Nasal Delivery Redifines Immunity: Fighting Melanoma Brain Metastases with a Cancer Nanovaccine

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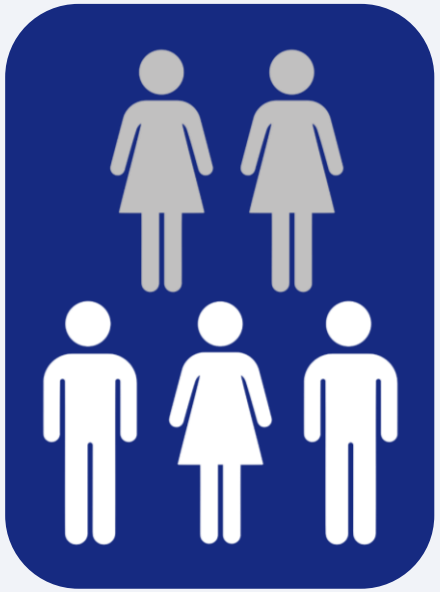
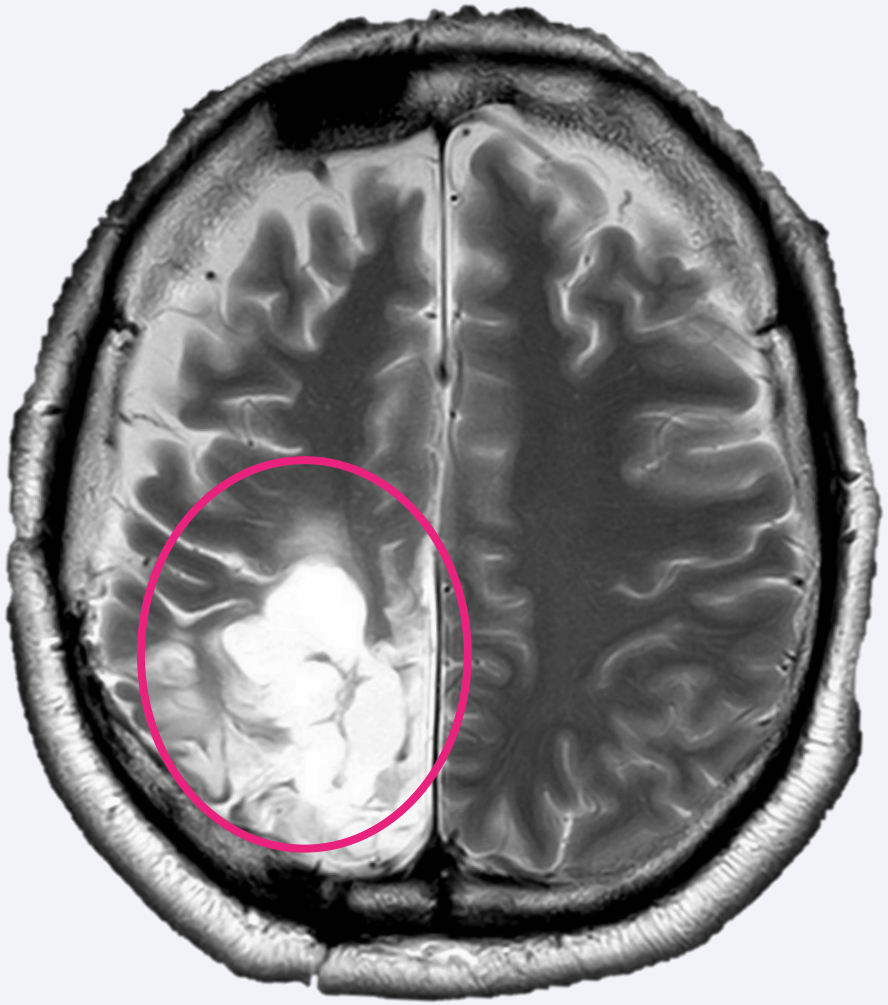
The Hurdle: Melanoma Brain Metastases

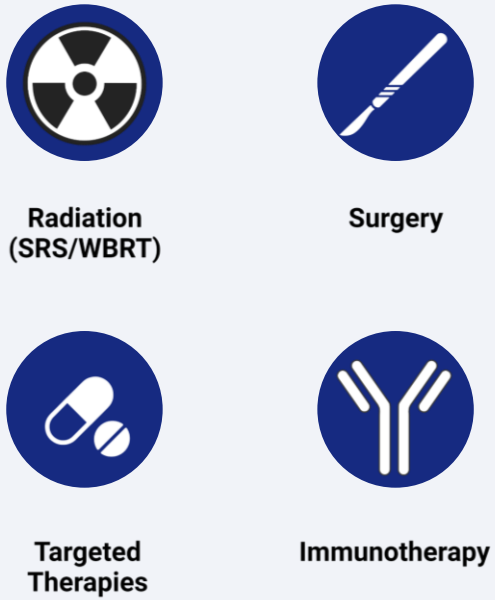
INCIDENCE



MORE THAN OF 60% OF MELANOMA PATIENTS WITH ADVANCED DISEASE WILL DEVELOP BRAIN METASTASES



CURRENT THERAPIES



POOR CLINICAL OUTCOME

1-year survival rate ≈15%

LIMITED PERMEABILITY THROUGH THE BBB

Our Approach: Multifunctional Nanovaccines

nature nanotechnology
ARTICLES
https://doi.org/10.1038/s41565-019-0512-0

Immunization with mannosylated nanovaccines and inhibition of the immune-suppressing microenvironment sensitizes melanoma to immune checkpoint modulators

João Conniot[1,2,7], Anna Scomparin[1,3,7], Carina Peres[2], Eilam Yeini[1], Sabina Pozzi[1], Ana I. Matos[2], Ron Kleiner[1], Liane I. F. Moura[2], Eva Zupančič[2,4], Ana S. Viana[5], Hila Doron[6], Pedro M. P. Gois[2], Neta Erez[6], Steffen Jung[4], Ronit Satchi-Fainaro[1*] and Helena F. Florindo[2*]

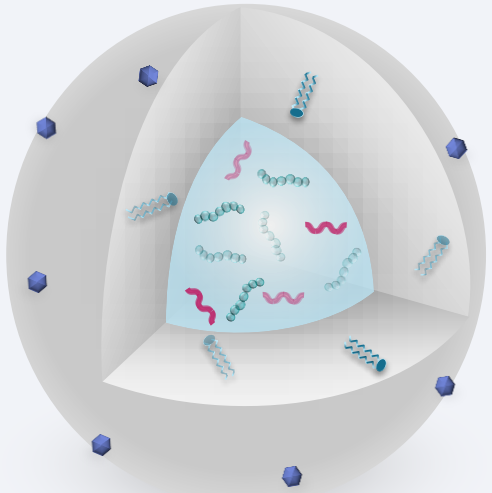
Primary Melanoma

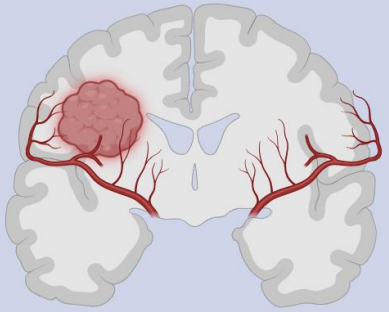
RESEARCH ARTICLE
ADVANCED SCIENCE
www.advancedscience.com

Polyoxazoline-Based Nanovaccine Synergizes with Tumor-Associated Macrophage Targeting and Anti-PD-1 Immunotherapy against Solid Tumors

Ana I. Matos, Carina Peres, Barbara Carreira, Liane I. F. Moura, Rita C. Acúrcio, Theresa Vogel, Erik Wegener, Filipa Ribeiro, Marta B. Afonso, Fábio M. F. Santos, Águeda Martínez-Barriocanal, Diego Arango, Ana S. Viana, Pedro M. P. Góis, Liana C. Silva, Cecília M. P. Rodrigues, Luis Graca, Rainer Jordan, Ronit Satchi-Fainaro, and Helena F. Florindo**

Breast Cancer





Prevention of Brain Metastases

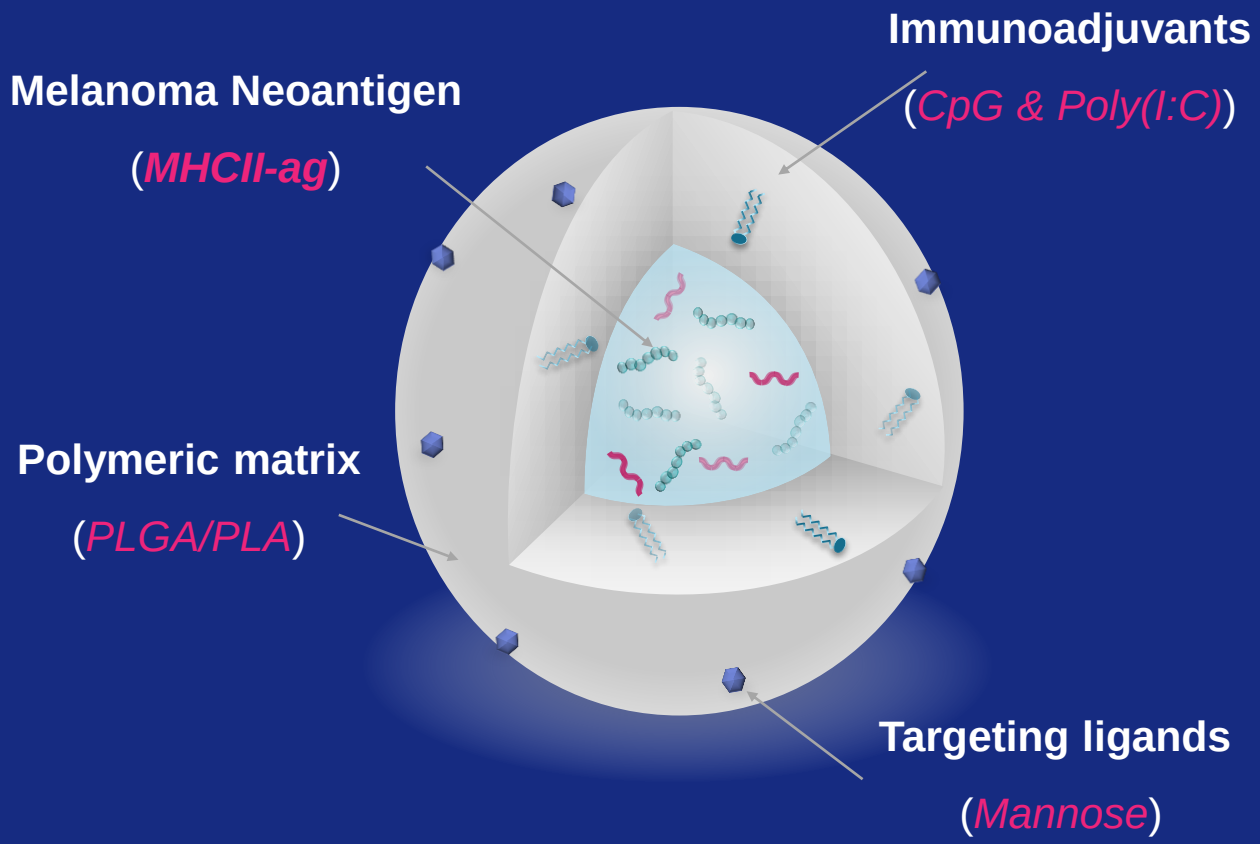
RESEARCH ARTICLE
ADVANCED FUNCTIONAL MATERIALS
www.afm-journal.de

Multifunctional Nanovaccine Sensitizes Breast Cancer to Immune Checkpoint Therapy

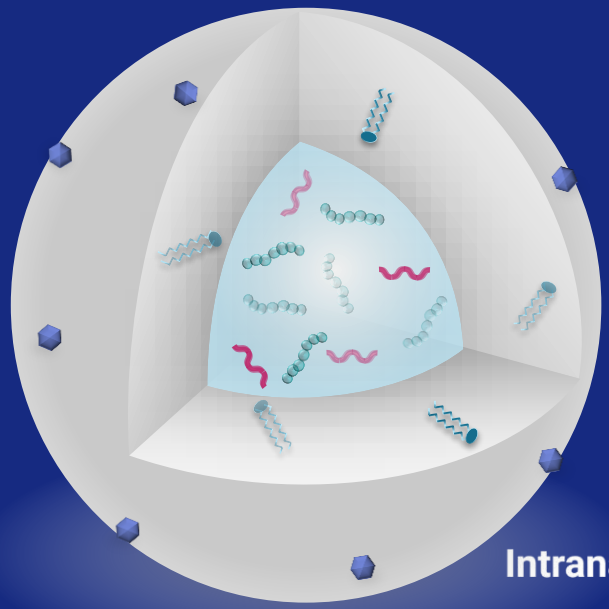
Carina Peres, Ana I. Matos, Bárbara Carreira, Liane I. F. Moura, Ron Kleiner, Daniella Vaskovich-Koubi, Keren Reshef, Shai Dulberg, Mafalda Verdial, João Conniot, Marta B. Afonso, Rita C. Acúrcio, Afonso P. Basto, Sofia Mensurado, Bruno Silva-Santos, Susana Constantino Rosa Santos, Ana S. Viana, Liana C. Silva, Cecília M. P. Rodrigues, Véronique Préat, Luís Graça, Asaf Madi, Ronit Satchi-Fainaro, and Helena F. Florindo**

Colorectal Cancer

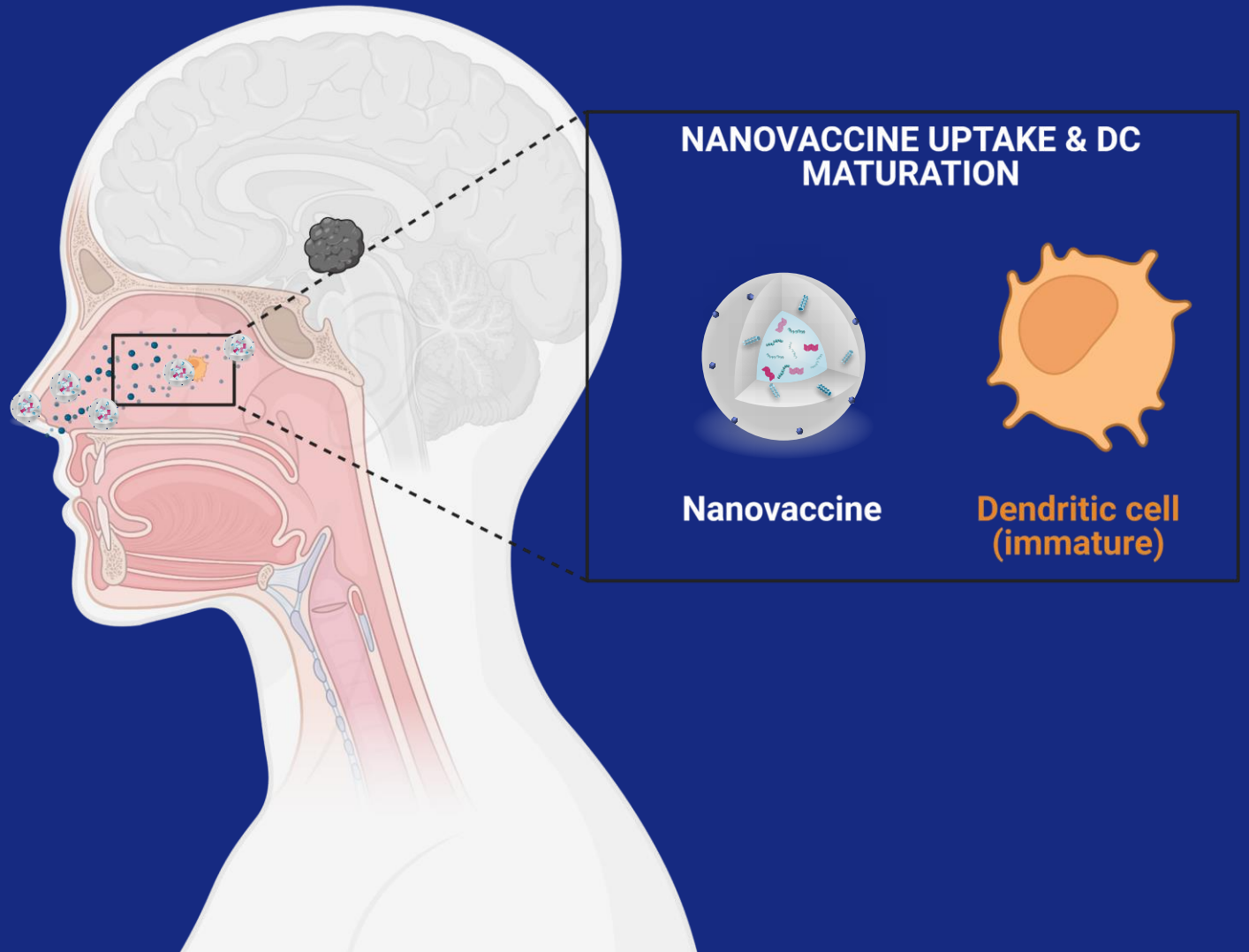
Cancer Nanovaccine



Cancer Nanovaccine: Mechanism of Action

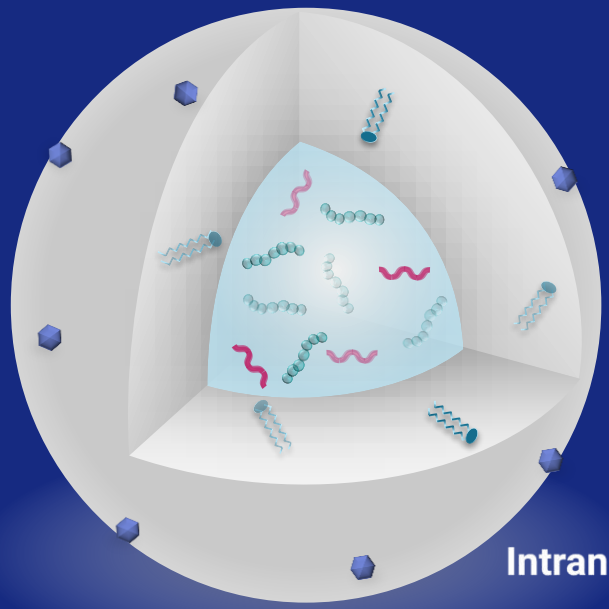


Nanovaccine
Intranasal delivery

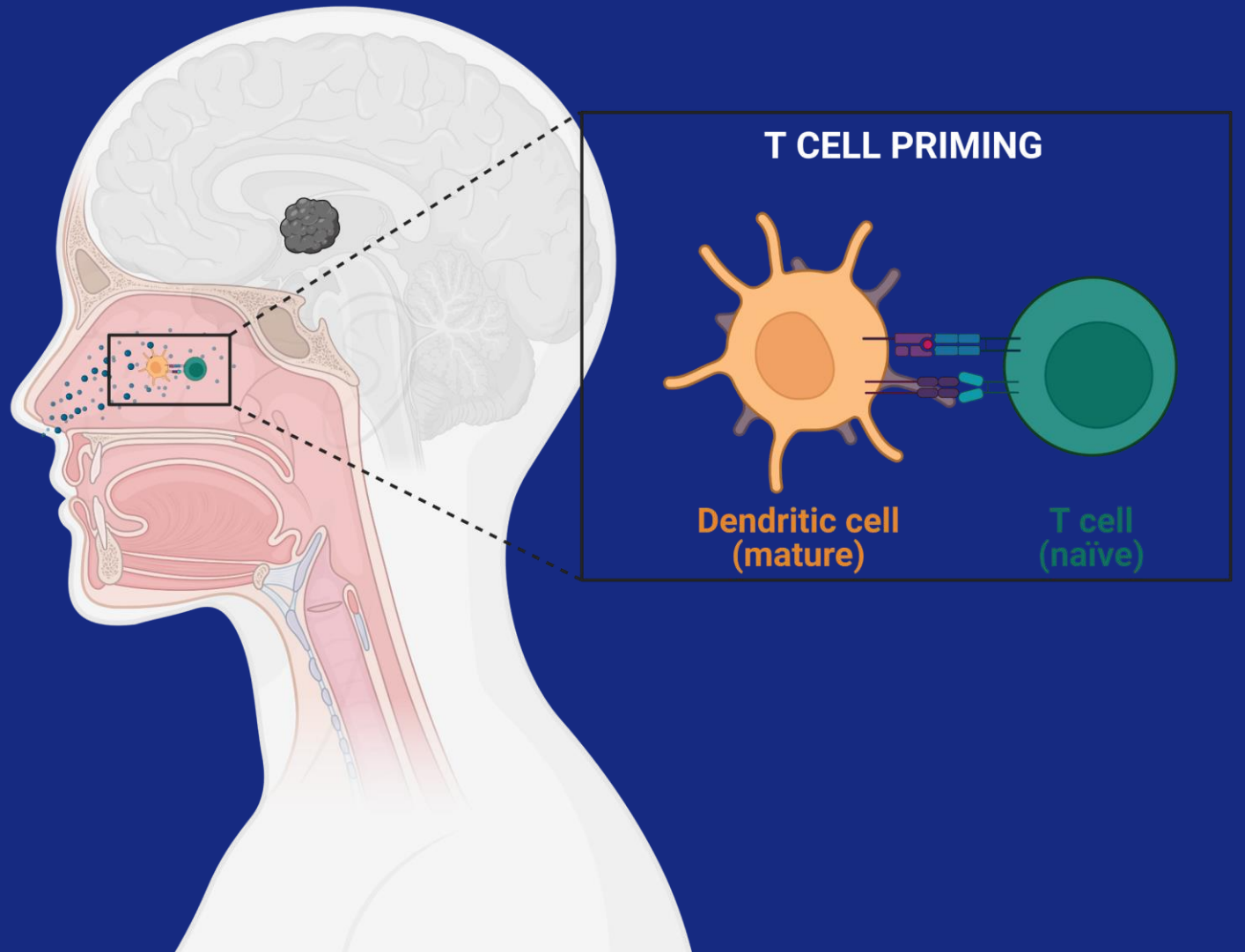


Conniot, Scomparin *et al. Nature Nanotechnology*, 2019 Sep;14(9):891-901.

Cancer Nanovaccine: Mechanism of Action



Nanovaccine
Intranasal delivery



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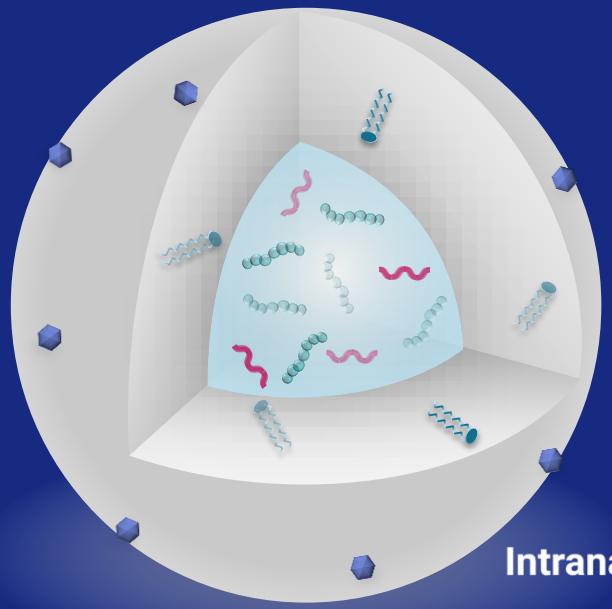
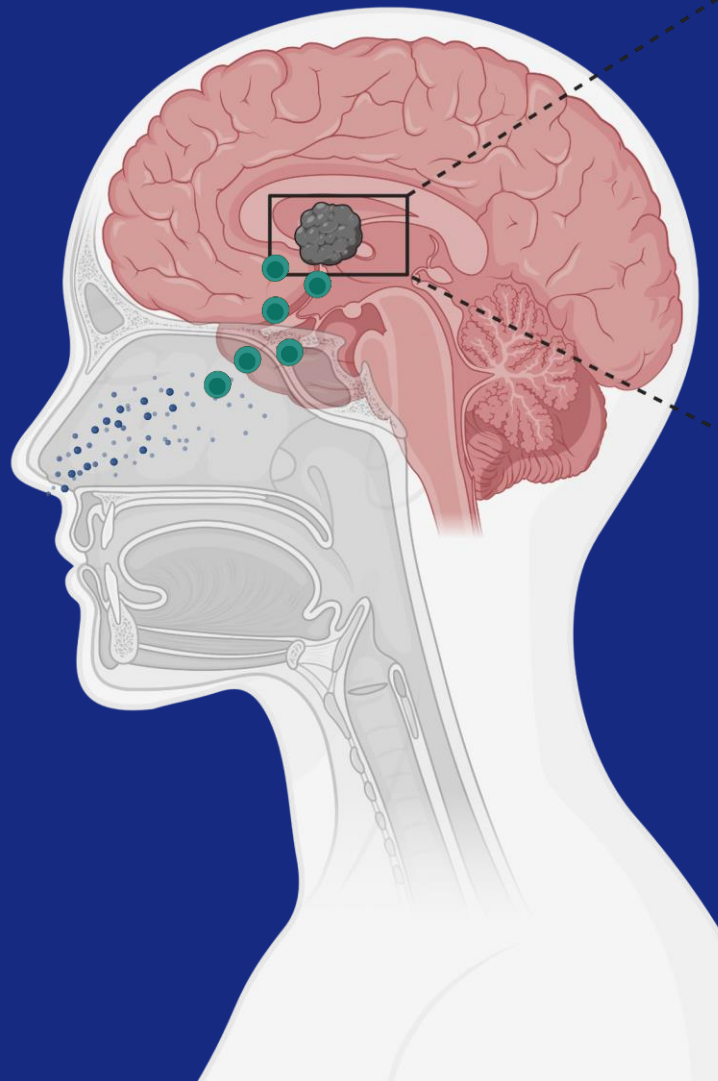
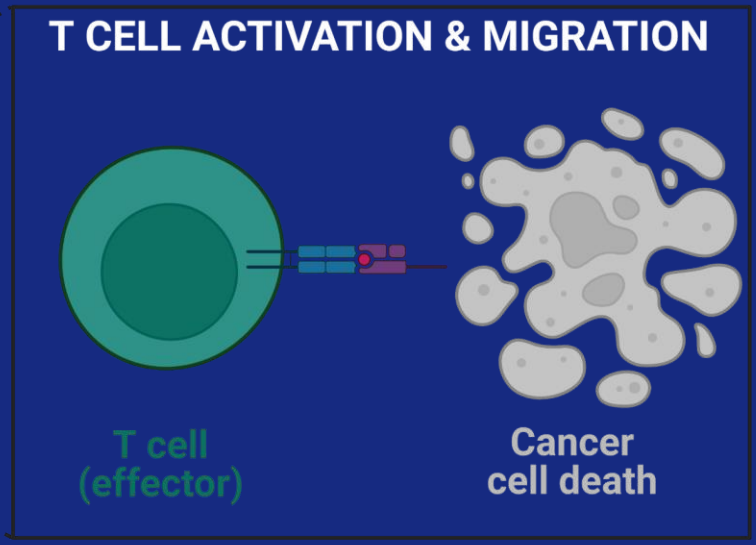
Cancer Nanovaccine: Mechanism of Action



Nanovaccine
Intranasal delivery





Conniot, Scomparin *et al. Nature Nanotechnology*, 2019 Sep;14(9):891-901.

Cancer Nanovaccine: Physicochemical Characterization

Table 1. Nanoparticle (NP) size, polydispersity index (Đ), entrapment efficiency (EE) and loading capacity (LC) of antigens into NP.

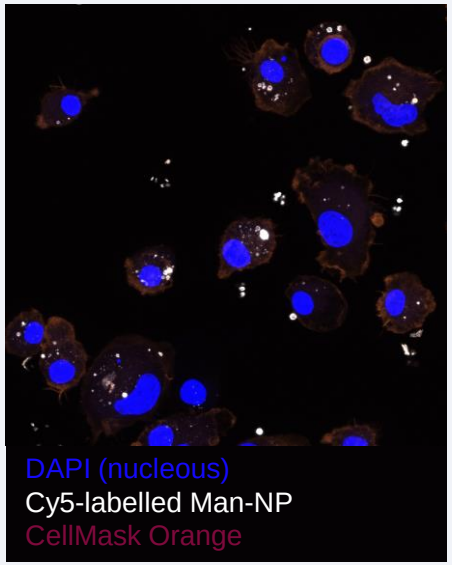
NP	Size[1] (nm ± SD[2])	PdI ± SD[2]	Z-Potential (mV ± SD[2])	Peptide EE (% ± SD[2])	Peptide LC (µg/mg ± SD[2])	Adj1 EE (% ± SD[2])	Adj1 LC (µg/mg ± SD[2])	Adj2 EE (% ± SD[2])	Adj2 LC (µg/mg ± SD[2])
man-NP	198 ± 2	0.16 ± 0.02	-4.48 ± 0.6	60.8 ± 3.7	30.4 ± 3.27	82.0 ± 5.2	4.6 ± 0.65	93.2 ± 5.2	10.4 ± 0.9

Target product specifications for optimal DC target & Activation
Size: < 200 nm
PDI: < 0.2

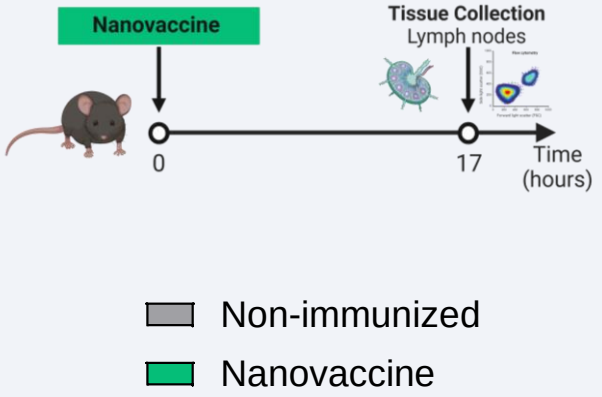
Peptides: Moderate entrapment efficiency

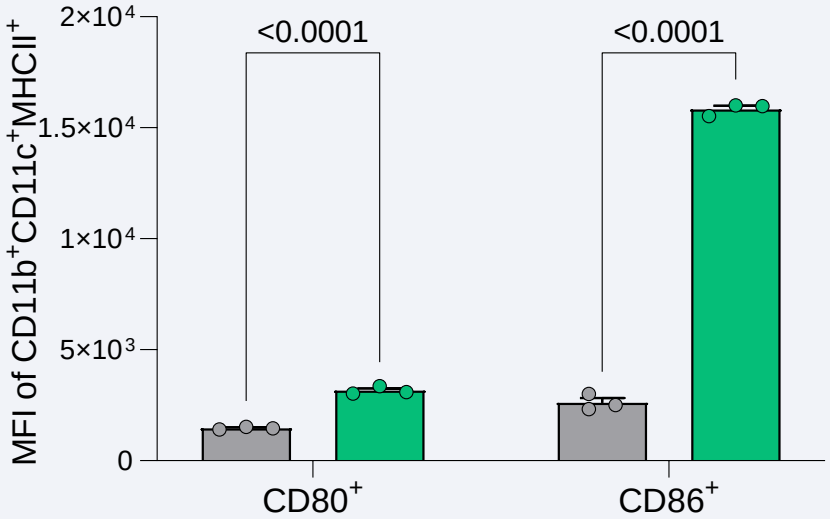
Adjuvants: High entrapment efficiency

NV are taken up by DC

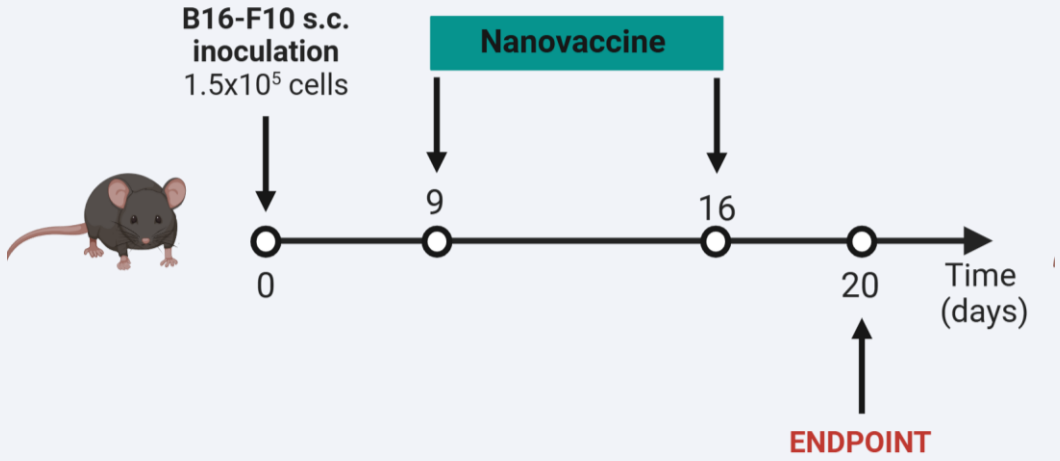


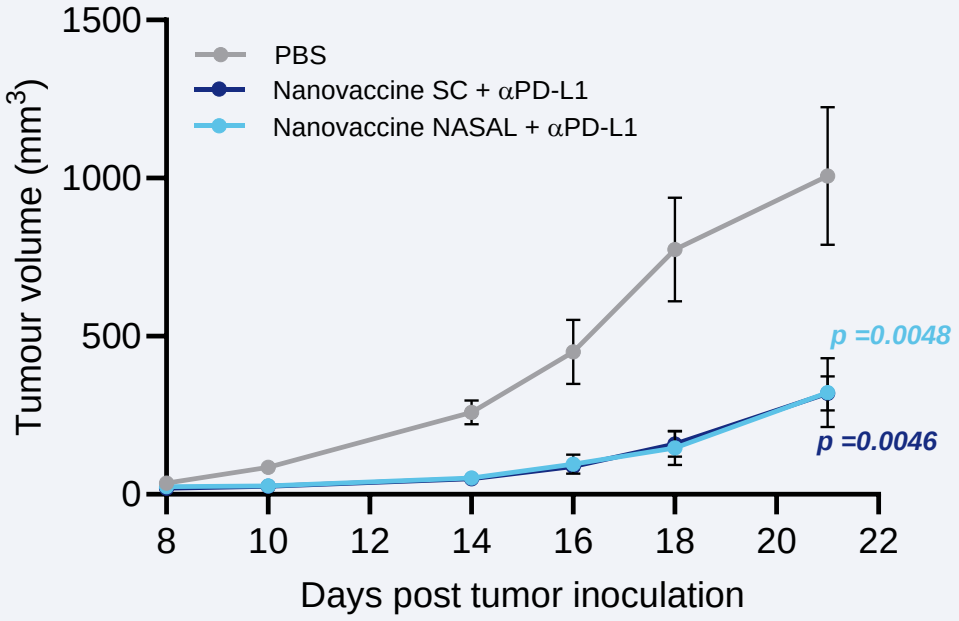
NV induce the activation of DC – upregulation of CD80 and CD86



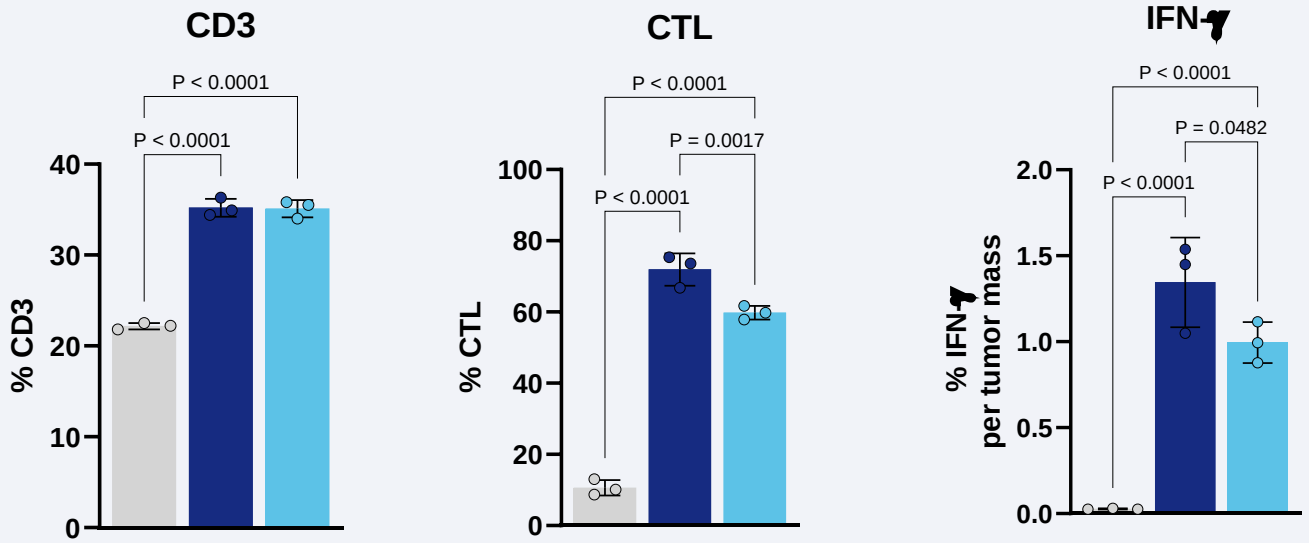


Cancer Nanovaccine: Restricts Melanoma in combination with anti-PD-L1

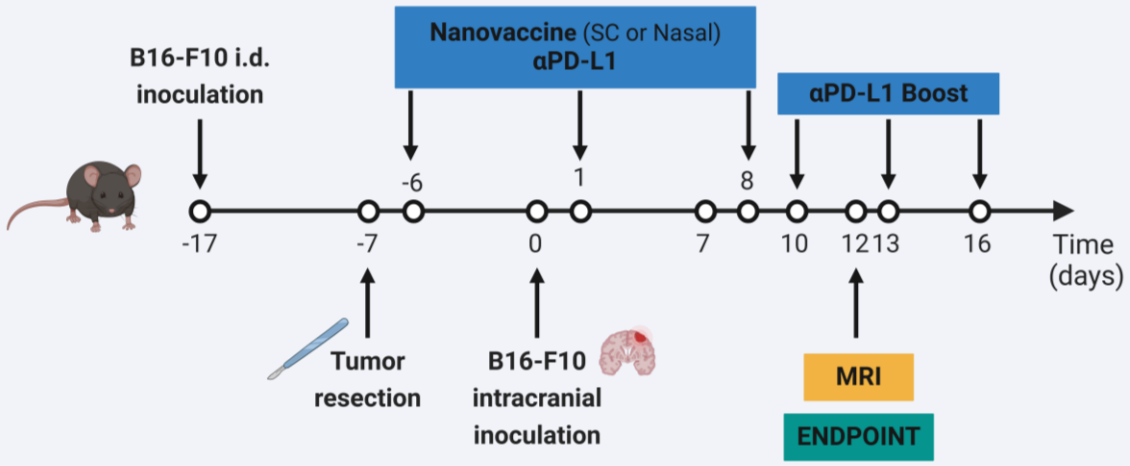


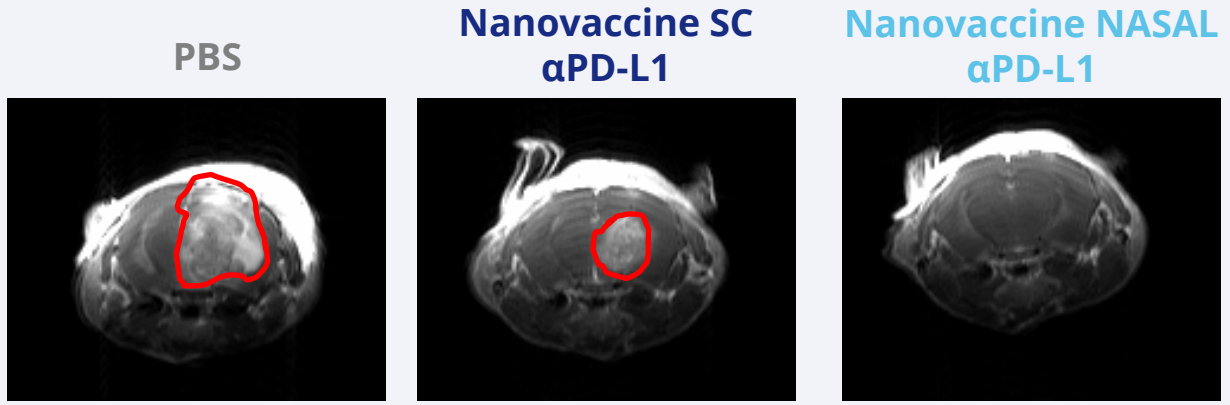


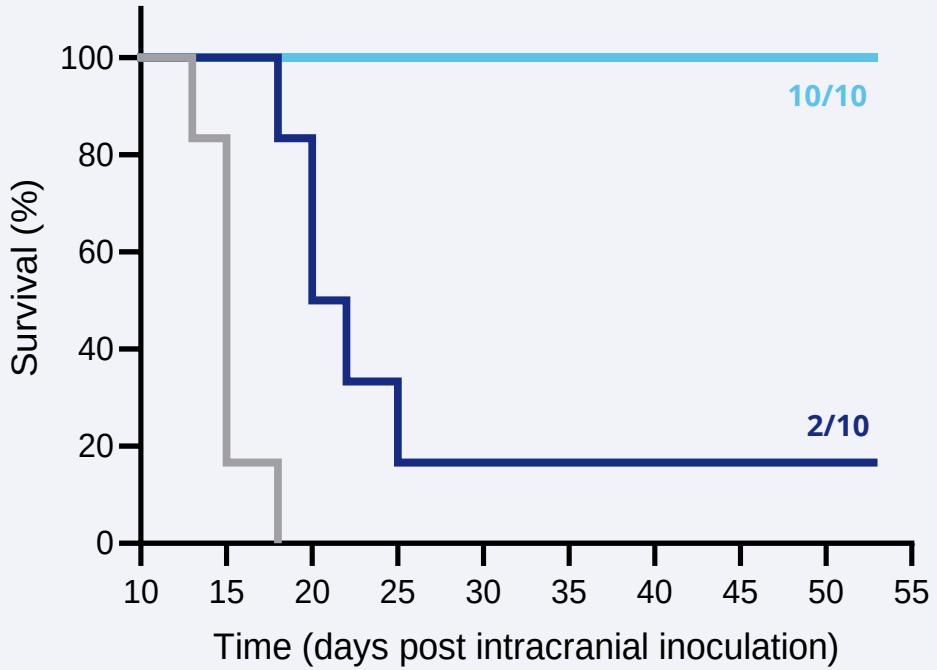
Increased expression of cytotoxic T cells within TME



Cancer Nanovaccine: Prevents Melanoma Brain Metastases



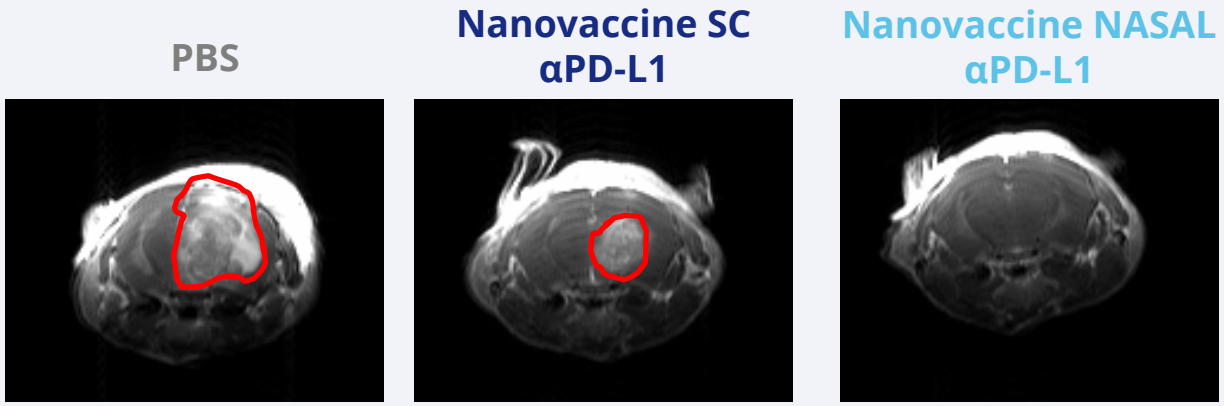


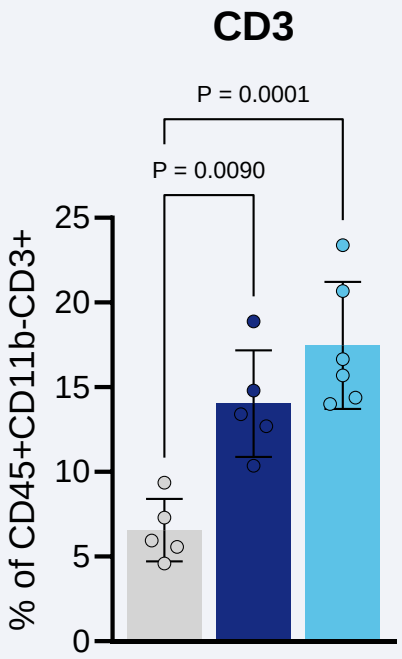


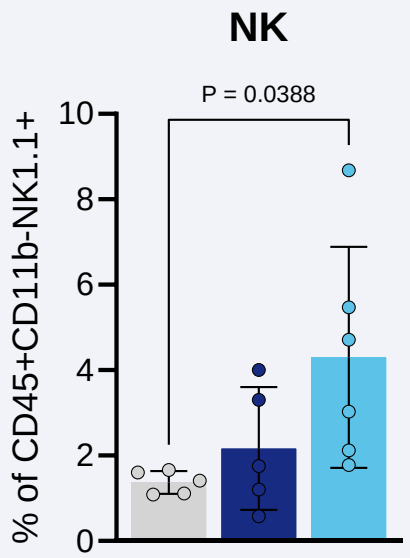
Nanovaccine NASAL prevented the development of melanoma brain tumors

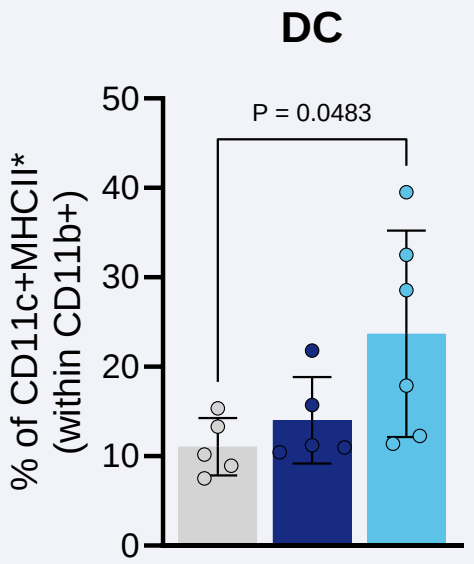
Cancer Nanovaccine: Prevents Melanoma Brain Metastases

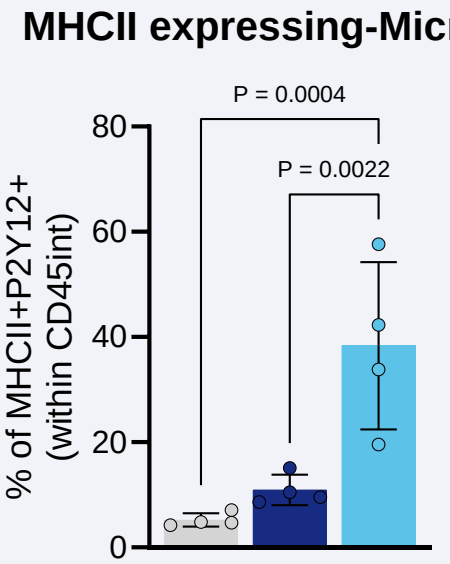
Nanovaccine NASAL triggered the infiltration of **T, NK, DC** and **MHCII-microglia** within TME



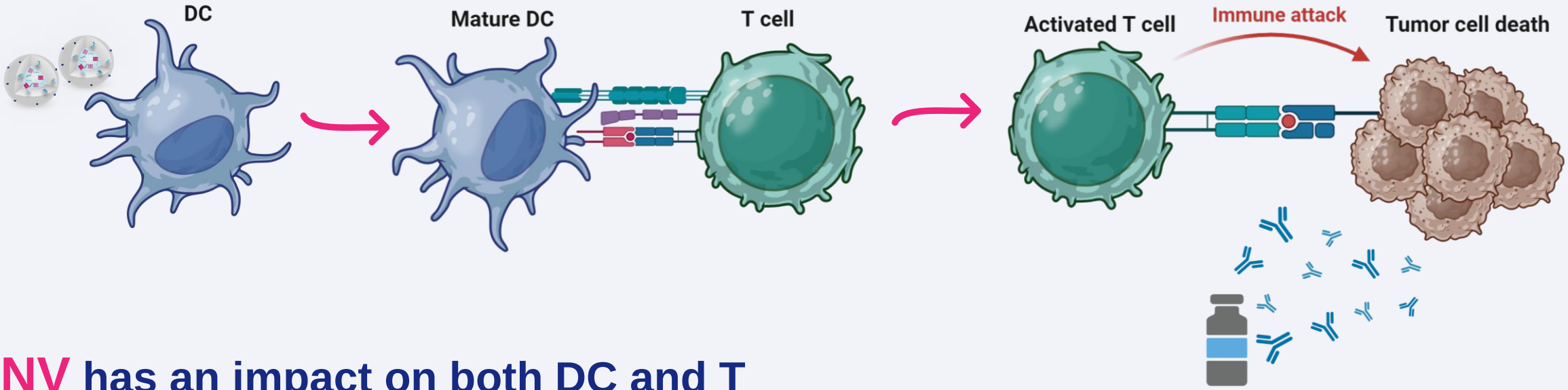








Main Conclusions



NV has an impact on both DC and T cell phenotypes, triggering their activation

Specific antigen anti-tumor immune response against primary and metastatic melanoma

Cancer vaccines constitute a potential strategy to improve response rates of metastatic cancer patients

Acknowledgments

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Thank you

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