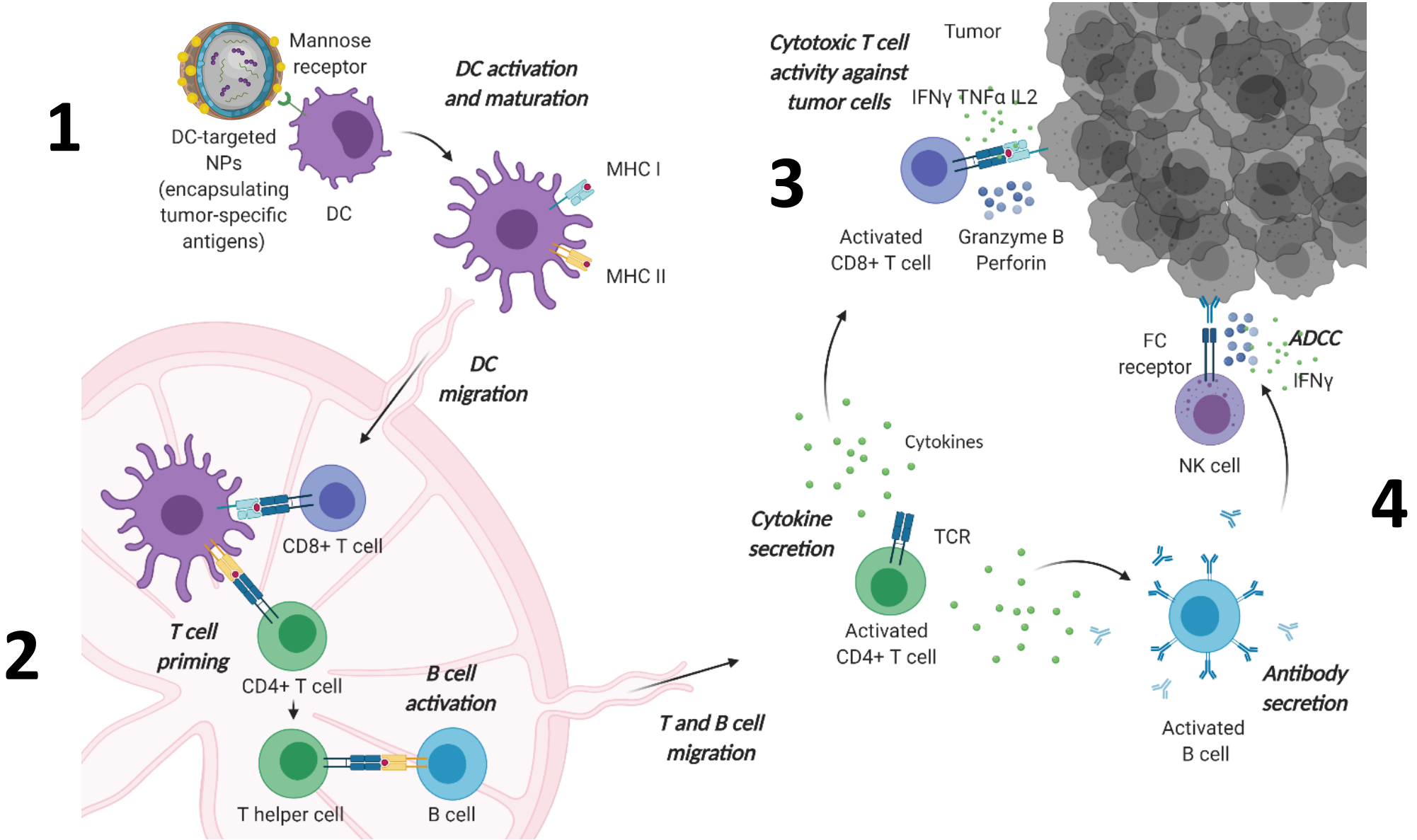
DC-Targeted Nano-Vaccine mechanism of action



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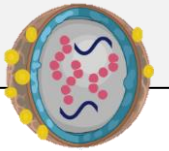
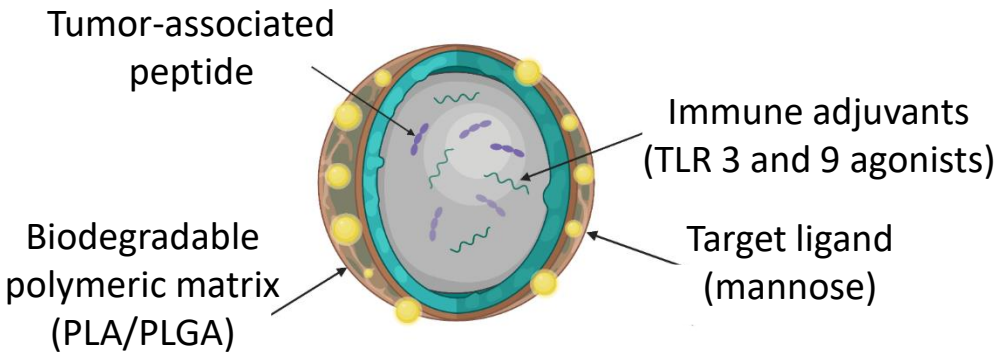
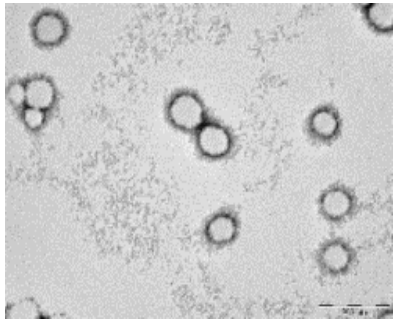
DC Nano-Vaccine characterization



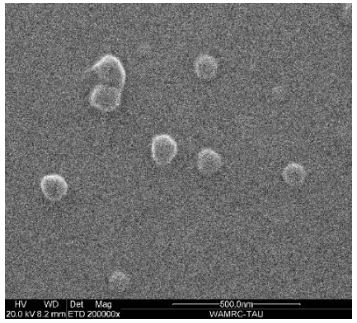


TEM image



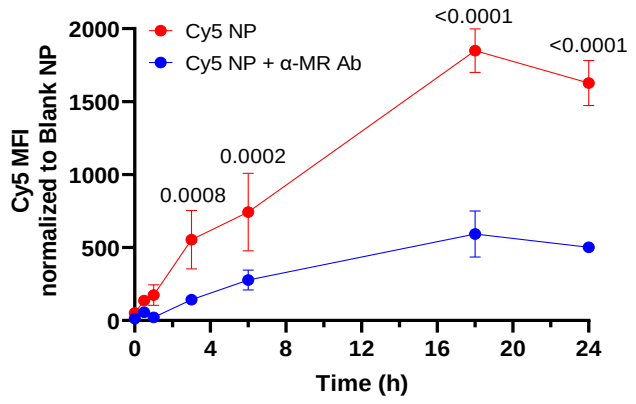
Diameter: 100 ± 20 nm.
Average of 25 nanoparticles.

SEM image

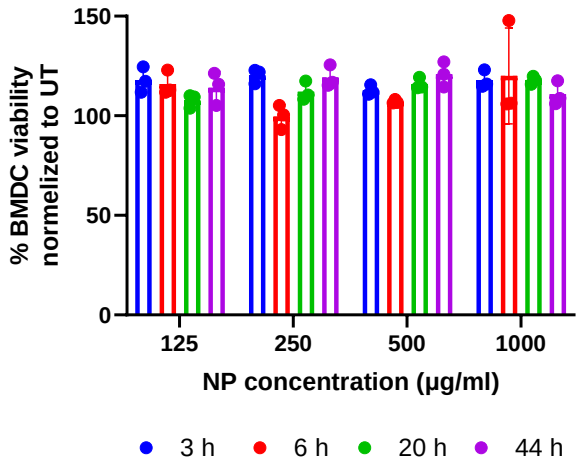


Diameter: 105 ± 10 nm.
Average of 25 nanoparticles.

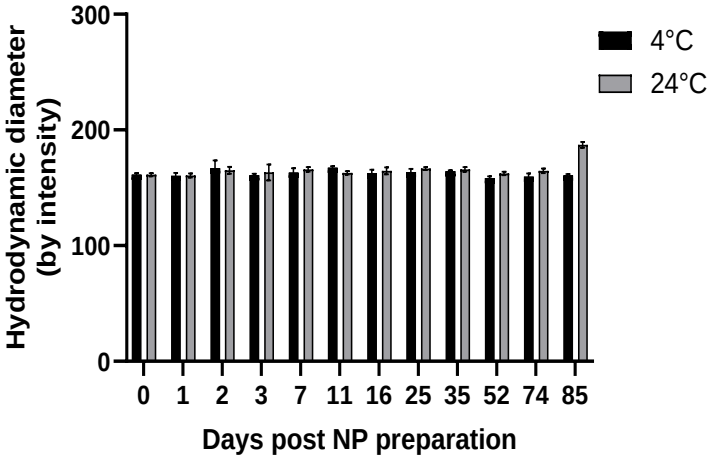
NP internalization into BMDC



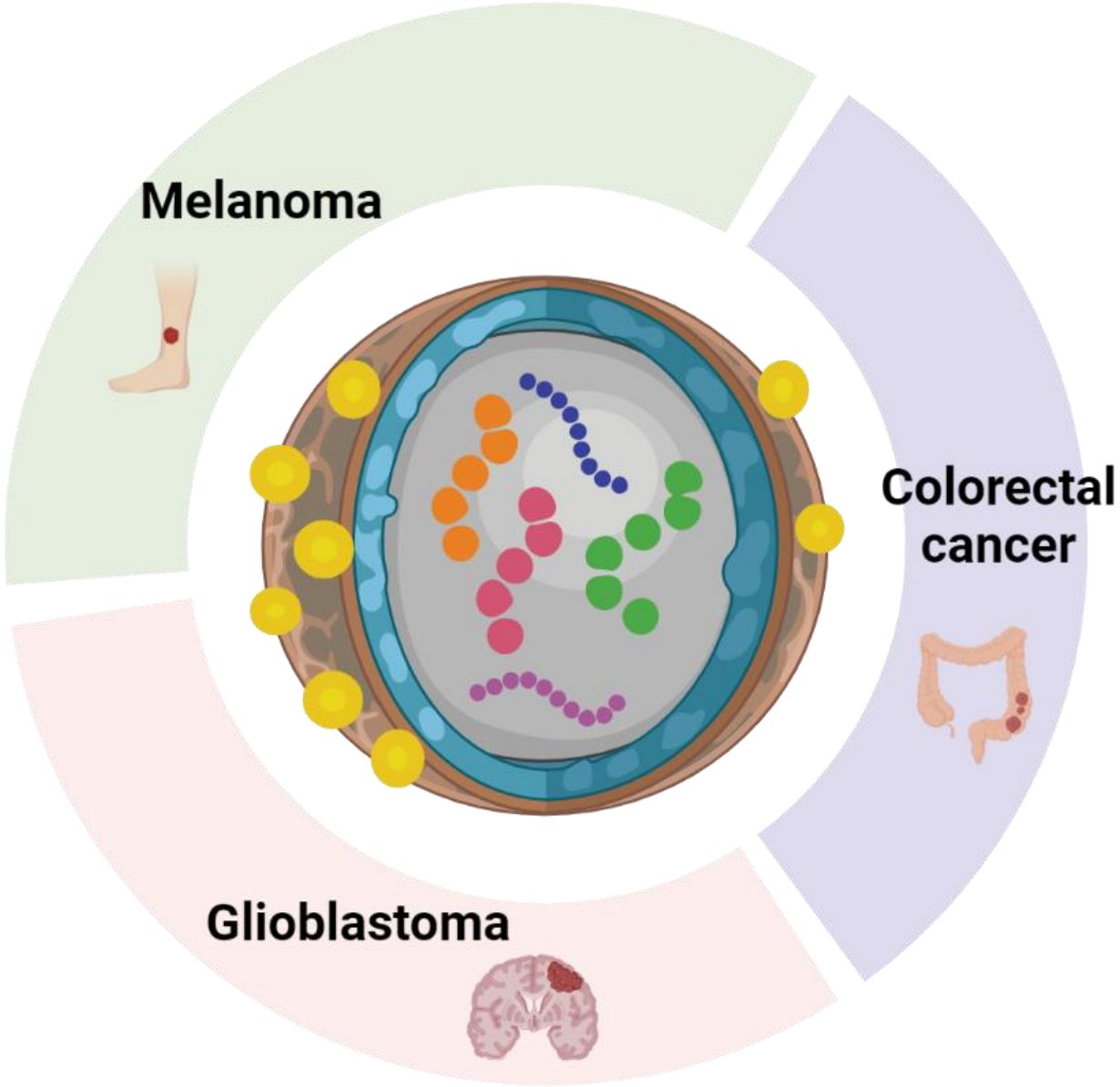
Biocompatibility



Stability over time



Cancer models



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DC-Targeted Nano-Vaccine for melanoma therapy

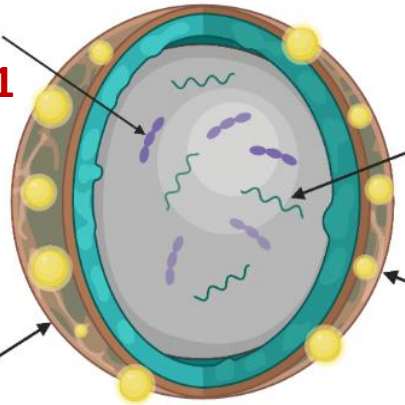
Melan-A/MART-1 – Overexpressed in melanoma

Tumor-associated peptide **Melan-A/MART-1**

Immune adjuvants (TLR 3 and 9 agonists)

Biodegradable polymeric matrix (PLA/PLGA)

Target ligand (mannose)



Melanoma

The most deadly form of skin cancer

Immunogenic

"Hot tumor"

Dr. João Conniot

Dr. Anna Scomparin

DC-Targeted Nano-Vaccine for melanoma therapy

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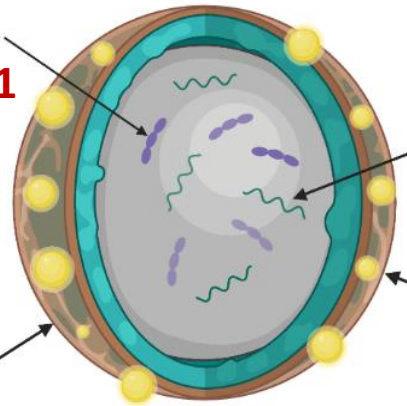
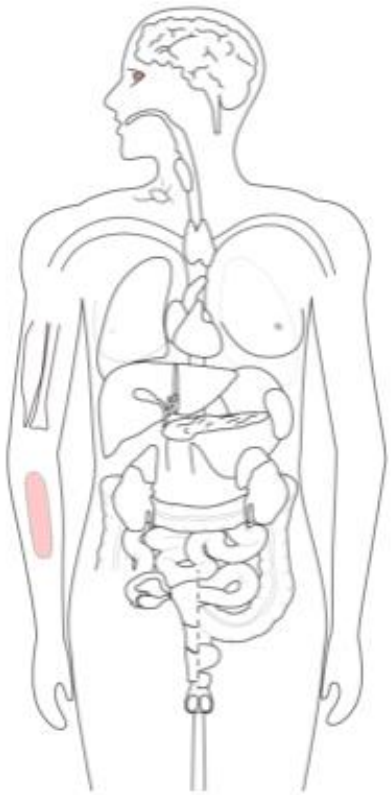


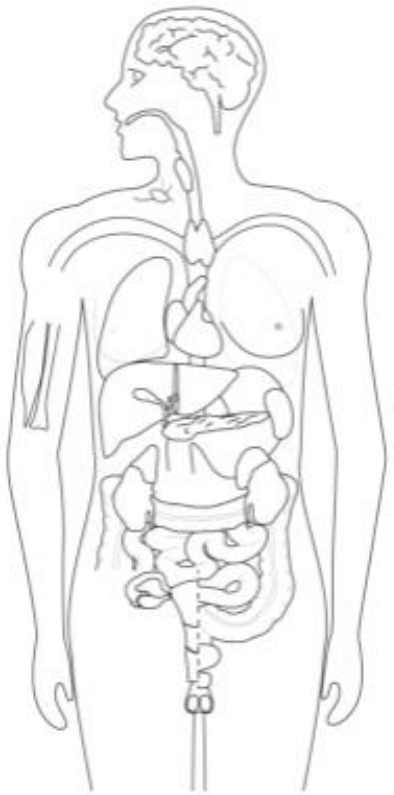
Dr. João Conniot

Dr. Anna Scomparin

Tumor



Normal

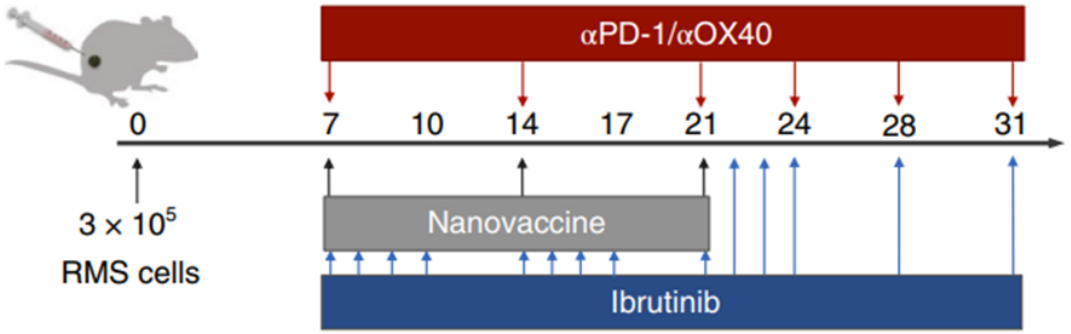


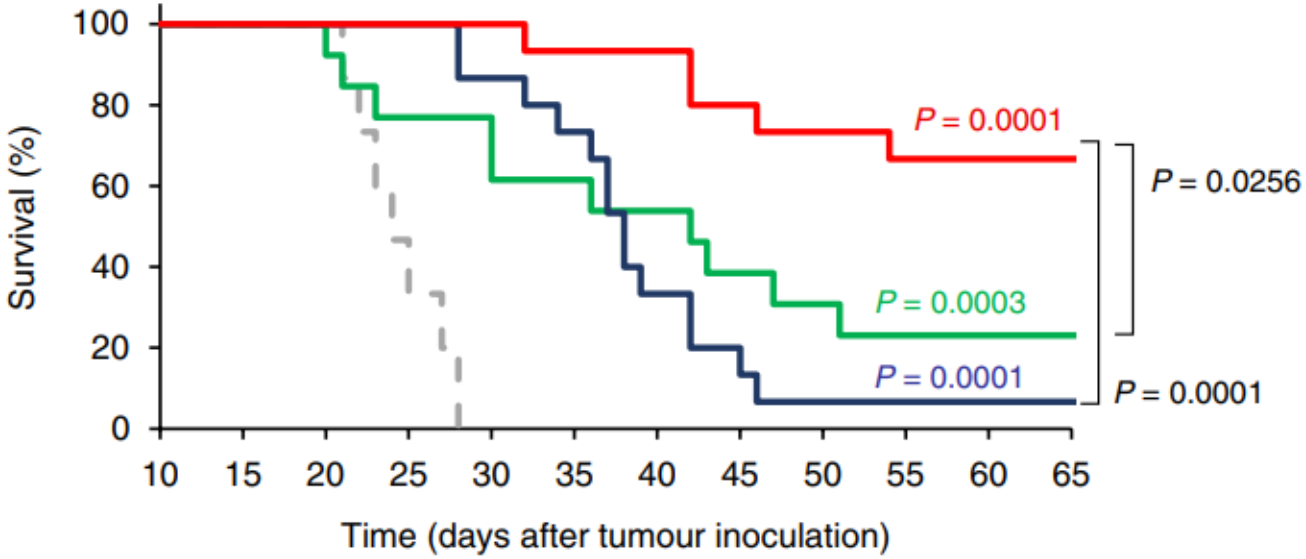
Tumor/ Normal ratio: 59.3

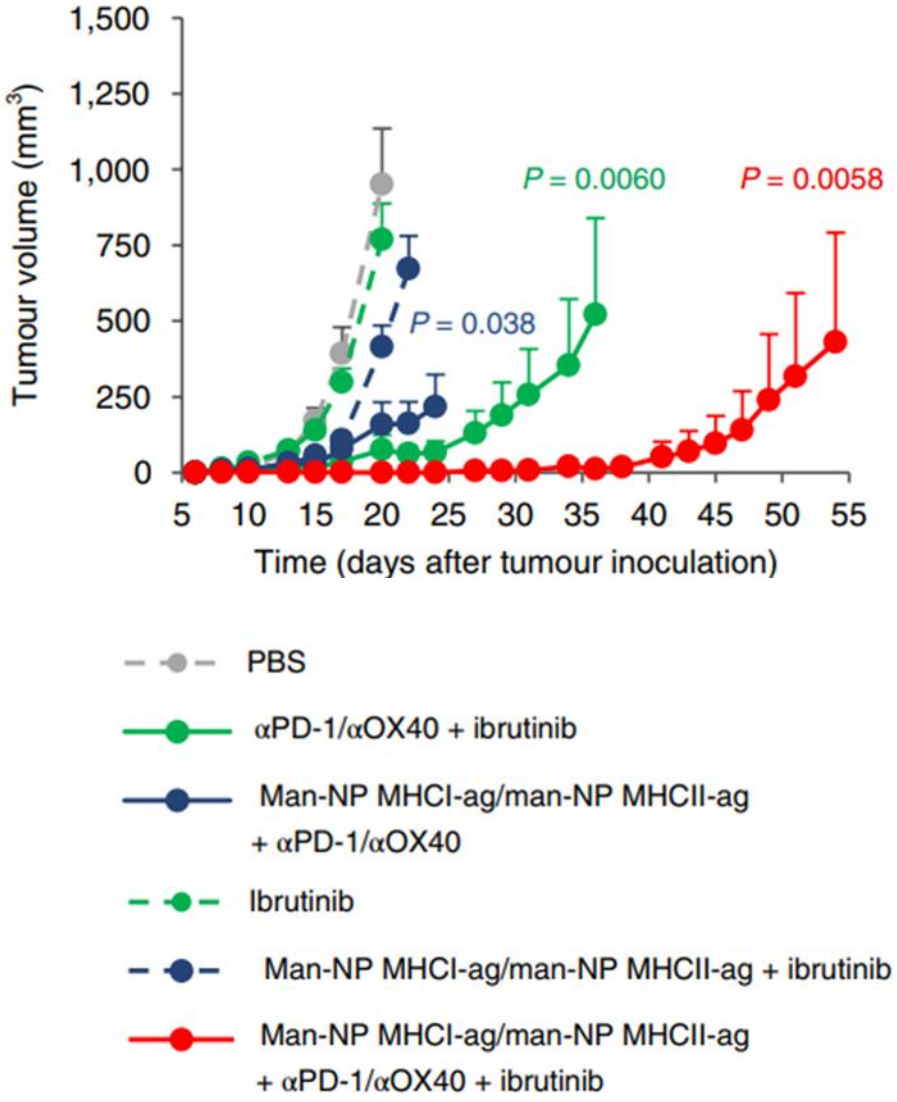
http://gepia.cancer-pku.cn/index.html

DC-Targeted Nano-Vaccine decreased melanoma tumor volume and increase mice survival *in vivo*

Melan-A/MART-1 – Overexpressed in melanoma







Conniot J*, Scomparin A*,…, Kleiner R, *et al*, *Nature Nanotechnology*, 2019

DC-Targeted Nano-Vaccine for CRC therapy

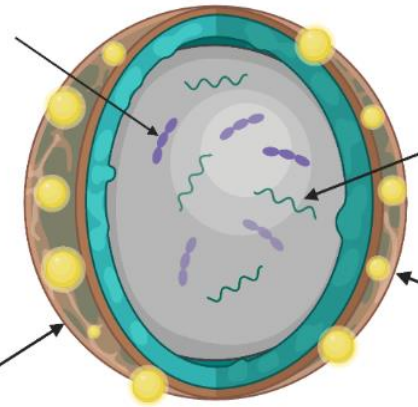
CEACAM5– Overexpressed in colorectal cancer

Tumor-associated peptide **CEACAM5**

Immune adjuvants (TLR 3 and 9 agonists)

Biodegradable polymeric matrix (PLA/PLGA)

Target ligand (mannose)



CRC

The third leading cause of cancer death

Immunogenic

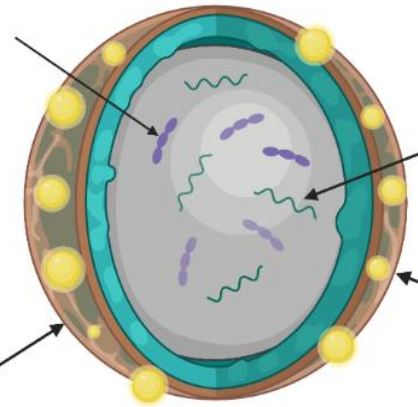
"Hot tumor"

Dr. Rita Acúrcio

DC-Targeted Nano-Vaccine for CRC therapy

CEACAM5– Overexpressed in colorectal cancer

Tumor-associated peptide **CEACAM5**

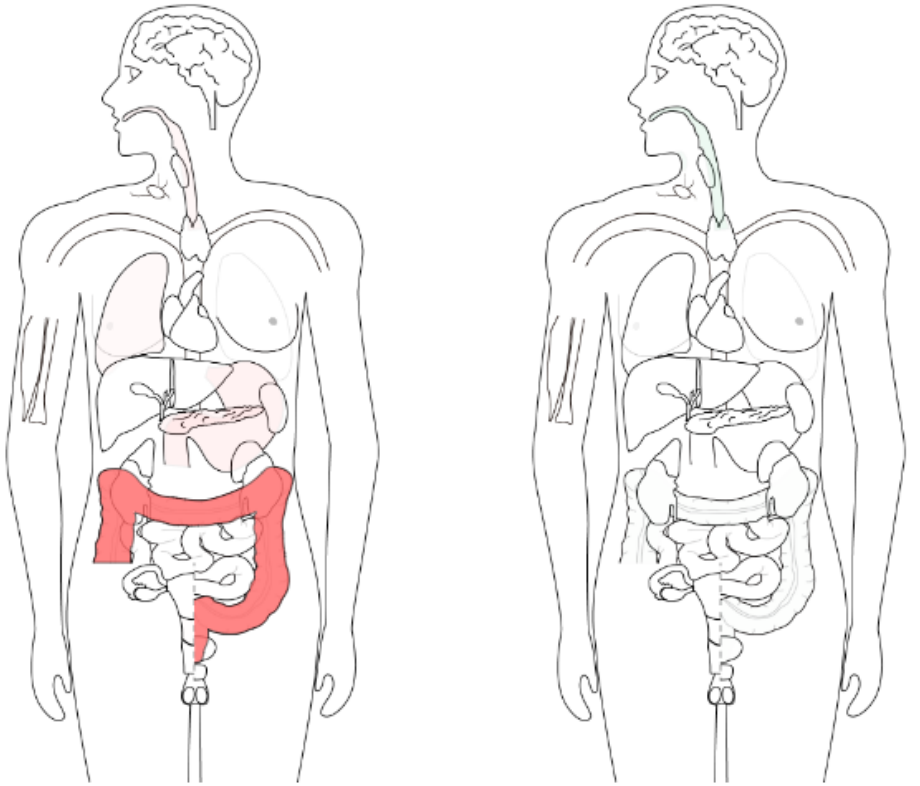


Immune adjuvants (TLR 3 and 9 agonists)

Biodegradable polymeric matrix (PLA/PLGA)

Target ligand (mannose)

Dr. Rita Acúrcio

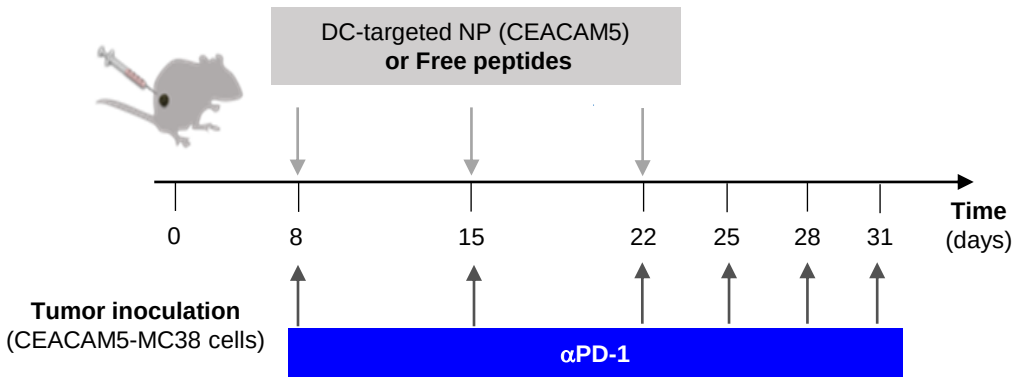


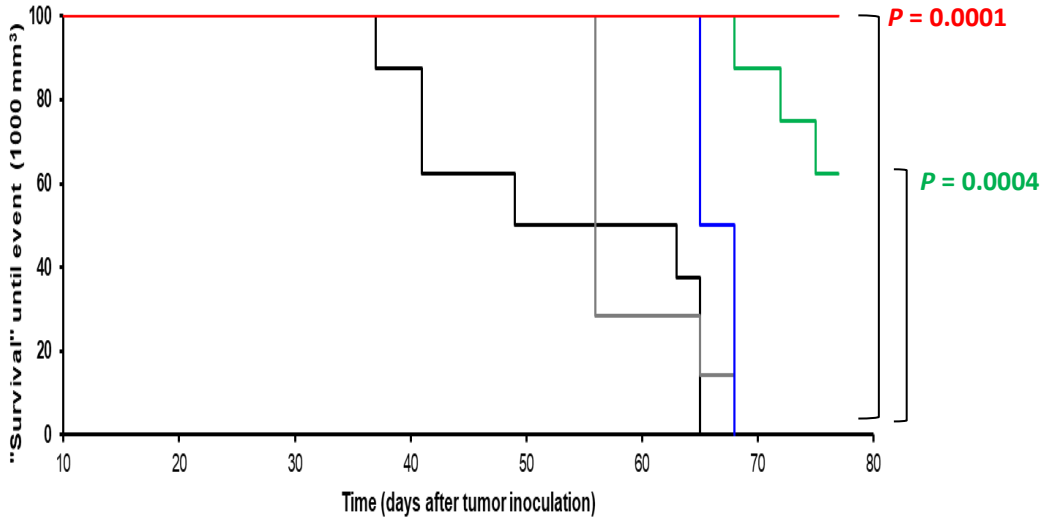
Tumor/ Normal ratio: 200.3

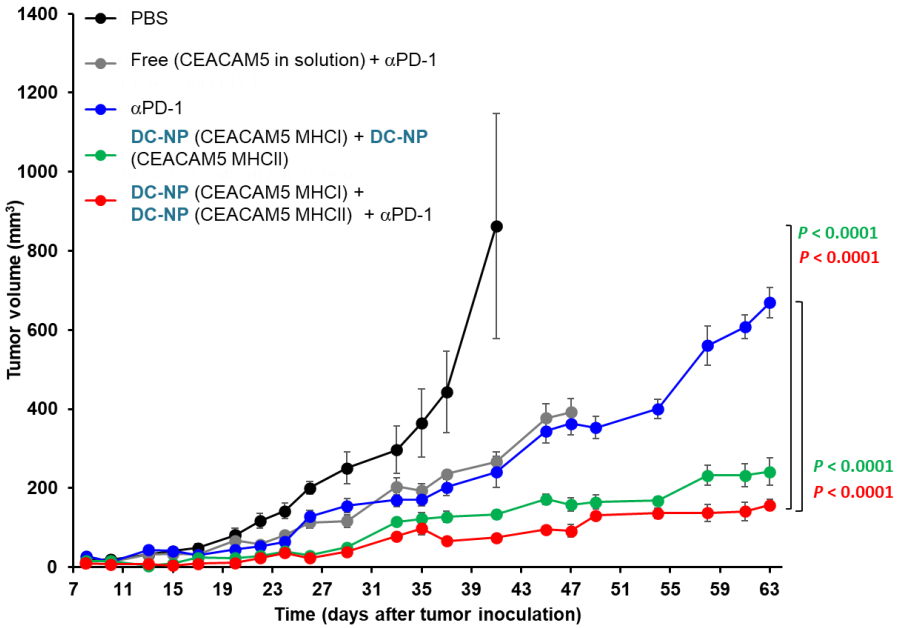
http://gepia.cancer-pku.cn/index.html

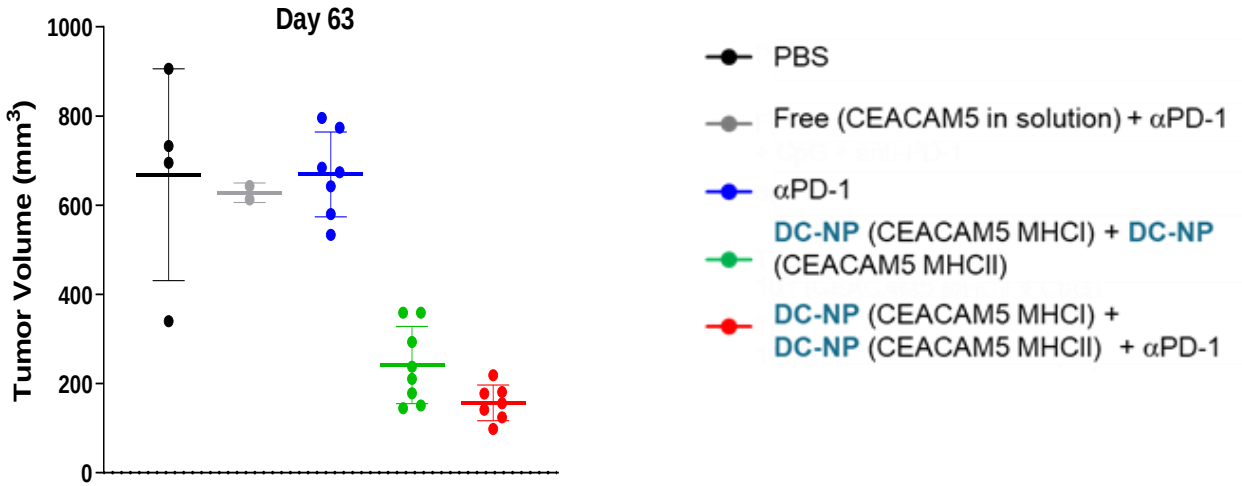
CEACAM5-NP sensitizes CRC-bearing mice to anti-PD-1 therapy leading to the inhibition of tumor growth and prolonged survival

CEACAM5– Overexpressed in colorectal cancer

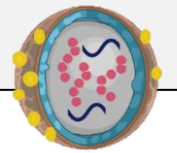






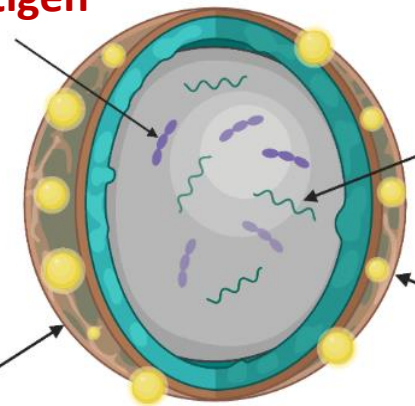


DC-Targeted Nano-Vaccine for glioblastoma therapy



Glioblastoma neoantigen

Tumor-associated peptide
Glioblastoma neoantigen



Immune adjuvants
(TLR 3 and 9 agonists)

Target ligand
(mannose)

Biodegradable
polymeric matrix
(PLA/PLGA)

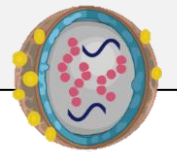
Glioblastoma

The most common and agressive primary brain tumor

Non-immunogenic

"Cold tumor"

DC-Targeted Nano-Vaccine for glioblastoma therapy



Glioblastoma neoantigen

Tumor-associated peptide
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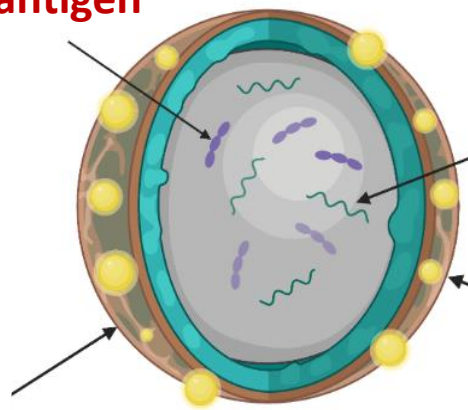

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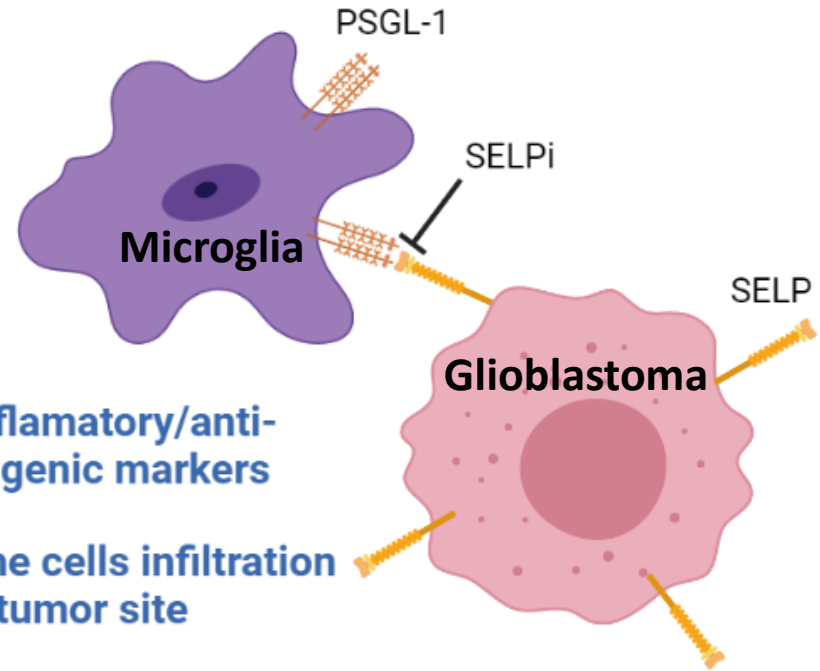
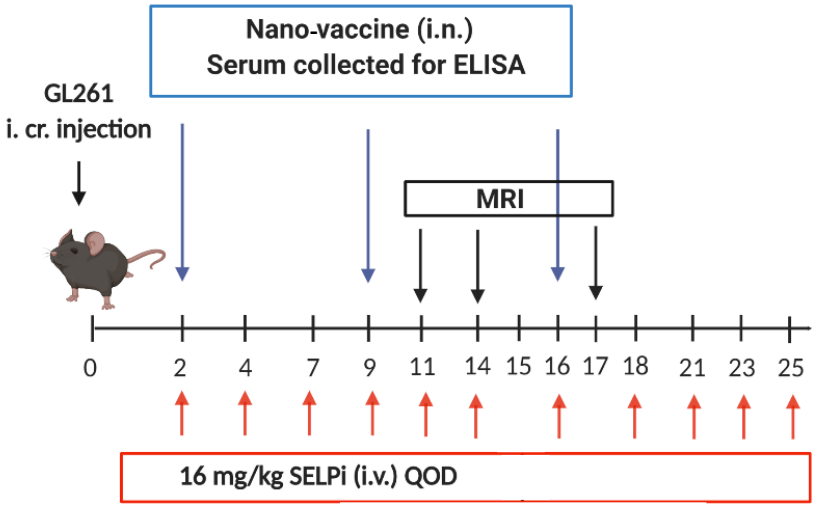


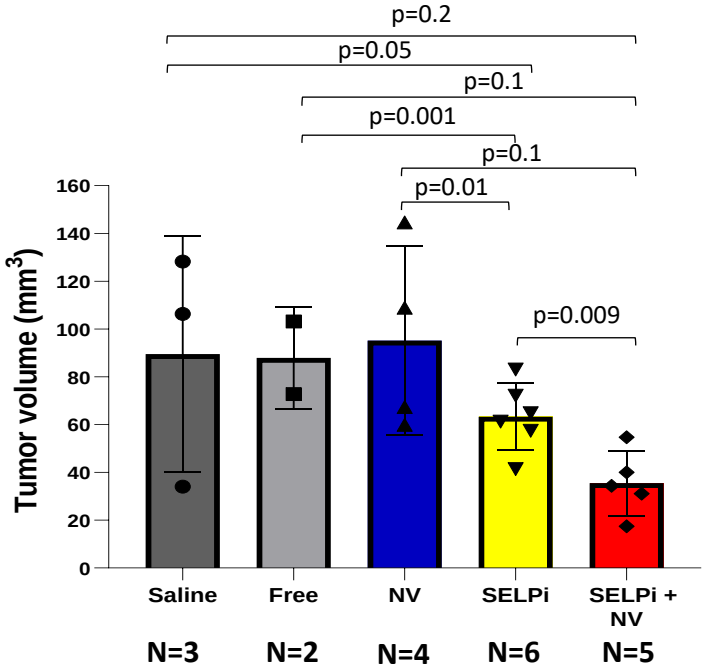
Dr. Eilam Yeini

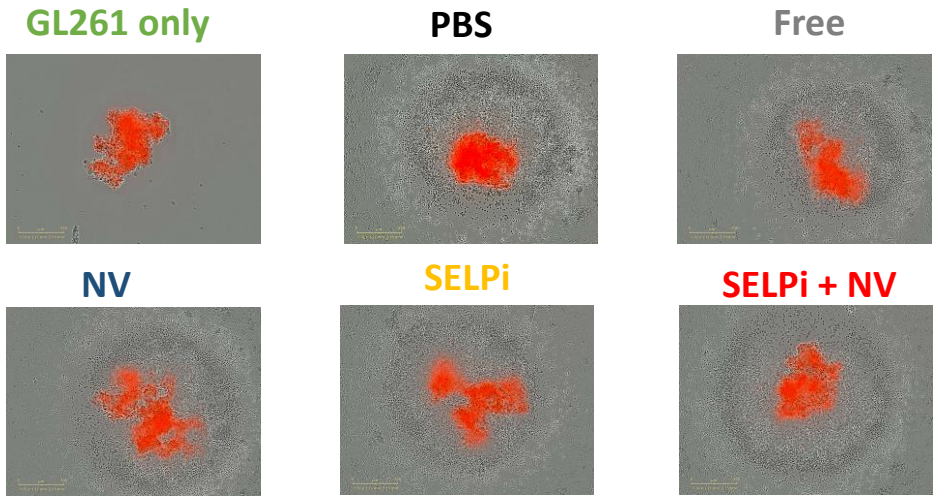
Yeini E,…, Kleiner R, *et al*, *Nature Communication*, 2021

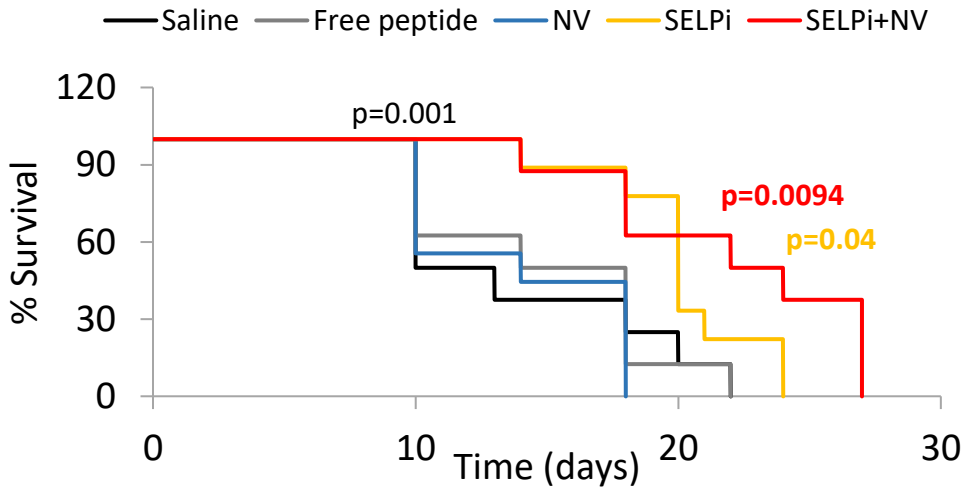
DC-Targeted Nano-Vaccine inhibit glioblastoma tumor growth in combination with P-selectin inhibitor *in vivo*

Glioblastoma neoantigen

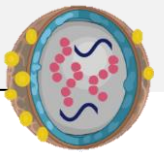




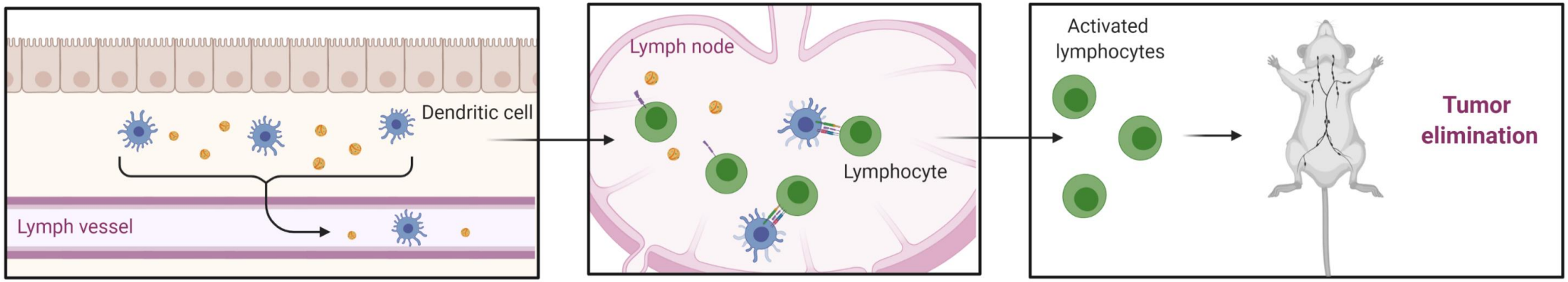




Conclusions



- The nano-vaccine is a **plug and play system** that can generate an immune response against distinct antigens expressed by tumor cells.
- DC-targeted nano-vaccine successfully induced a **specific activity** of effector immune cells.
- The nano-vaccine effectively **sensitize glioblastoma, CRC** and **melanoma** murine models to other immunotherapies.
- **Prolonged survival and decreased tumor growth** were achieved in **glioblastoma, CRC** and **melanoma** murine models, following treatments with a combination of nano-vaccine and immunosuppressive tumor microenvironment modulators.



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RSF's Multidisciplinary research team

The whole is greater than the sum of its parts …

Biology | **Medicine** | **Engineering** | **Chemistry**

Establishment and molecular characterization of pairs of dormant vs fast-growing, primary vs metastatic and resistant vs drug-sensitive orthtopic tumor models

Eilam Yeini
Sabina Pozzi
Sahar Dangoor
Opal Avramoff
Yael Shtilerman
Christian Burgos
Paula Ofek, PhD
Anat Eldar-Boock, PhD
Yulia Liubomirski, PhD
Galia Tiram, PhD
Shiran Ferber, PhD
Hadas Gibori, PhD
Dikla Ben-Shushan, PhD
Noa Reisman
Sapir Golan
Roni Blatt
Keren Miller, PhD
Liron Stern
Nitzan Albeck

Patient-derived tumor models

Daniella Vaskovich
Lidar Fridrich
Rachely Grossman, MD
Miki Goldenfeld
Shelly Sofer, MD
Roni Shreberk-Atidim, MD
Ilanit Shetzigovski-Meller, MD
Gal Bachar, MD

3D tumor models

Lena Neufeld
Ron Kleiner
Gal Shenbach
Tal Zur
Zohar Shatsberg
Ehud Segal, PhD
Liora Omer

Design, synthesis and characterization of 20 novel nanomedicines

Shani Koshrovski
Daniel Rodriguez
Yana Epshtein
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