

4th Cuneo City ImmunoTherapy Conference (CCITC)

Immunotherapy in Hematological Malignancies 2024

CUNEO

October 10-12, 2024

Spazio Incontri Fondazione CRC

Personalized Oncolytic immunotherapy

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CEINGE and University of Naples Federico II

Organized by Prof. Massimo Massaia, SC Ematologia AO S.Croce e Carle, Cuneo - Italy and
Centro Interdipartimentale di Biotecnologie Molecolari "Guido Tarone" (MBC), Torino - Italy

Immunotherapy in Hematological Malignancies 2024

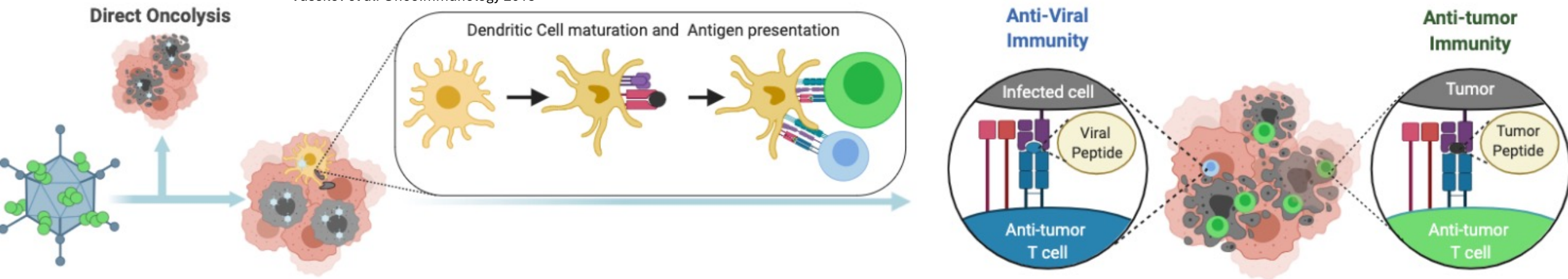
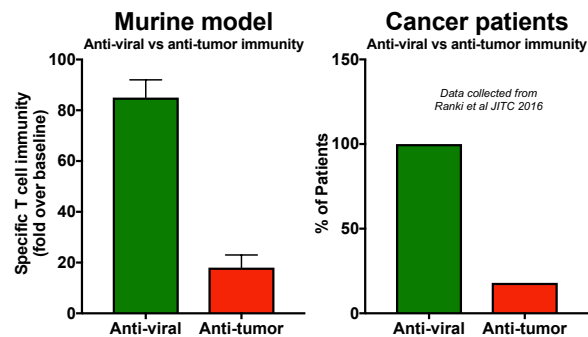
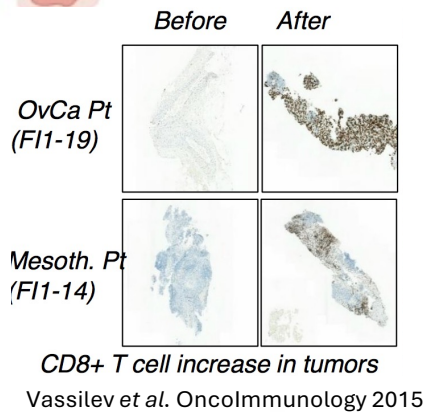
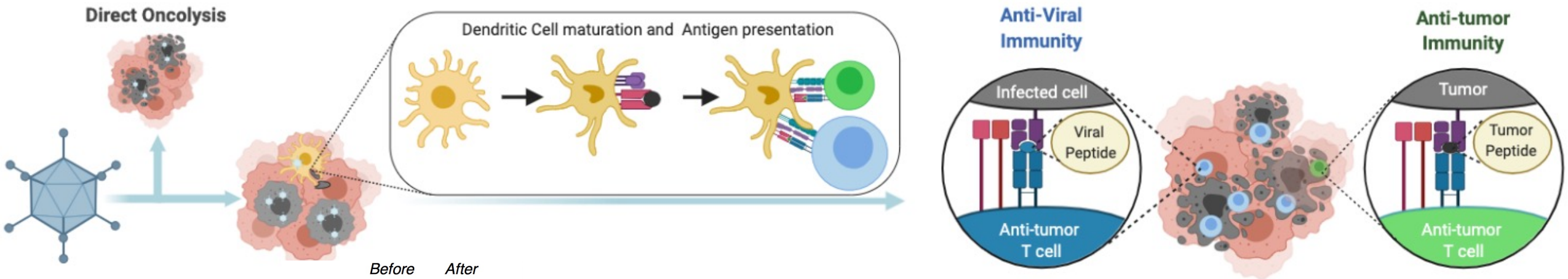
Disclosures of Vincenzo Cerullo

<u>Company name</u>	<u>Research support</u>	<u>Employee</u>	<u>Consultant</u>	<u>Stockholder</u>	<u>Speakers bureau</u>	<u>Advisory board</u>	<u>Other</u>
<u>VALO Therapeutics</u>			X	X		X	

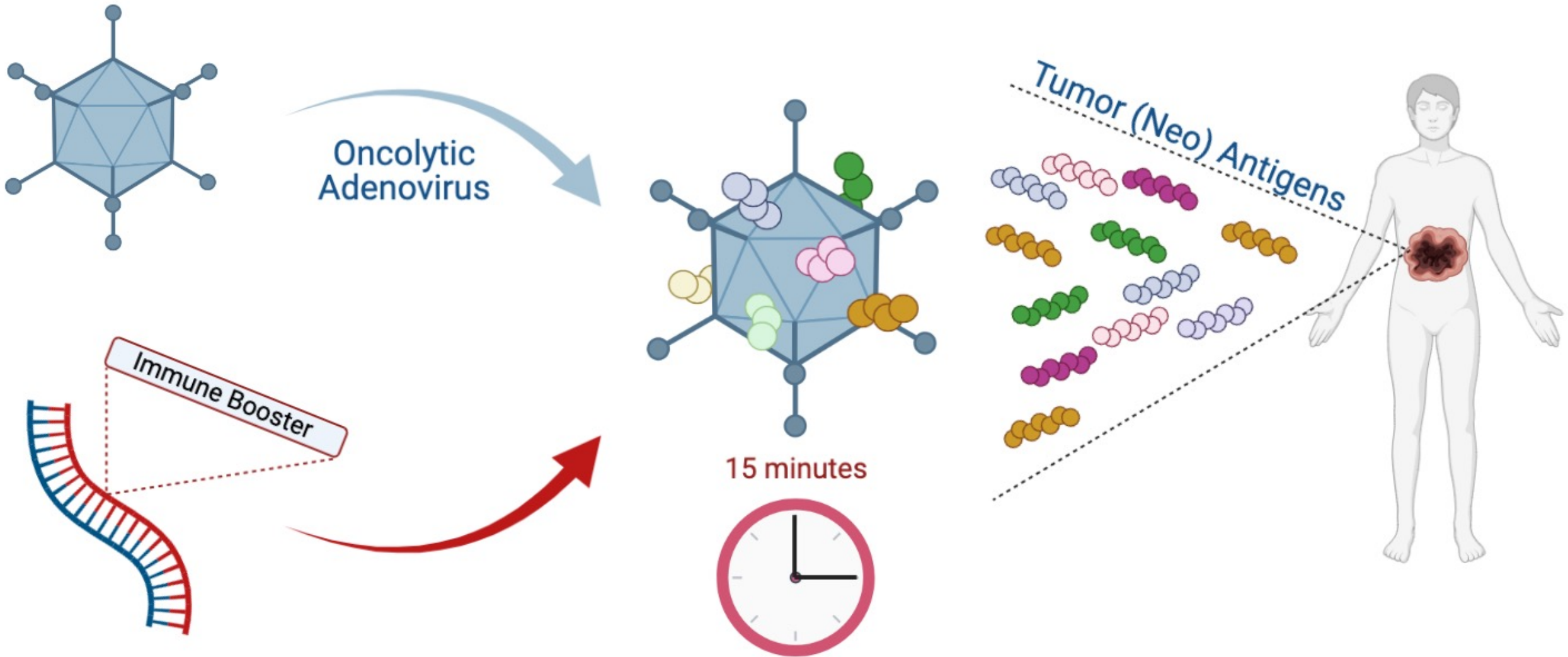


Personalized Oncolytic immunotherapy:
Dressing up viruses to fool cancer

Oncolytic vaccines – Dual Mode of Action



Peptide-coated Conditionally Replicating Adenovirus

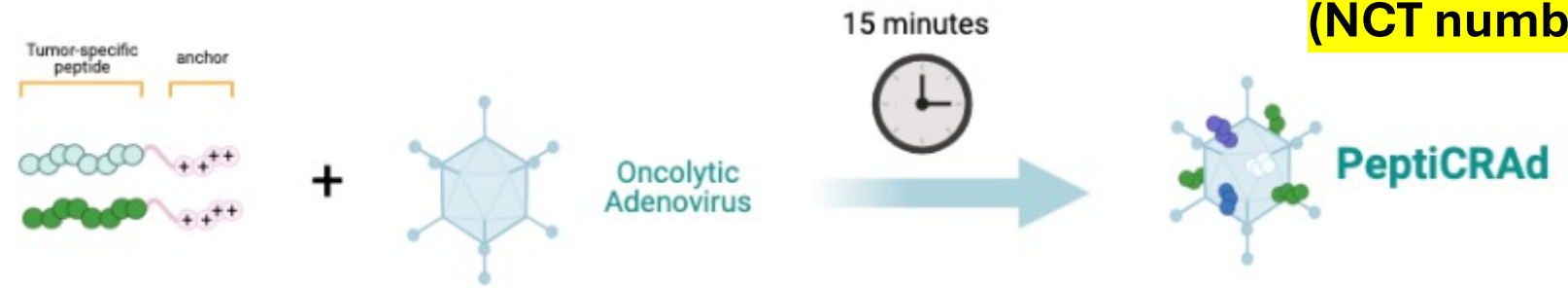




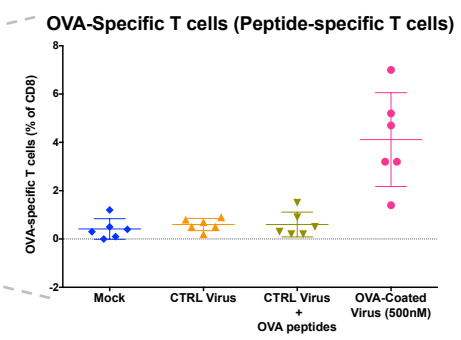
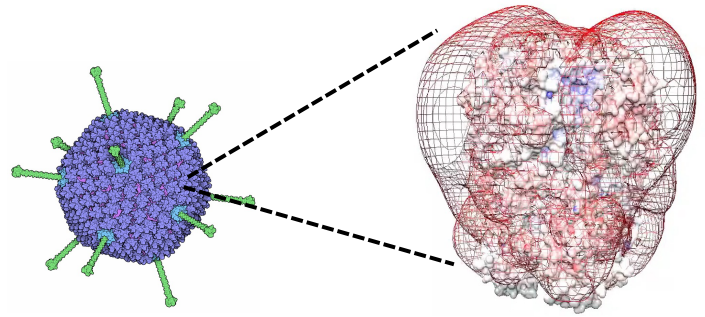
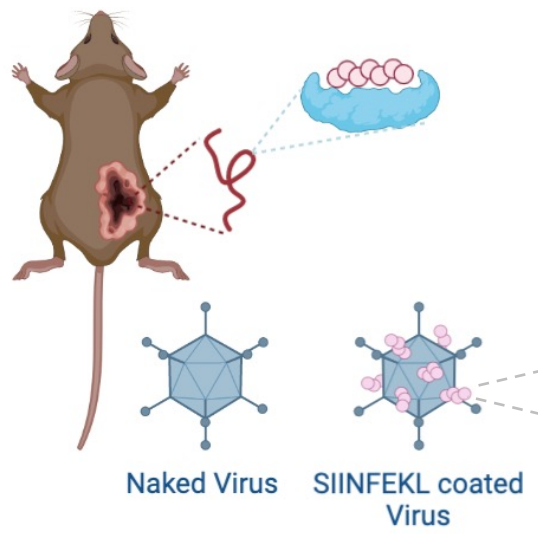
Cristian Capasso, PhD Student

Example 1: PeptiCRAd

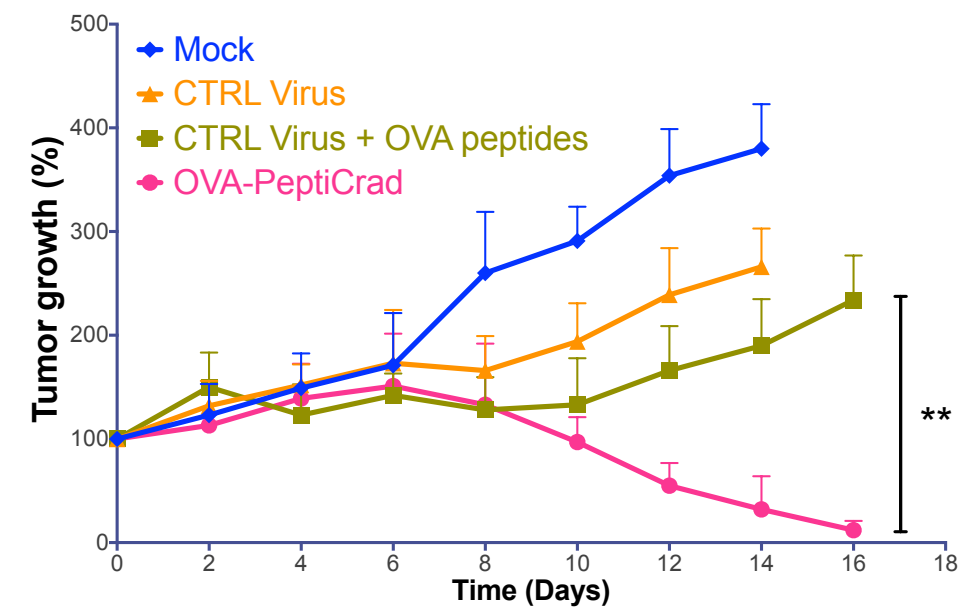
ClinicalTrials.gov identifier
(NCT number): NCT05492682



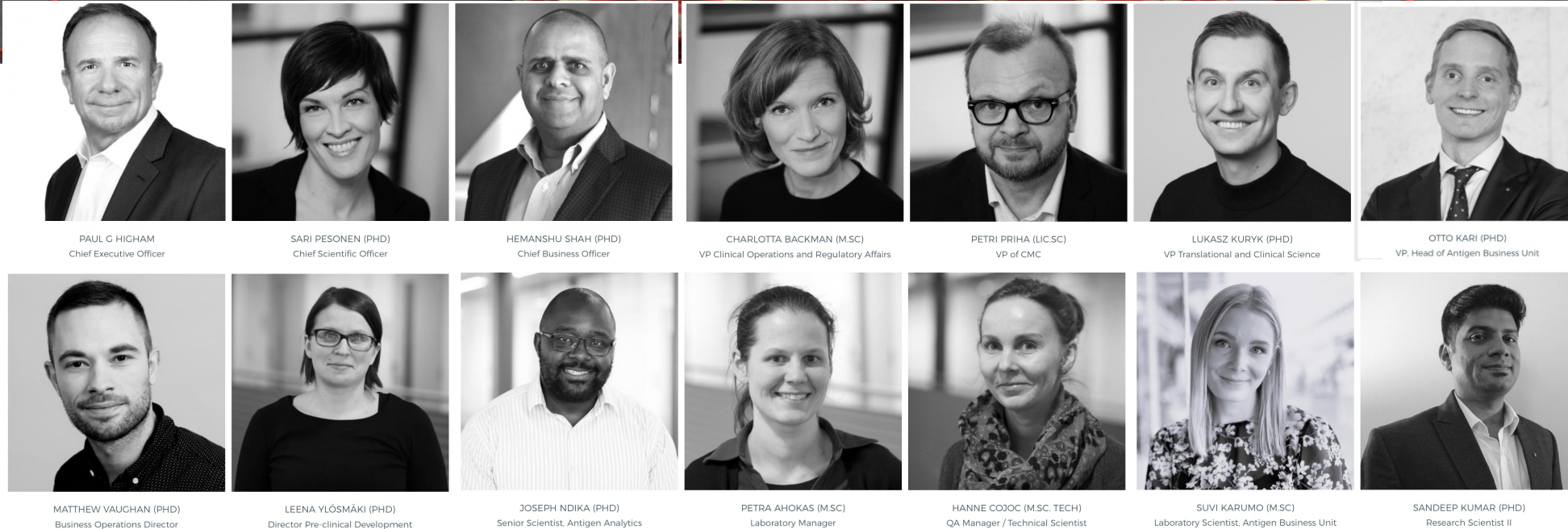
Murine Melanoma expressing chicken ovalbumin and presenting SIINFEKL on its MHC-I



**B16-OVA -
Primary treated tumors**

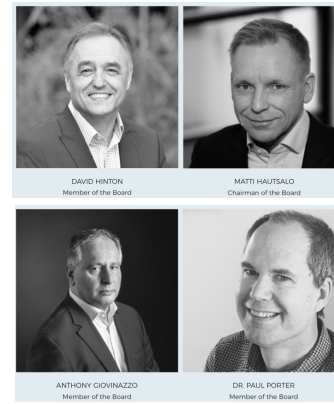


Reinventing Immunotherapy in Oncology and Infectious Disease

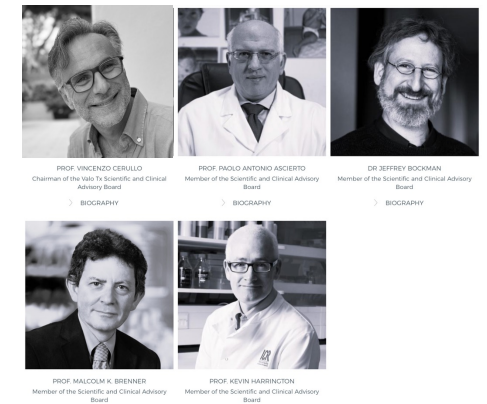


- Spun out from the University of Helsinki (UH) in 2016
- Leadership team with over 50 years combined cancer immunotherapy experience
- 25+ million € invested to date
- VC Round of minimum €15m

Board of the directors



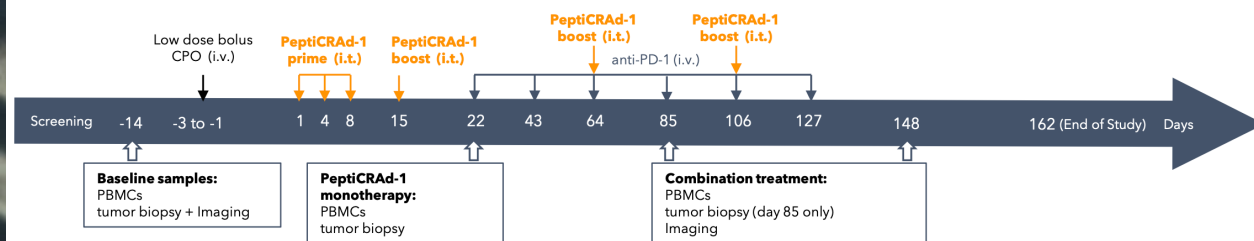
Scientific Advisory Board



First in human of PeptiCRAd

ClinicalTrials.gov
identifier
(NCT number):
NCT05492682

PeptiCRAd-1 - Phase 1b Study Treatment Schedule and Assessment Plan



RECRUITING
NCT05492682
START: Safety and Anti-Tumor Activity of PeptiCRAd-1 in Treatment of Cancer

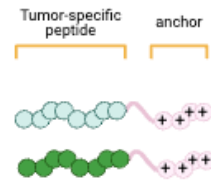
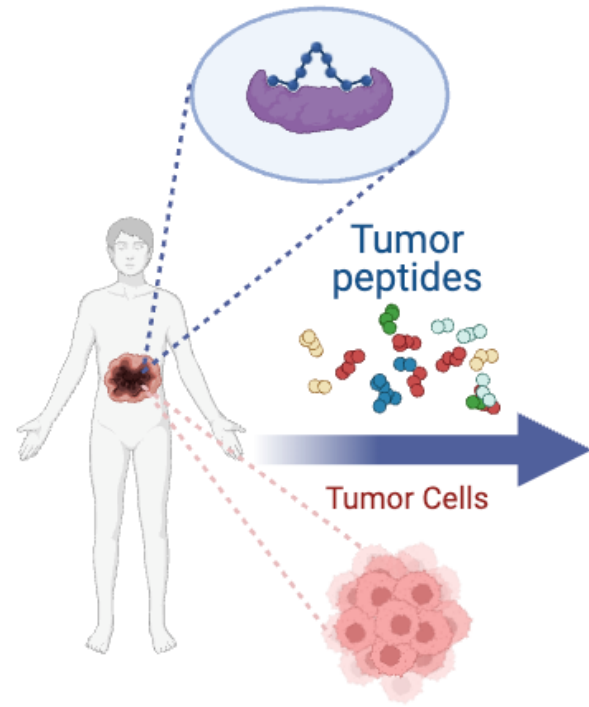
Conditions

[Colorectal Cancer](#) [Melanoma \(Skin\)](#) [Myxoid Liposarcoma](#) [Non-Small Cell Lung Cancer](#) [Synovial Sarcoma](#)
[Triple-Negative Breast Cancer](#) [Show fewer conditions](#)

Locations

[Frankfurt, Germany](#) [Heidelberg, Germany](#)
[Tubingen, Germany](#)

Cancer Immunotherapy



+



Oncolytic Adenovirus

15 minutes



PeptiCRAd

Capasso et al. *Oncoimmunology*. 2015, 2017
Feola et al. *Oncoimmunology*. 2018
Tahtinen et al. *Cancer Res.* 2020
Ylosmaki et al. *Mol Therapy Onc* 2021
Chiaro et al., *Nature Comm* 2023
Feodorof et al., *Oncoimmunology* 2024
PATENTED / LICENSED



Erkko Ylösmäki,
Postdoc

Example 2: PeptiENV



+

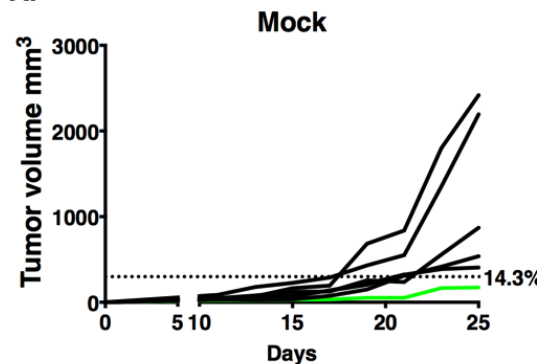


Oncolytic
Enveloped Virus

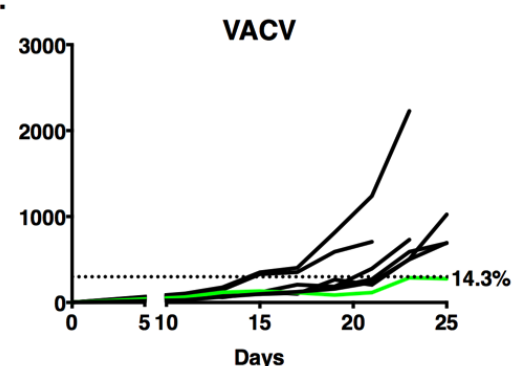


PeptiENV

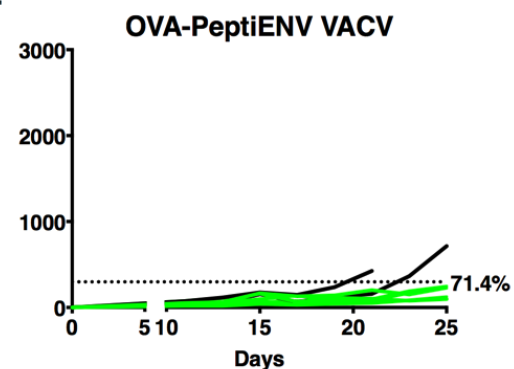
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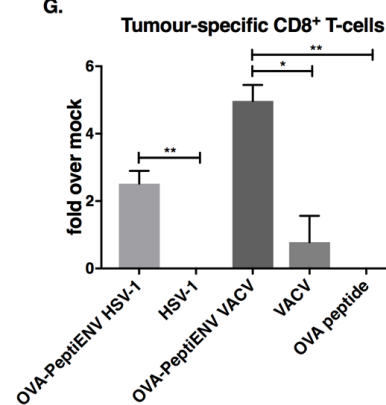
B.



C.

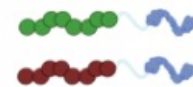


G.



Ylösmäki et al. Mol Ther. 2018 Sep 5;26(9):2315-2325

Example 3: PeptiBAC



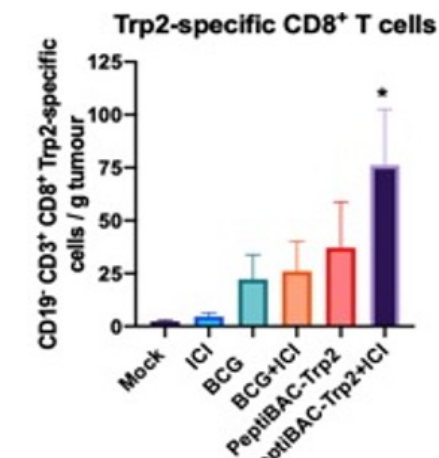
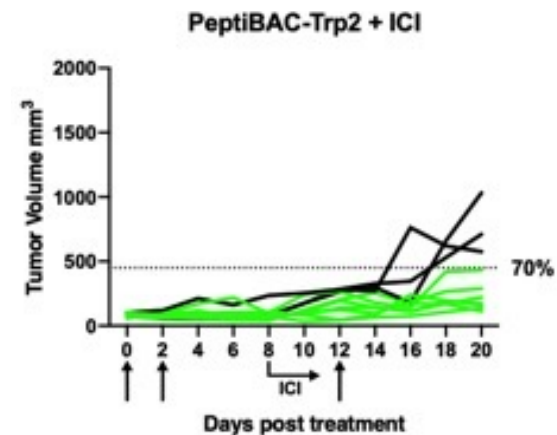
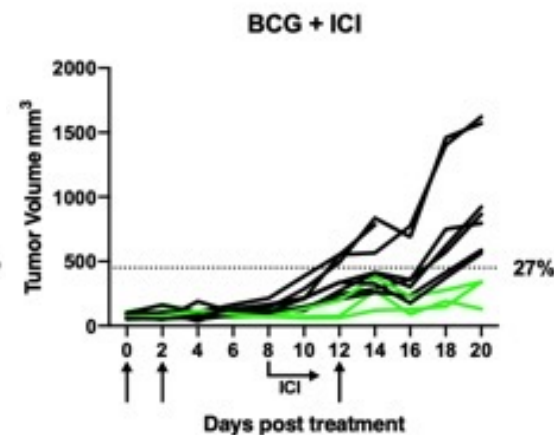
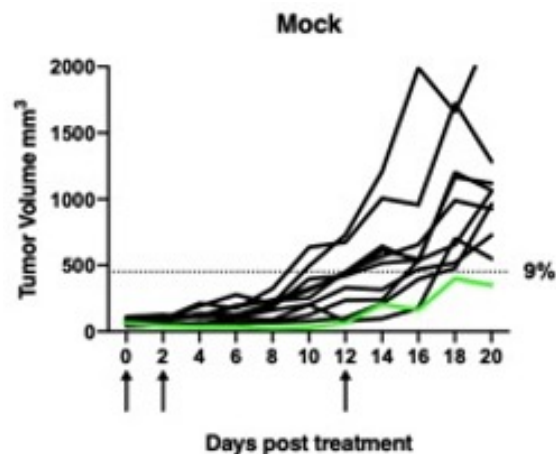
+



Bacteria
(BCG)



PeptiBAC

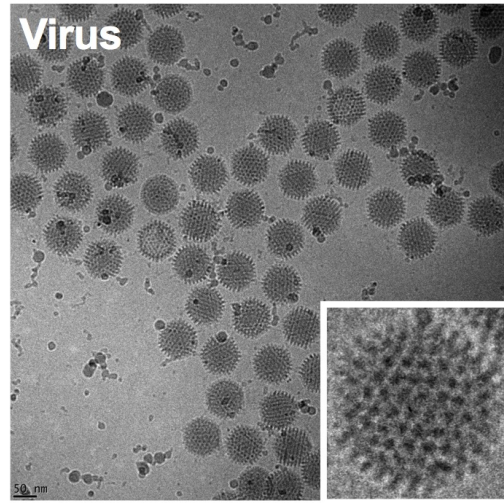


Ylosmaki et al., J Immunother Cancer. 2021 Jul;9(7)

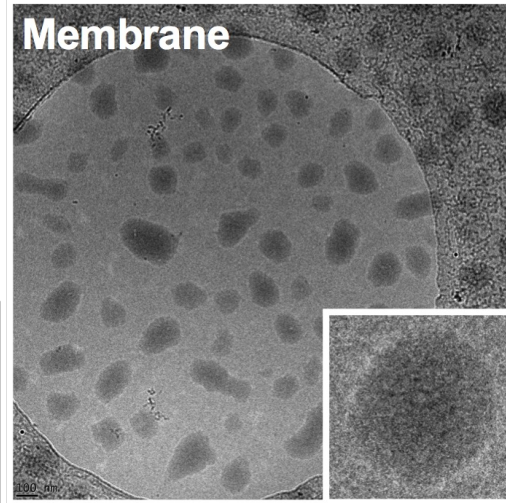
Example 4: ExtraCRAd



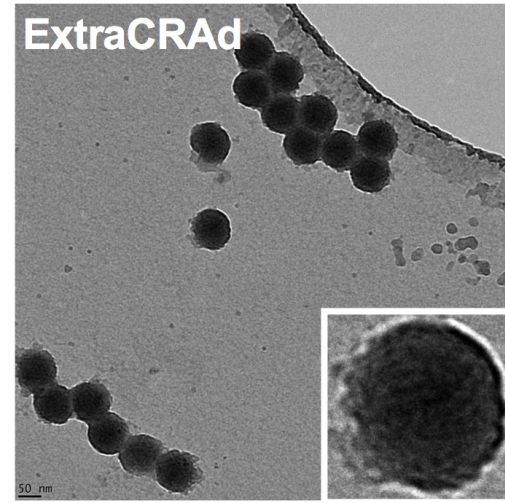
Manlio Fucciello,
PhD student



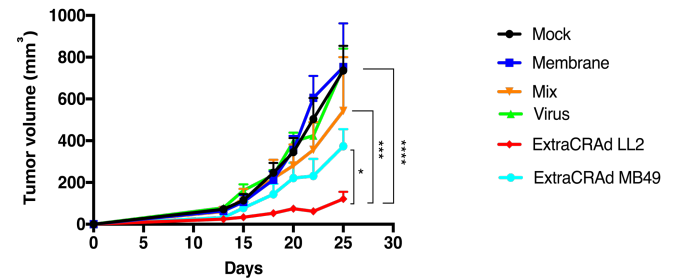
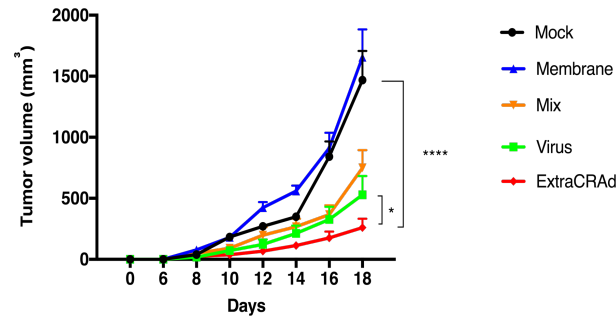
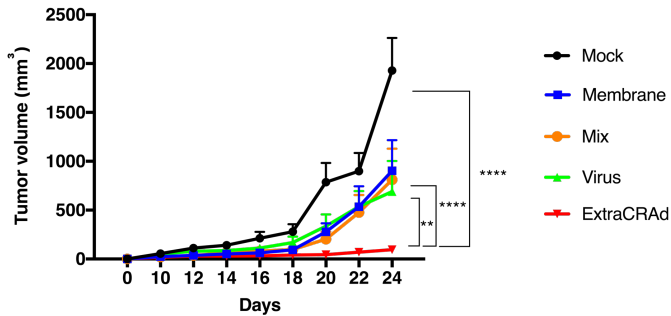
Melanoma (B16OVA)



Melanoma (B16F10)



Lung Carcinoma (LL2)





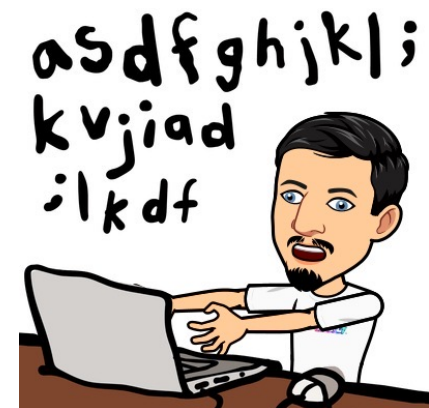
Coated viruses are effective to trigger
anti-tumor immune response

What do we coat the viruses with?

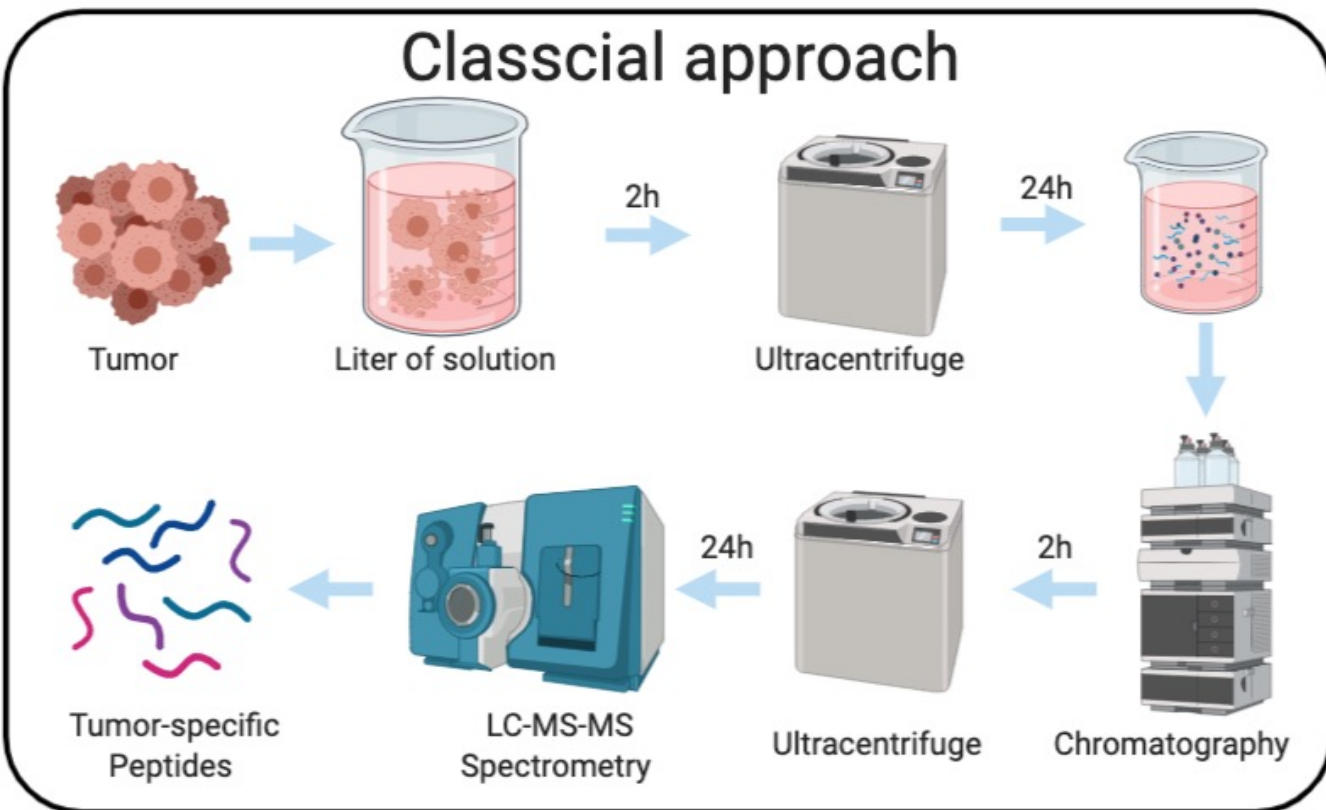
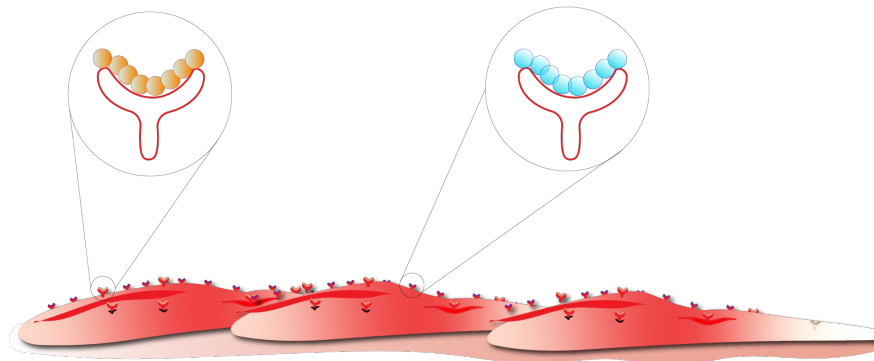
Tumor MHC-I ligandome, PeptiCHIP and HEX



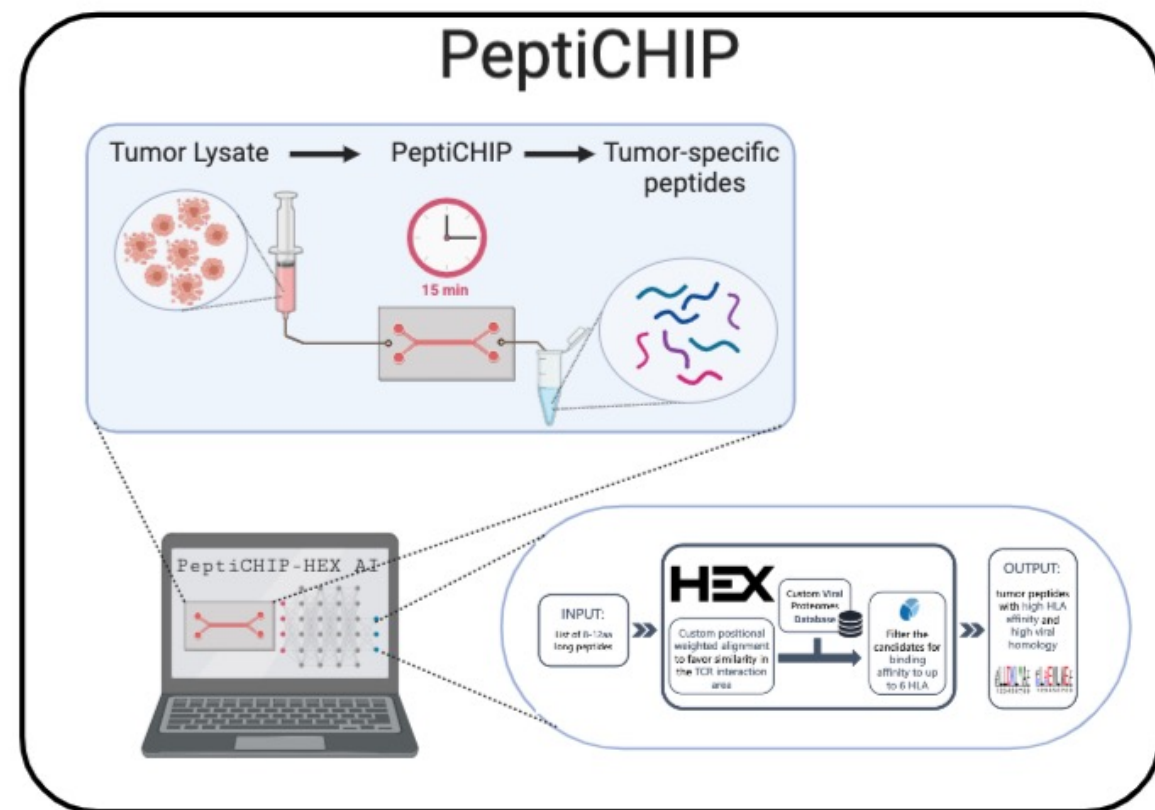
Sara Feola, Postdoc



Jacopo Chiaro, PhD Student



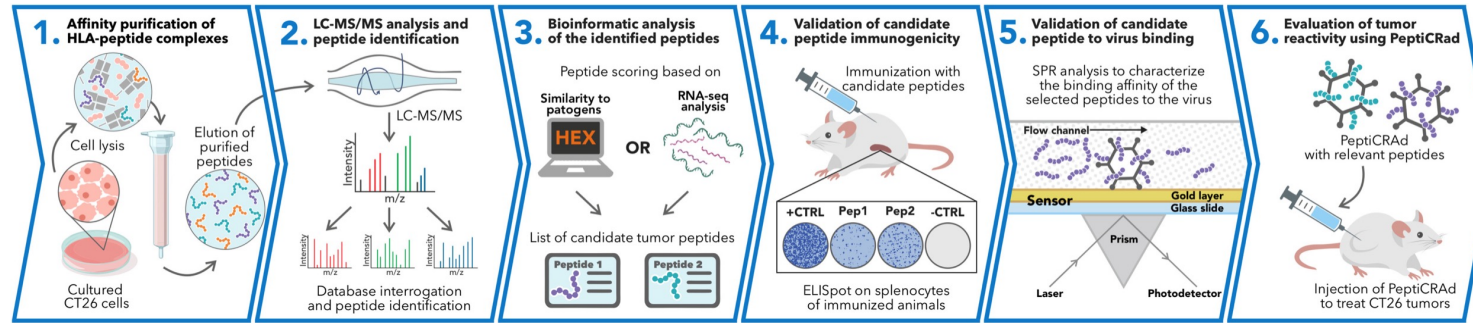
Peltonen et al., *Cancers* Jul 7;13(14):3408



Chiaro et al., *Cancer Immunol Res.* 2021 Aug;9(8):981-993

Feola et al., *ACS Nano*, September 2021

Precision oncolytic immunotherapy pipeline



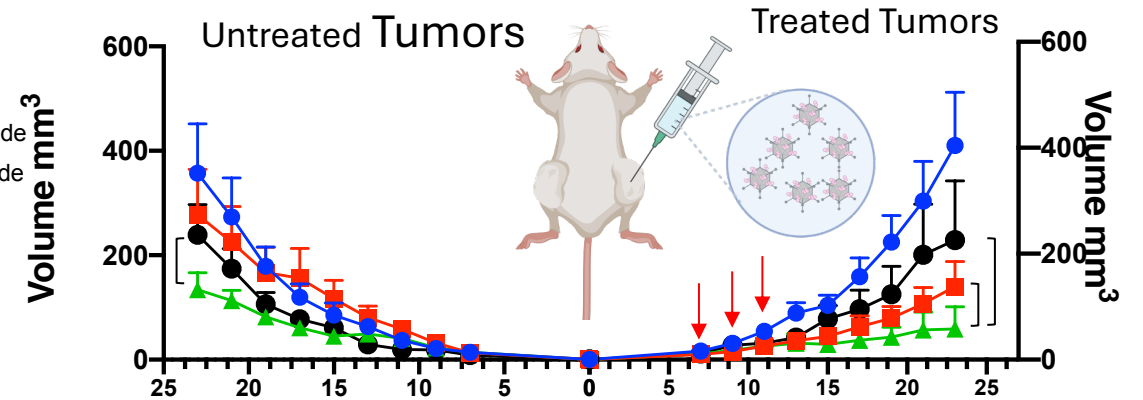
Colorectal cancer

Feola et al., *Elife*. 2022 Mar 22;11:e71156. doi: 10.7554/eLife.71156.



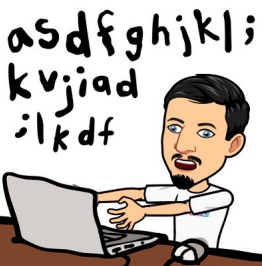
Sara Feola,
Postdoc

- Mock
- OV-naked
- ▲ PeptiCRAd-HEX peptide
- PeptiCRAd-AH1 peptide

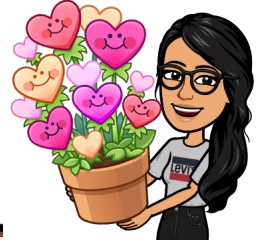


Mesothelioma

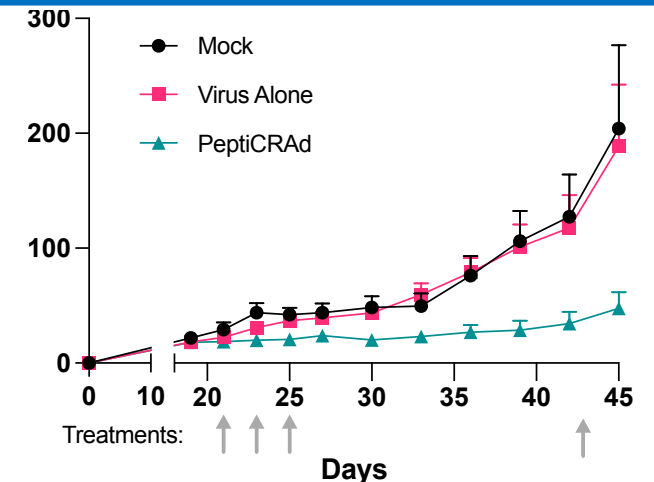
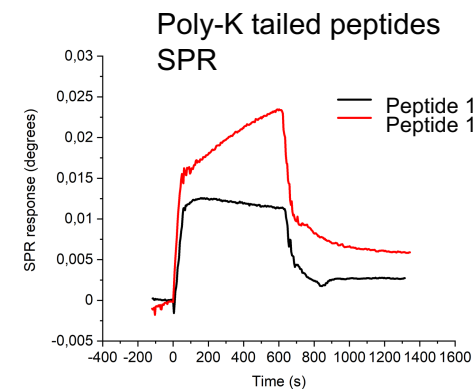
Chiaro and Antignani et al., *Nature Communications* 2023 Nov 3;14(1):7056



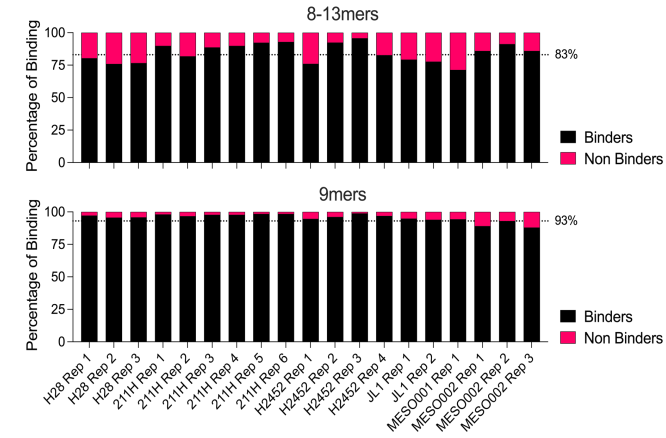
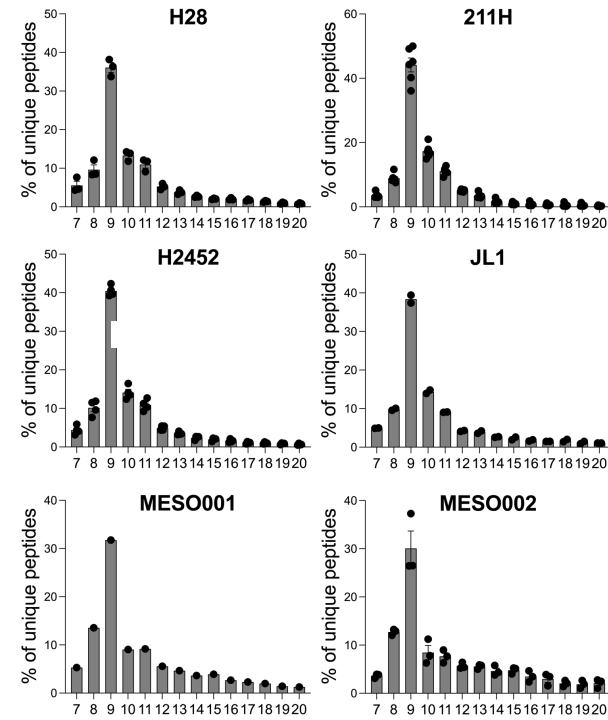
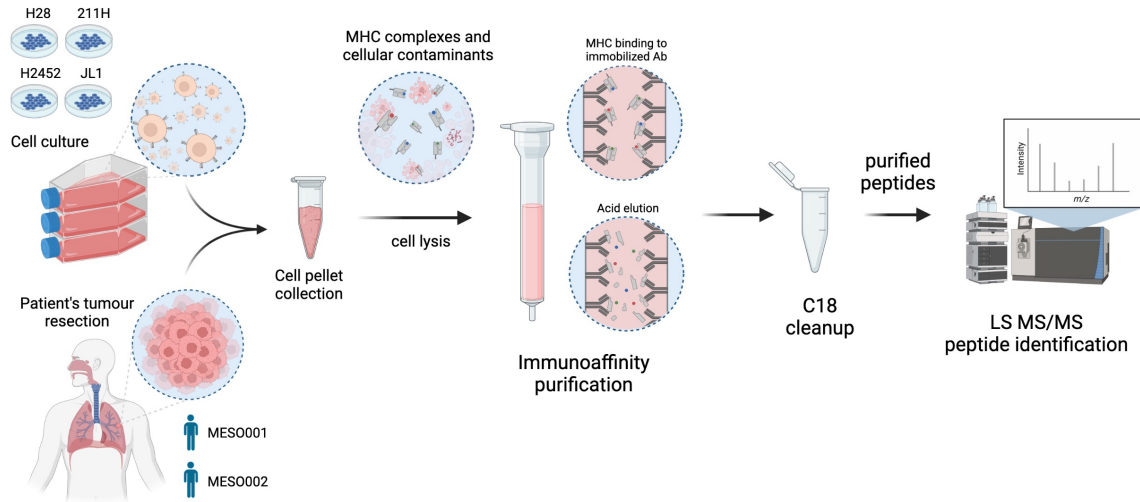
Jacopo Chiaro,
PhD Student



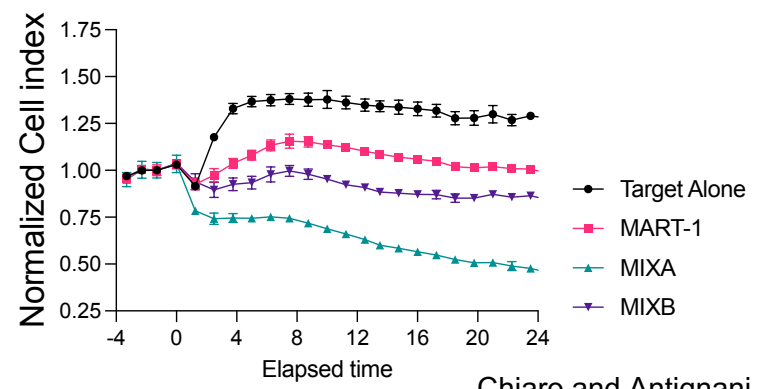
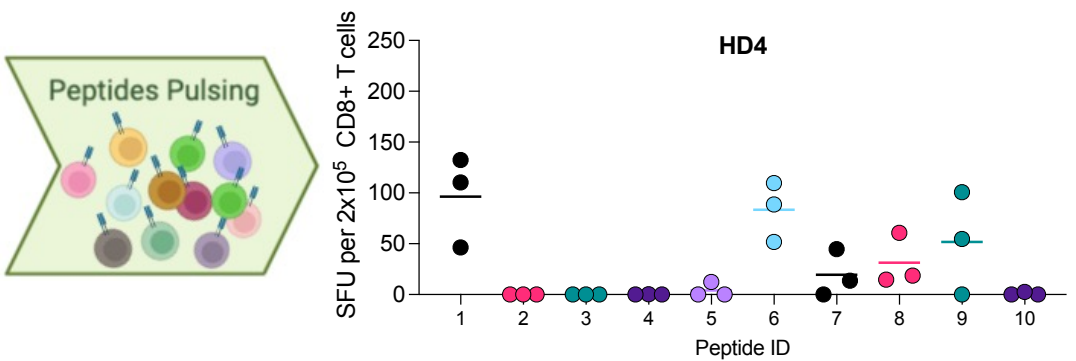
Gabriella Antignani
PhD student



Human Mesothelioma

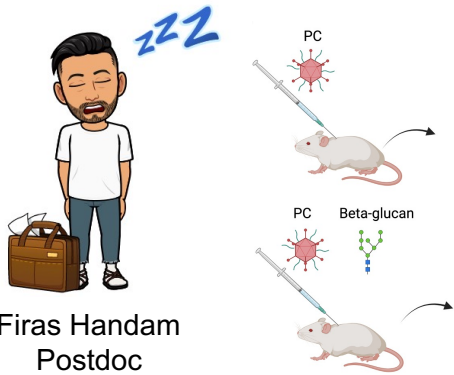


Expansion of specific T cell clones

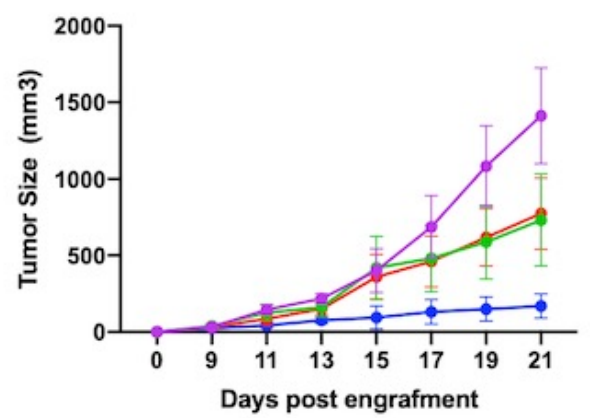
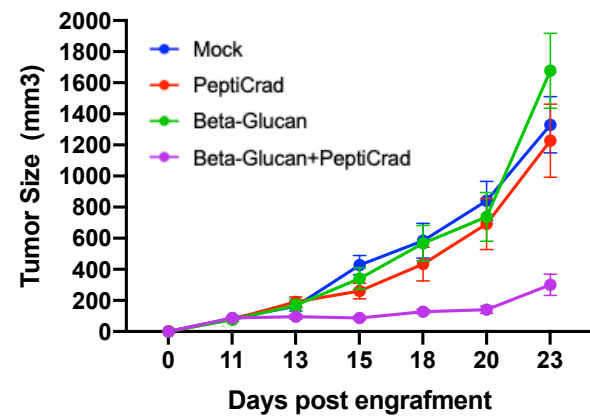




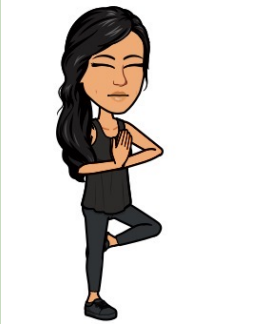
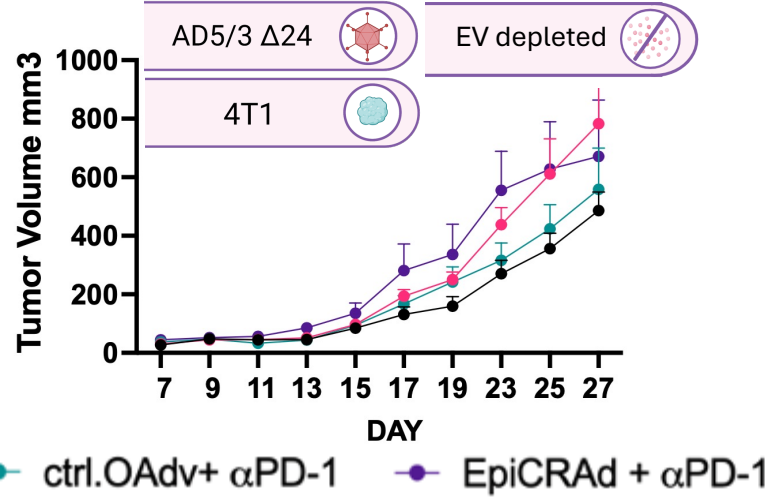
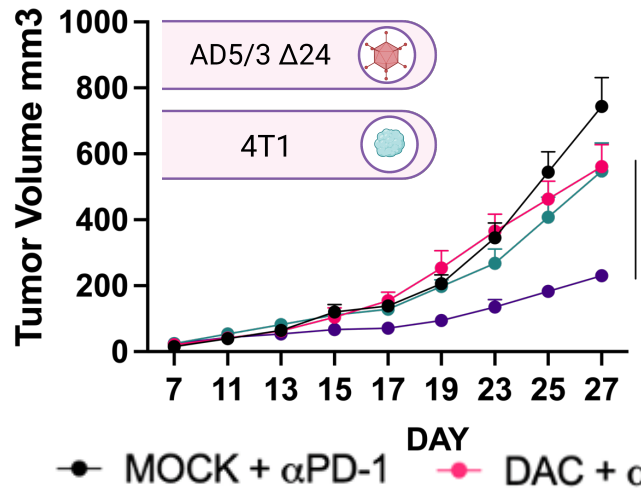
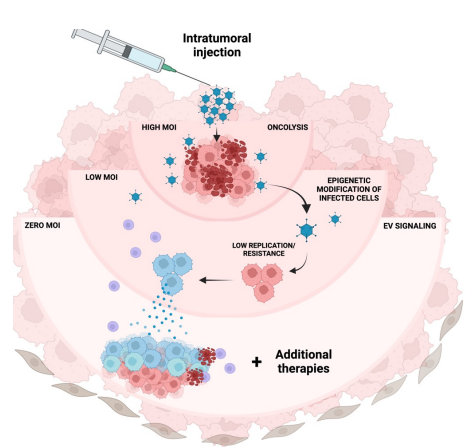
TRAINED IMMUNITY



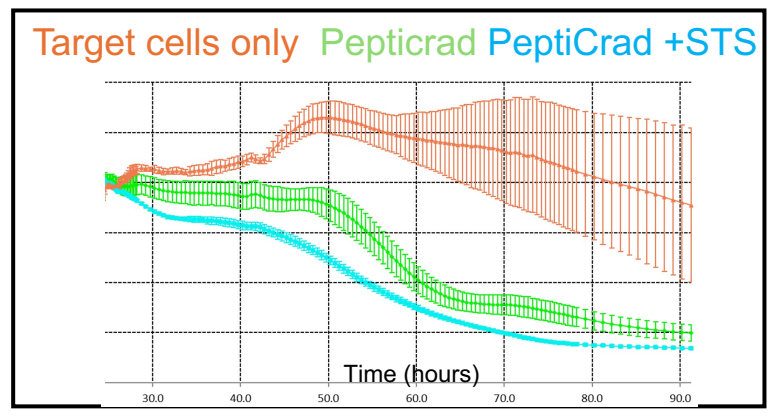
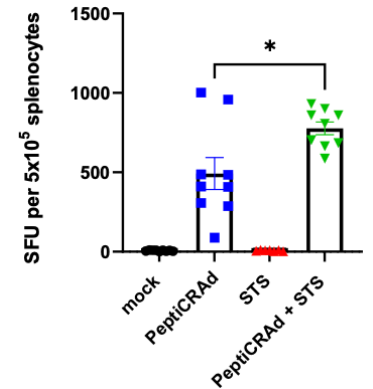
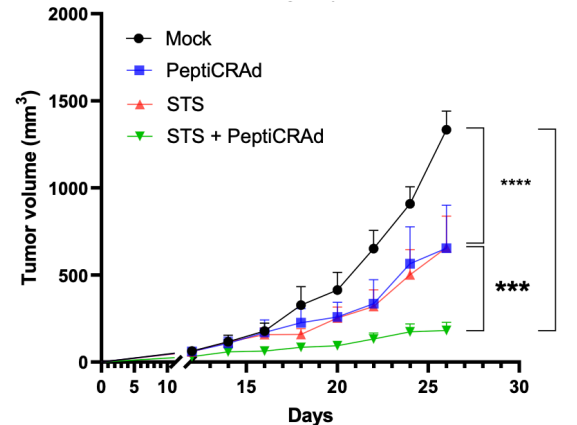
Firas Handam
Postdoc
unpublished data



Salvatore Russo
PhD student
unpublished data



Salvatore Russo
PhD student
unpublished data

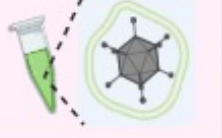


Towards precision cancer oncolytic immunotherapy


3 Improve Efficacy and Storage

Thermostable formulations
Environmental-friendly

GLOBEVAC

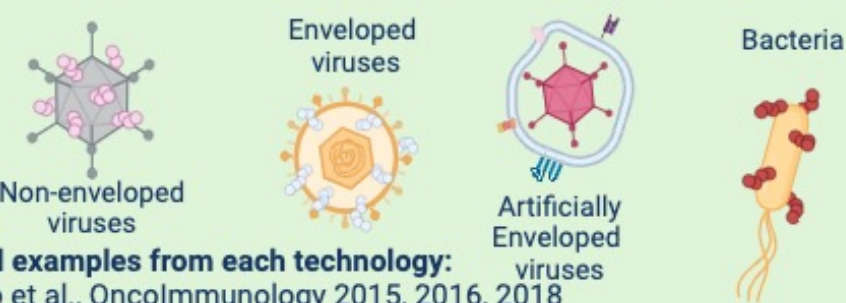


Epigenetic manipulation of
Tumor, TME and Immune system



EpiCRAd*
BetaCRAd
PeptiFAST

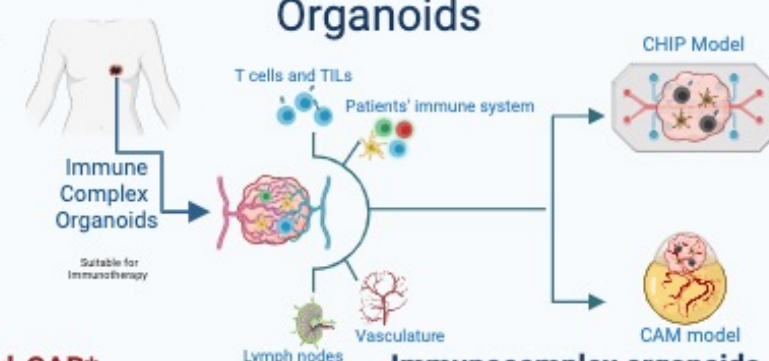
3 Platforms vaccine development



Non-enveloped viruses Enveloped viruses Artificially Enveloped viruses Bacteria

Selected examples from each technology:
Capasso et al., Oncolimmunology 2015, 2016, 2018
Ylösmäki et al., Molecular Therapy 2018
Fusciello et al., Nature Communciations 2019
Ylösmäki et al., JITC 2021
Hamdan et al., Mol Ther Onc 2023
Tripodi et al., iScience 2023

1 Organoids



Immune Complex Organoids
Suitable for Immunotherapy

T cells and TILs Patients' immune system

CHIP Model


Lymph nodes Vasculature

CAM model

Ad-CAB*
Hamdan et al., JITC 2021

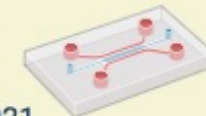
Immunocomplex organoids
Grönholm et al., Cancer Res 2020

2 Tumor antigens and neo-antigens discovery




Ligandome
Peltonen et al., Cancers 2021
Feola et al., eLIFE 2022
Chiaro et al., Nature Comm 2023

PeptiCHIP*
Feola et al., ACS Nano 2021
Manfredi et al., Science Adv 2023



2 Tumor antigens and neo-antigens discovery



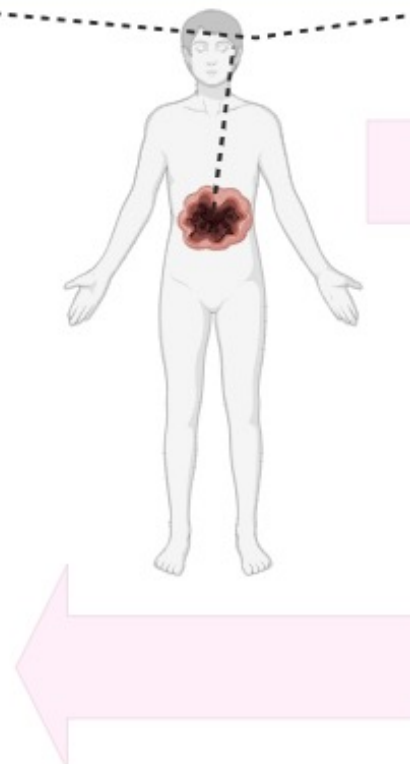
PeptiCHIP-HEX AI

Recognition of tumor peptide similar to viral peptide

Tumor peptide

Cross-reactive Anti-viral and anti-tumor T cells killing cancer cells

HEX*
Chiaro et al., Cancer Immunology Research 2021



ImmunoViroTherapy LAB (IVT Lab)



Thank to

Collaborators (short list, *only the one involved in the project presented today*):

Tapani Viitala – Drug Research Program, University of Helsinki FI

Helder Santos & Flavia Fontana – University of Groningen Netherland NL

Janne Lehtio & Rui Branca – Karolinska Institute and ScinceLifeLab Stockholm SE

Barbara Szomolay - Systems Immunity Research Institute Cardiff University UK

Satu Mustjoki – Translational Immunology Program University of Helsinki FI

Antti Rannikko and Vilja Pietilainen – Finnish Institute of Molecular Medicine (FIMM)& HUS FI

Seppo Vainio & Ilya Skovorodkin – Oulu University FI

Maria Resigno – Humanitas University IT

Lucio Pastore – University of Naples Federico II IT

Chiara Bonini and Eliana Ruggiero, San Raffaele Milano IT

Mario Squadrito and Luigi Naldini, San Raffaele Milano IT



ERC-Consolidator Grant
ERC-PoC Grant PeptiCHIP
ERC-PoC Grant GlobeVAC



Magnus Ehrnrooth Foundation



JANE JA AATOS
ERKON SÄÄTIÖ



DIGITAL PRECISION CANCER MEDICINE
FOR DISCOVERIES AND
IMPROVED TREATMENTS



Medicinska Understödsföreningen
Liv och Hälsa r.f.

