3D-bioprinted cancer models for prediction of nanomedicine response driven by H&E-based AI algorithm

http://SatchiFainaroLab.com
ronitsf@tauex.tau.ac.il
@RSFLab

CRS, Philadelphia, 15th July, 2025

Prof. Ronit Satchi-Fainaro, Ph.D.
Head, Cancer Research and Nanomedicine Laboratory
Kurt and Herman Lion Chair in Nanosciences and Nanotechnologies
Director, Kahn 3D-BioPrinting Initiative
Director, Cancer Biology Research Center
Head, Gray School of Medical Sciences, Tel Aviv University, Israel

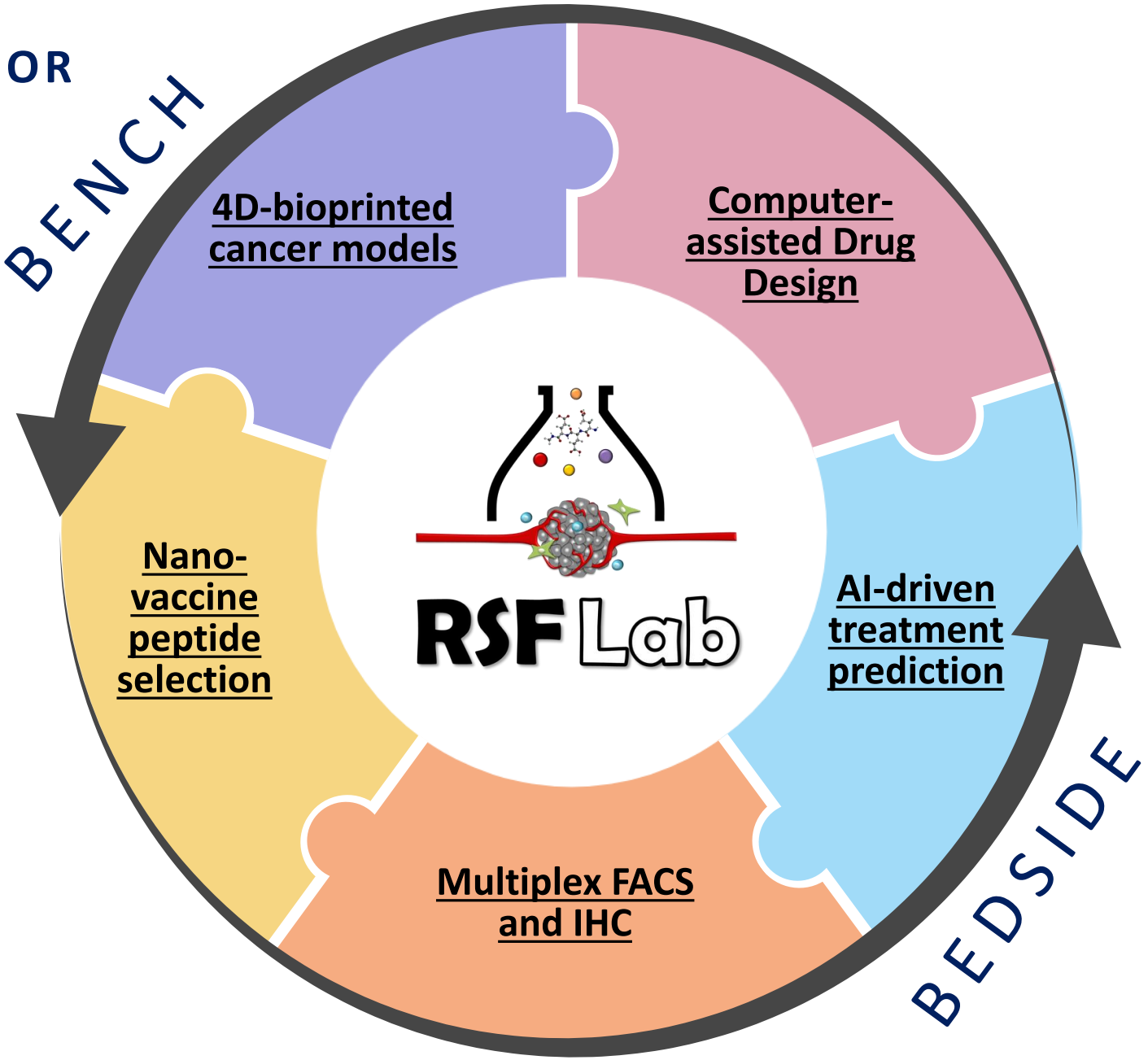
CRS 2025 ANNUAL MEETING & EXPOSITION
PHILADELPHIA, PA
JULY 13-18, 2025

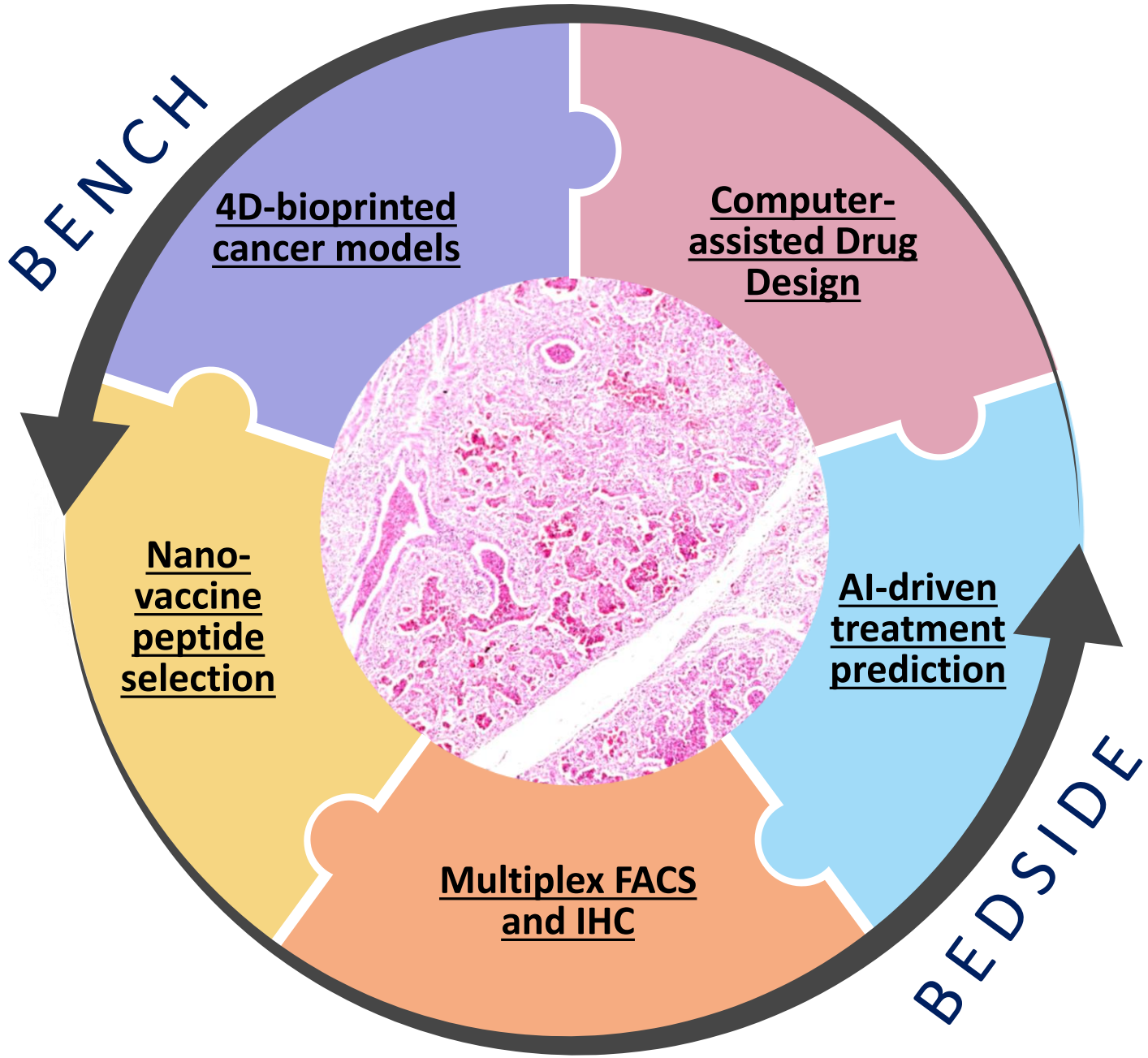
NEXT-GENERATION DELIVERY INNOVATIONS

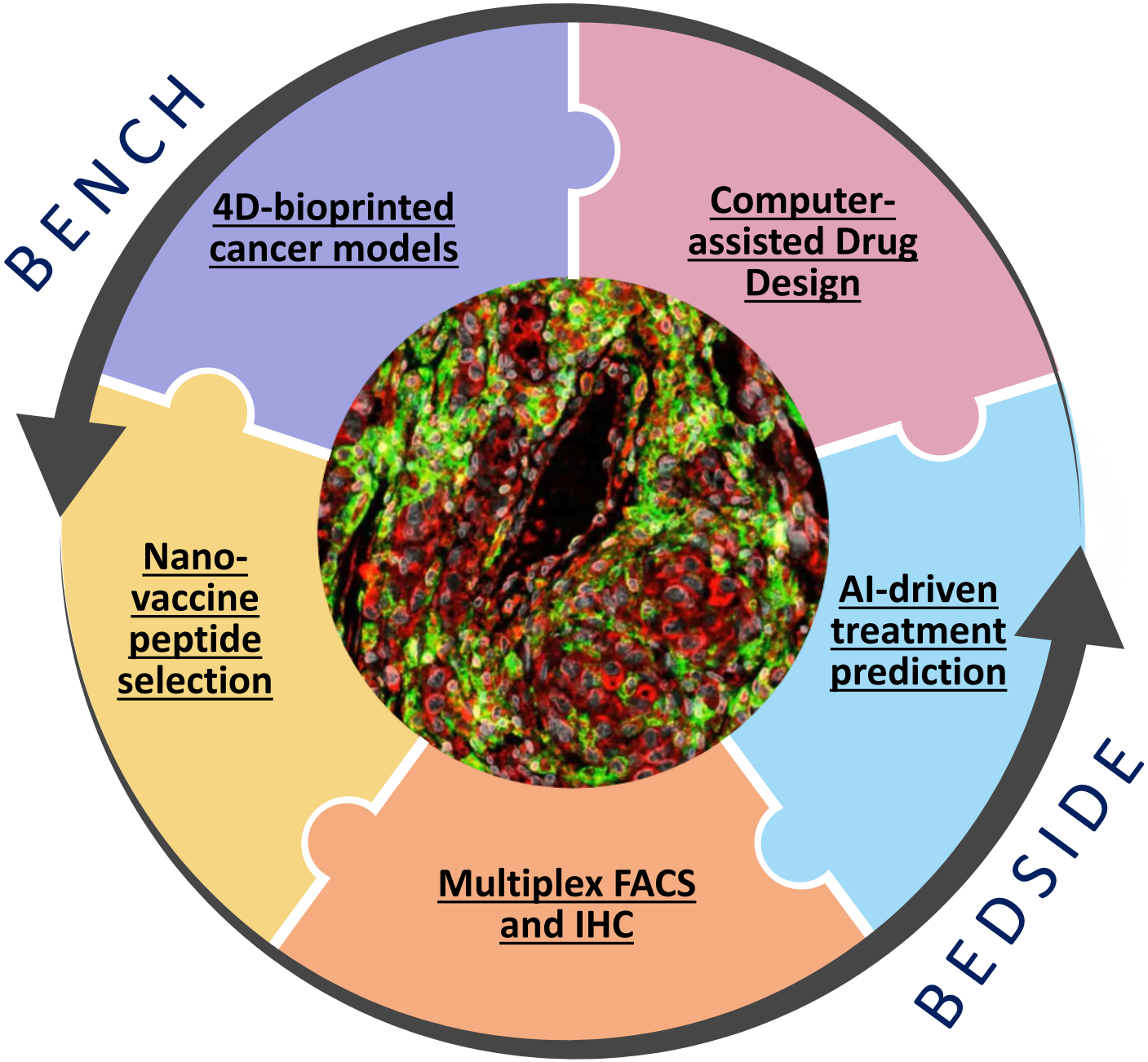
Disclaimers

Co-Founder, Selectin Therapeutics Inc.
Co-Founder, ImmuNovation Ltd.
Founder, 3DCanPredict Ltd.
Director, BoD, Teva Pharmaceutical Industries Ltd.
Sponsored Research, Merck

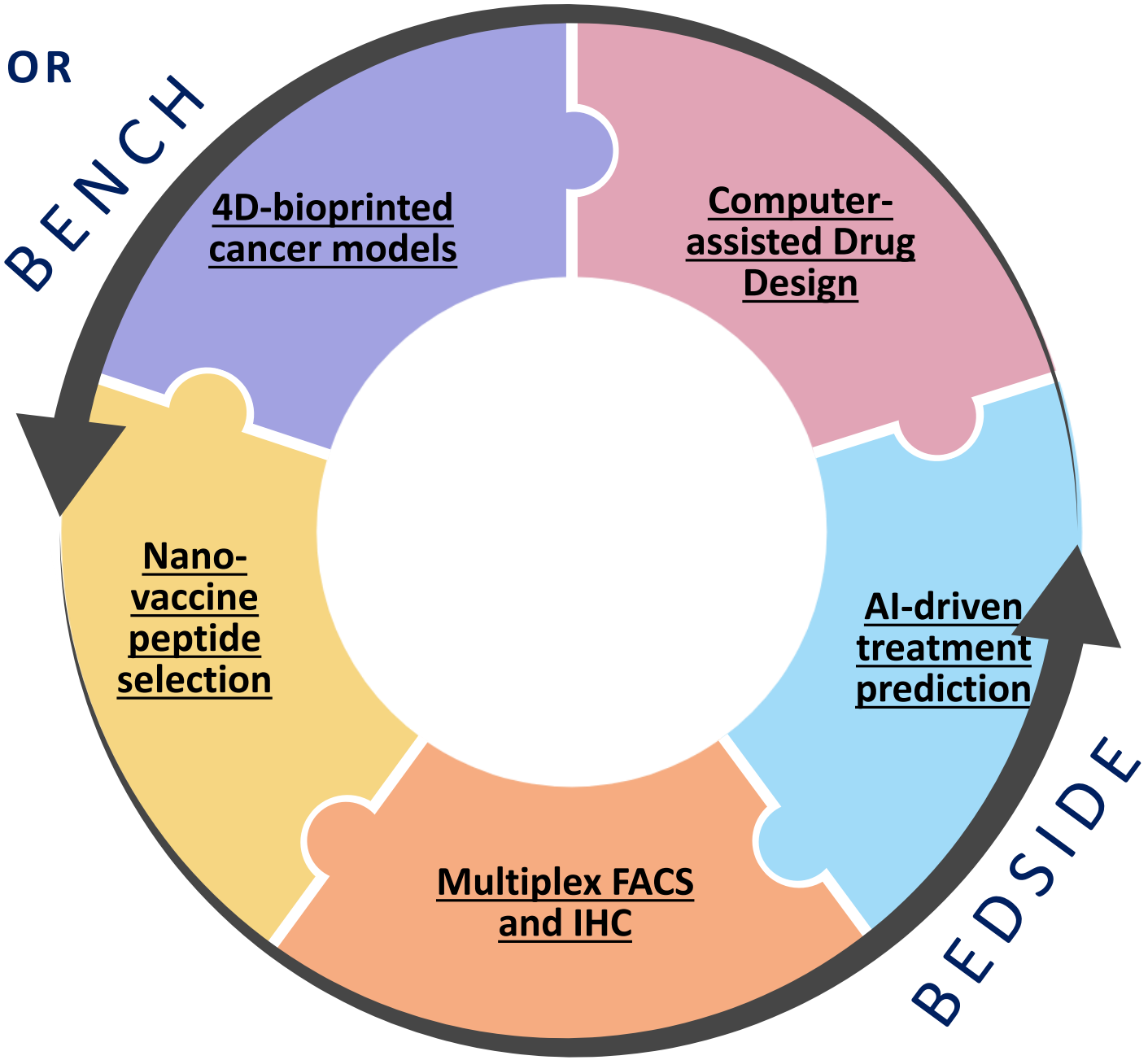
CUTTING-EDGE TECHNOLOGIES FOR BREAKTHROUGH DISCOVERIES

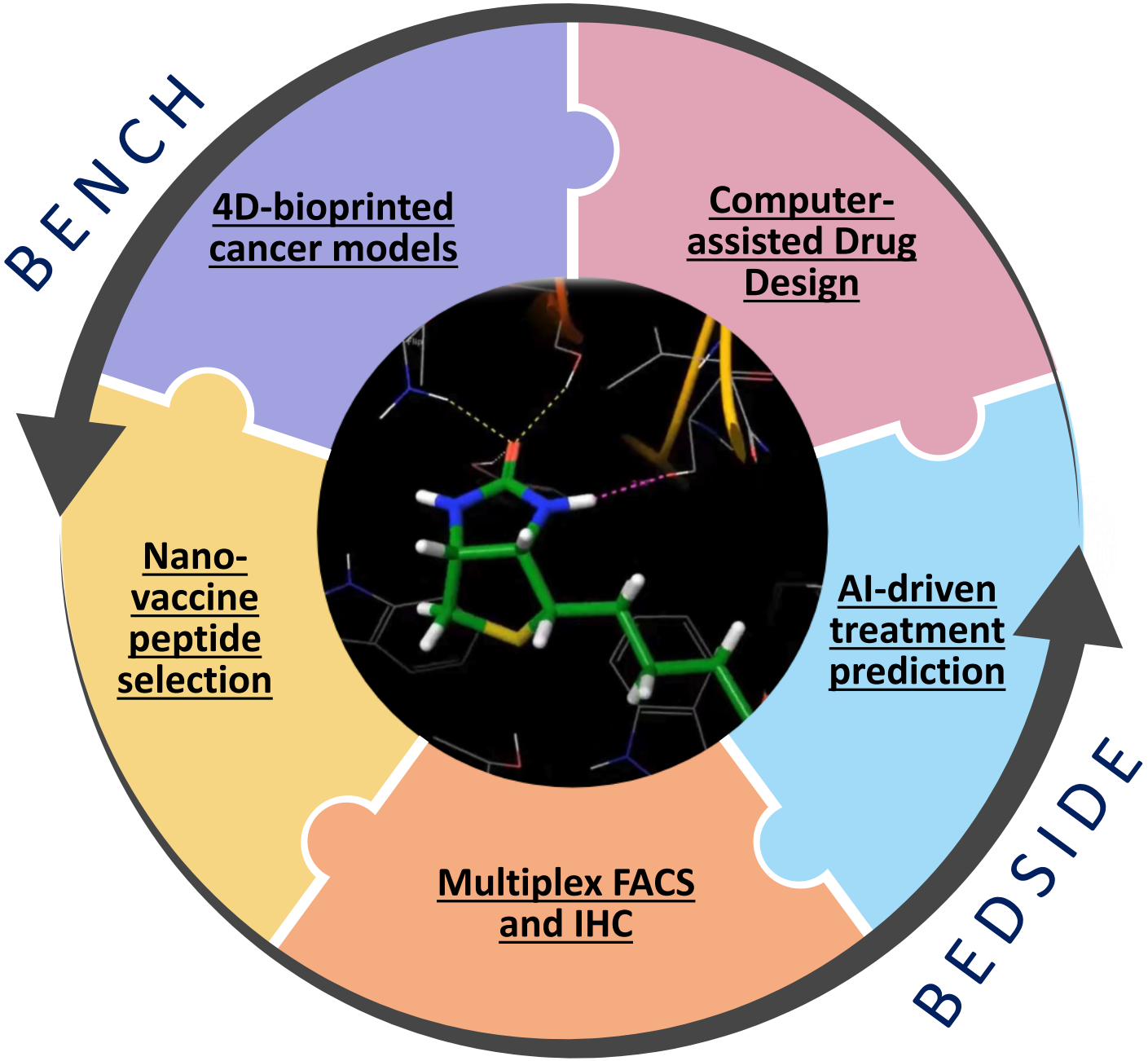


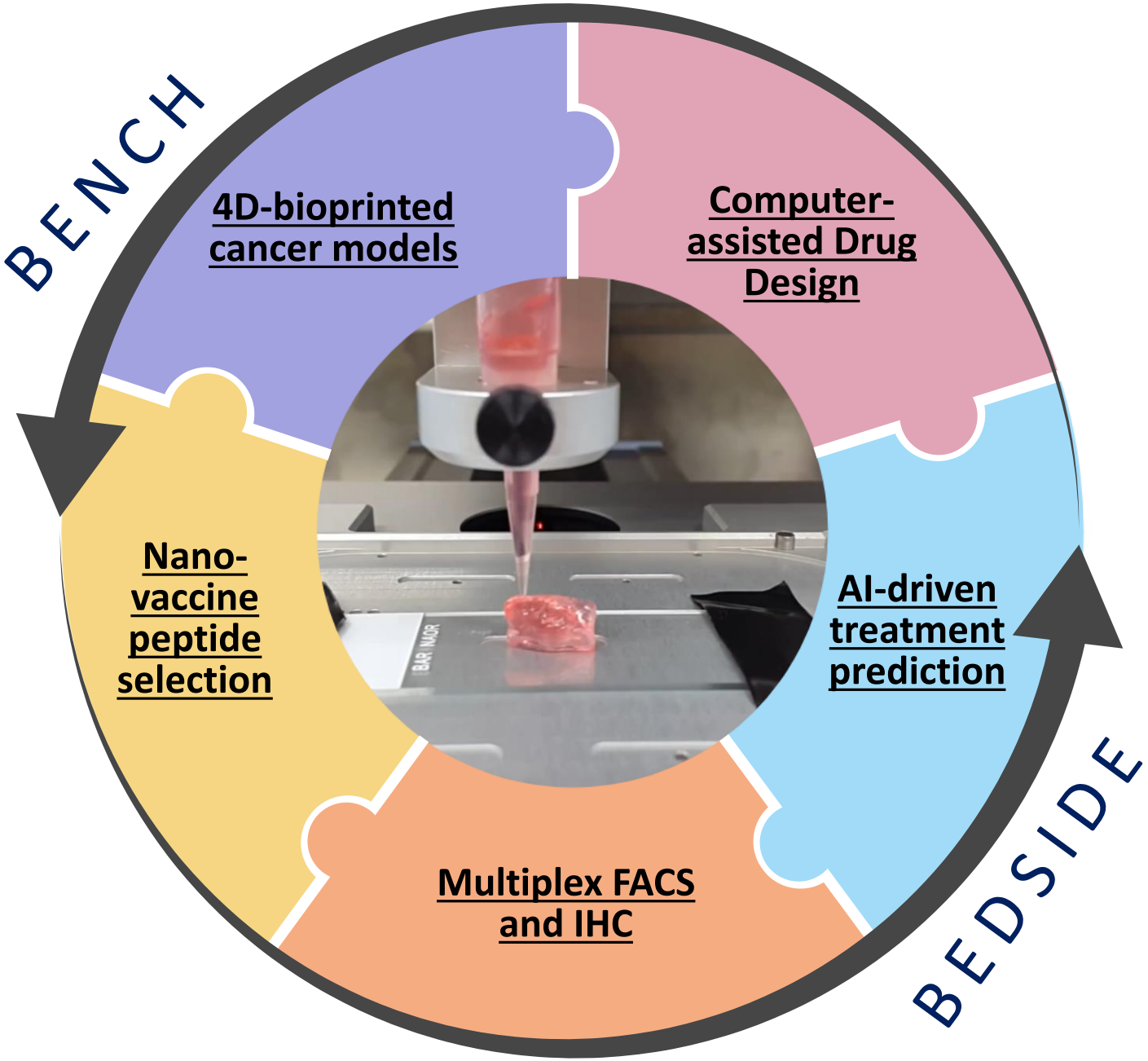

BENCH
4D-bioprinted cancer models
Computer-assisted Drug Design
AI-driven treatment prediction
BEDSIDE
Multiplex FACS and IHC
Nano-vaccine peptide selection


BENCH
4D-bioprinted cancer models
Computer-assisted Drug Design
AI-driven treatment prediction
BEDSIDE
Multiplex FACS and IHC
Nano-vaccine peptide selection

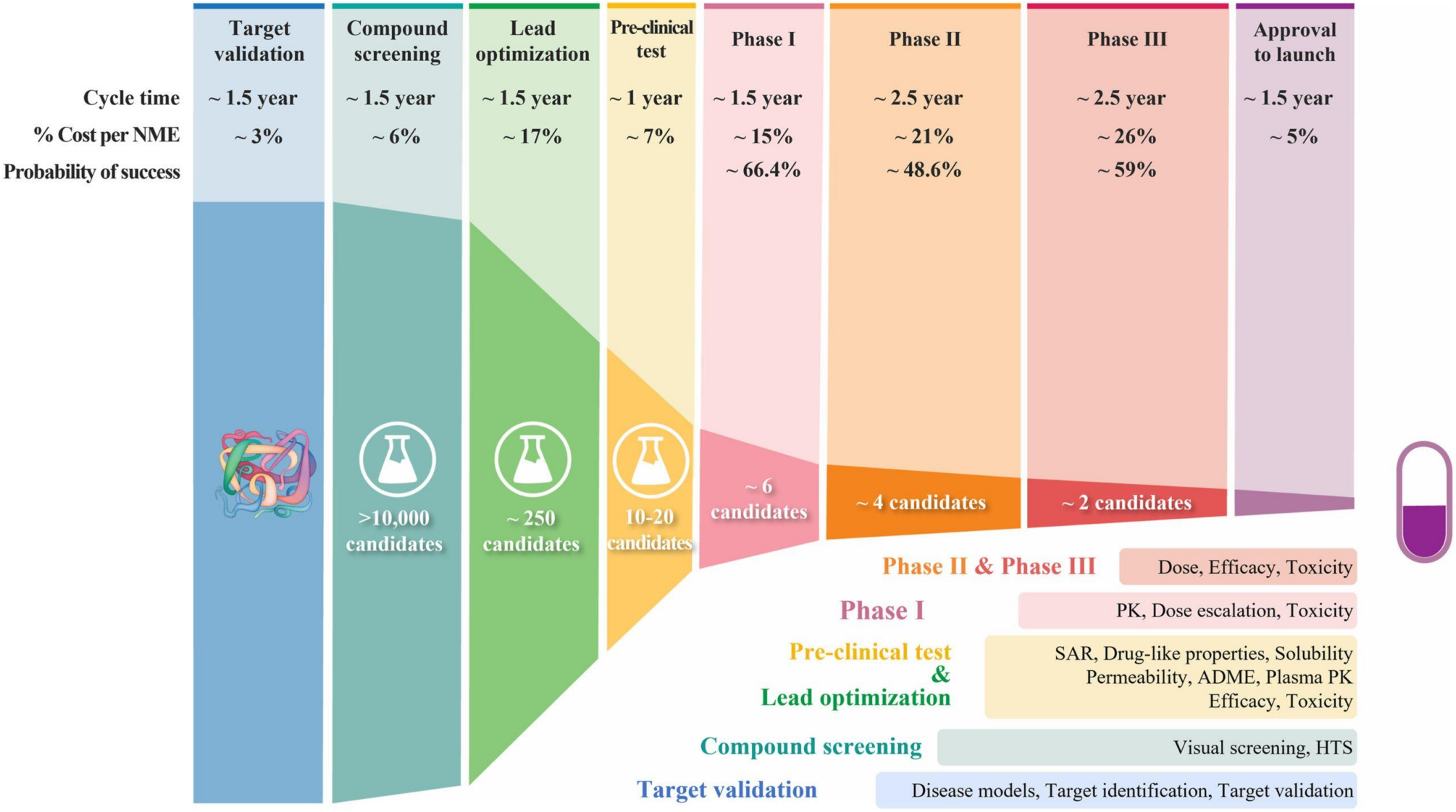
CUTTING-EDGE TECHNOLOGIES FOR BREAKTHROUGH DISCOVERIES




BENCH
4D-bioprinted cancer models
Computer-assisted Drug Design
AI-driven treatment prediction
BEDSIDE
Multiplex FACS and IHC
Nano-vaccine peptide selection


BENCH
4D-bioprinted cancer models
Computer-assisted Drug Design
AI-driven treatment prediction
BEDSIDE
Multiplex FACS and IHC
Nano-vaccine peptide selection

Biopharmaceutical drug development: Attrition rates



https://www.sciencedirect.com/science/article/pii/S2211383522000521

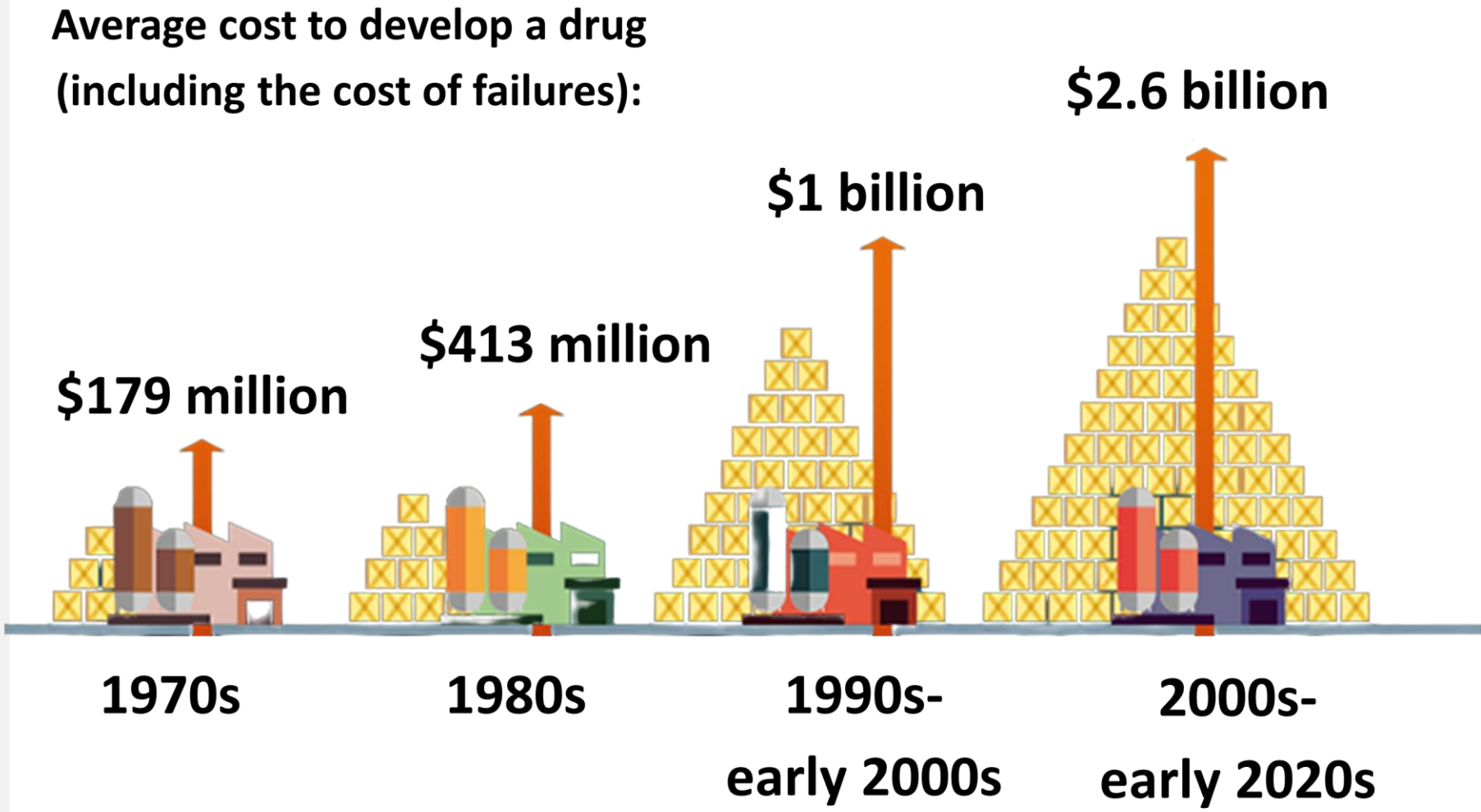
RSF Lab

TEL AVIV UNIVERSITY
Pursuing the Unknown

Development costs

Success rates in bringing a drug from discovery through to commercialization are low and getting worse.

Only 11.3% of drugs that enter clinical testing will be approved in the United States, down from a 16.4% success rate ten years ago.



1. PhRMA, 2016
2. A New Look at the Arsenal of Tech Solutions, Applied Clinical Trials, October 1, 2015, Kenneth A. Getz

RSF Lab

TEL AVIV UNIVERSITY
Pursuing the Unknown

Likelihood of approval from Phase I

The overall likelihood of approval (LOA) from Phase I for all developmental candidates over 2011–2020 was 7.9%.

Unmet clinical needs in cancer, especially the advanced stage of this disease

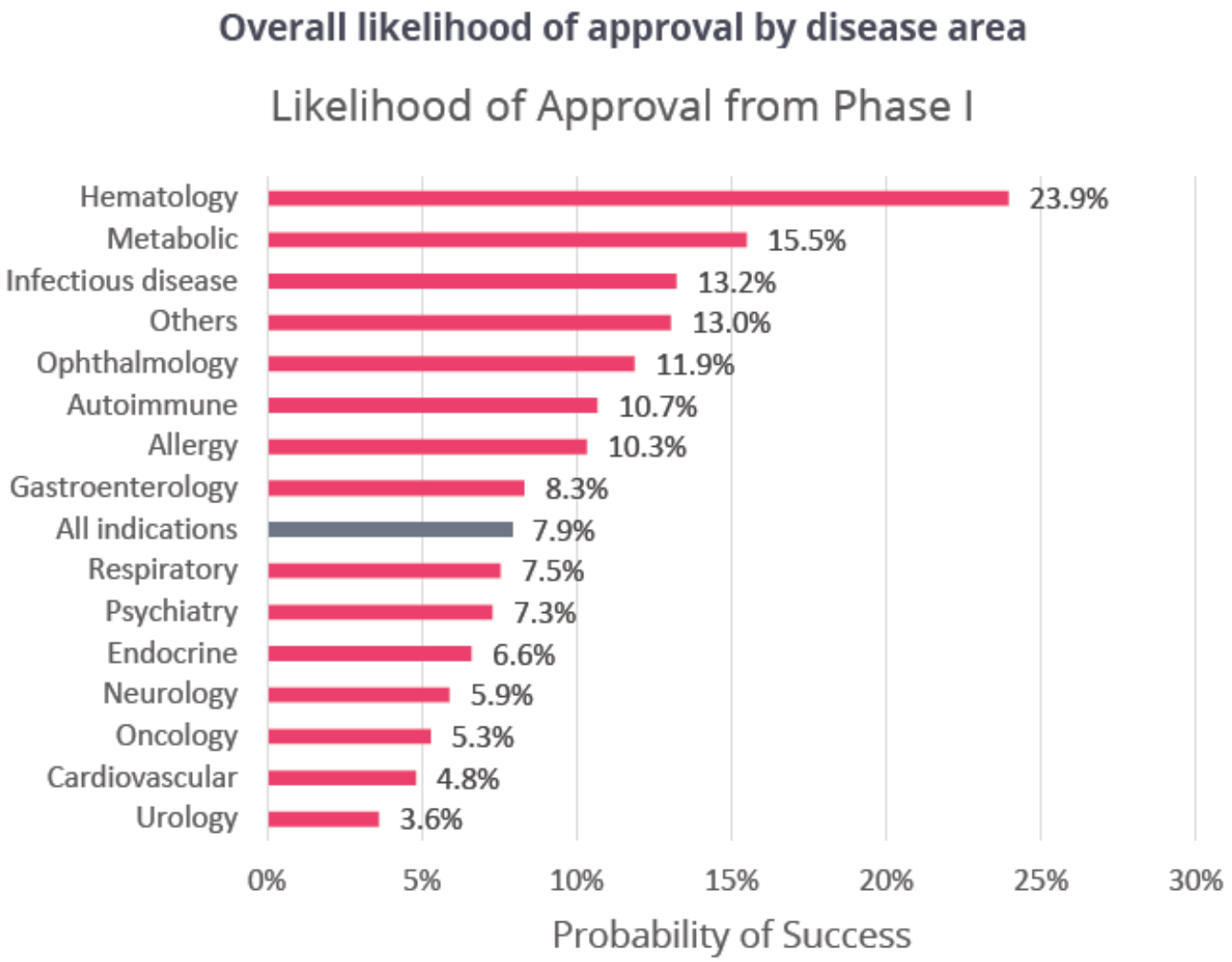


FIgure 5a: Chart of LOA from Phase I, displayed highest to lowest by disease area. Source: Biomedtracker® and Pharmapremia®, 2020

TEL AVIV UNIVERSITY
Pursuing the Unknown

How to address these challenges?

Modernization Act 2.0

DID YOU KNOW?

117TH CONGRESS
2D SESSION

S. 5002

To allow for alternatives to animal testing for purposes of drug and biological product applications.

IN THE SENATE OF THE UNITED STATES

SEPTEMBER 29, 2022

Mr. PAUL (for himself, Mr. BOOKER, Mr. BRAUN, Mr. CRAPO, Mr. MARSHALL, Ms. COLLINS, Mr. KING, Mr. PADILLA, Mr. SANDERS, Mr. TUBERVILLE, Mr. LUJÁN, and Mr. SCOTT of Florida) introduced the following bill; which was read twice, considered, read the third time, and passed

---

A BILL

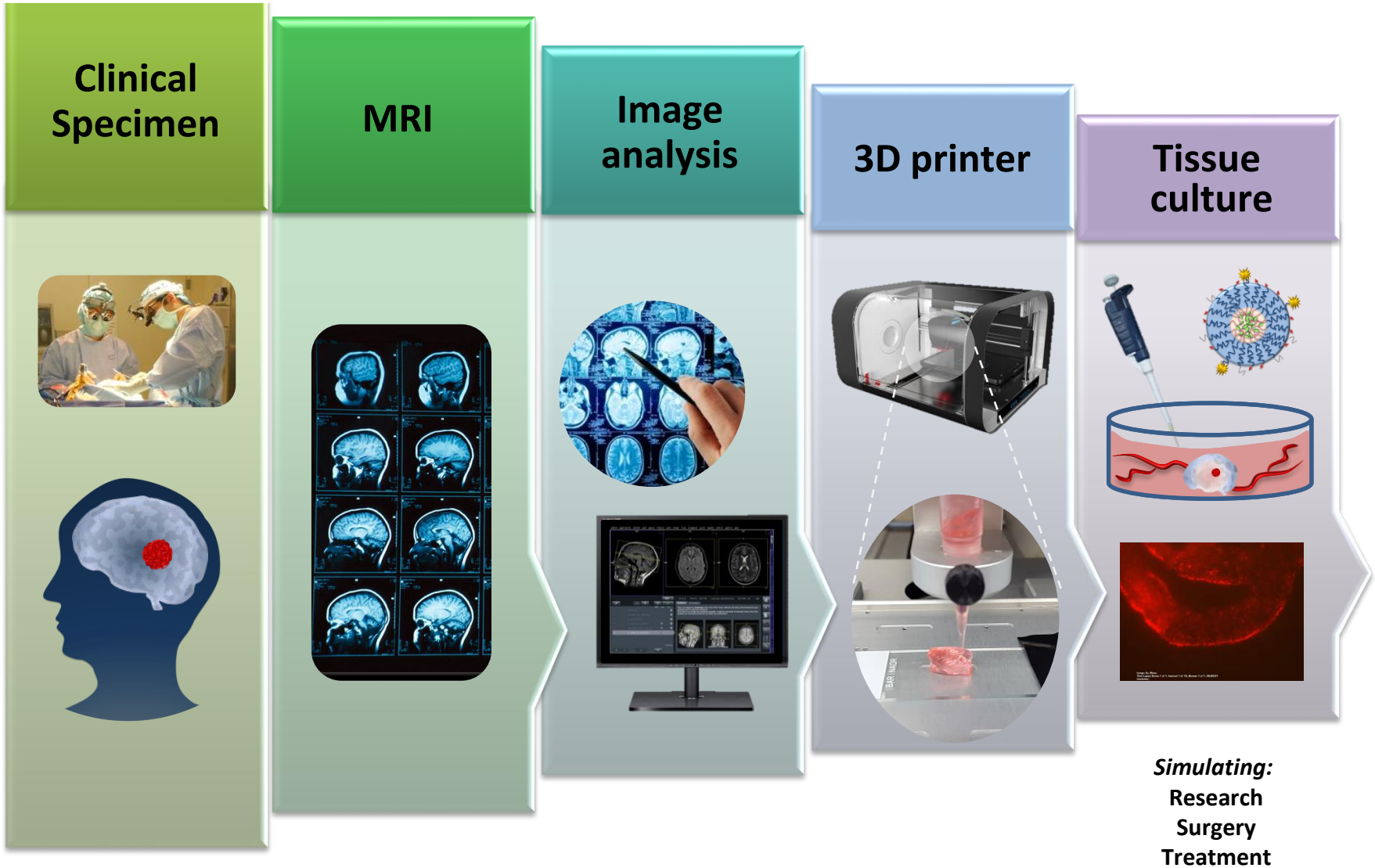
To allow for alternatives to animal testing for purposes of drug and biological product applications.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

How to address these challenges? – 3D-bioprinted tumors for simulations of research, surgery, and treatment

Lena Neufeld

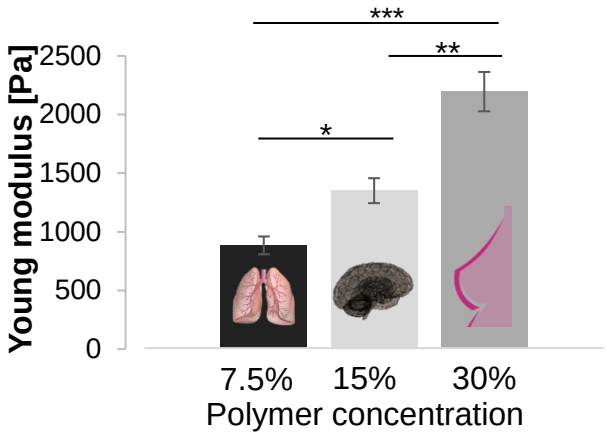
A simulation-based process that takes only 2 weeks!



Simulating:
Research
Surgery
Treatment

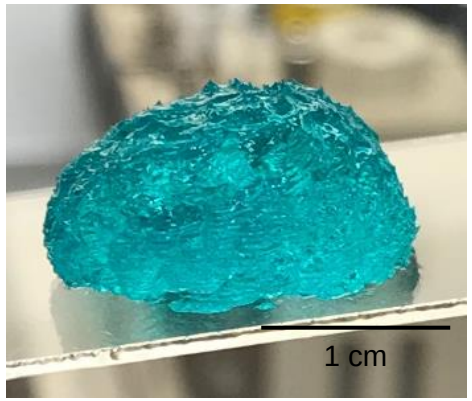
Proof of concept: Generation of 4DCanPredict platform

Bio-ink characterization



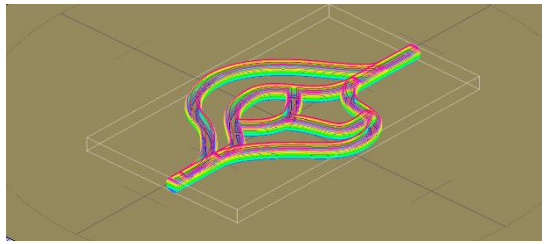
3D-BioPrinted brain

~ 10 minutes per model

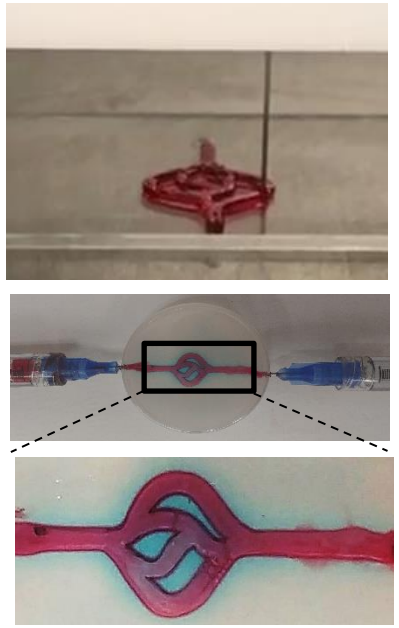


4DCanPredict vascular network

Computational design of blood vessels

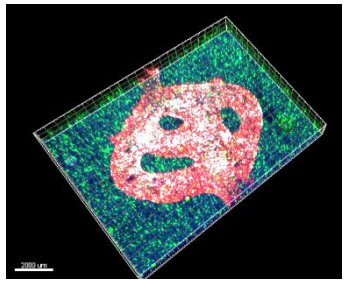


3D-BioPrinted vascularized tumor model created with 2 bio-inks

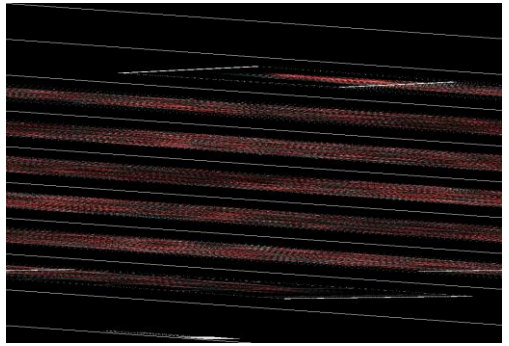


Recapitulating tumor microenvironment

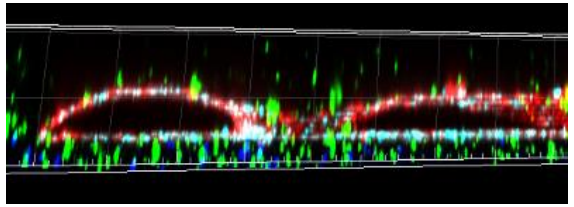
3D-BioPrinted tumor



Endothelial cells hPericyte
Cancer cells hAstrocytes hMicroglia

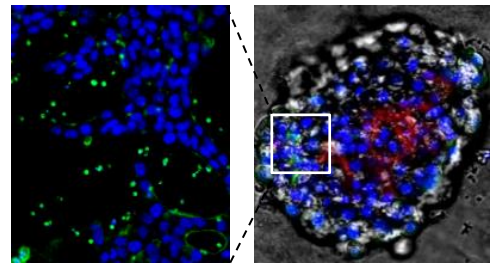


Confocal Z-stack



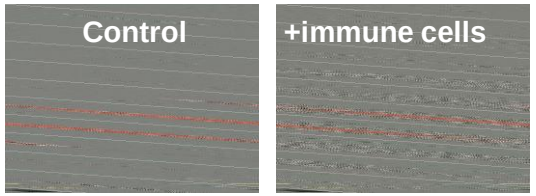
Immunology and drug permeability

Infiltration of immune cells into spheres



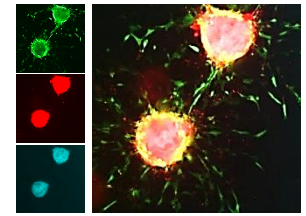
Cancer cells T cells CD8⁺ DAPI

Immune cells cytotoxicity



Cancer cells immune cells

Internalization of drugs



Cancer cells Endothelial cell
hAstrocytes Cy5-labeled drugs

4DCanPredict has established the first immunocompetent personalized 4D-BioPrinted vascularized & perfusable cancer model

Pozzi et al., Advanced Drug Delivery Reviews (2020)

Neufeld, et al., Nature Reviews Cancer (2022)

Neufeld, et al., Science Advances (2021)

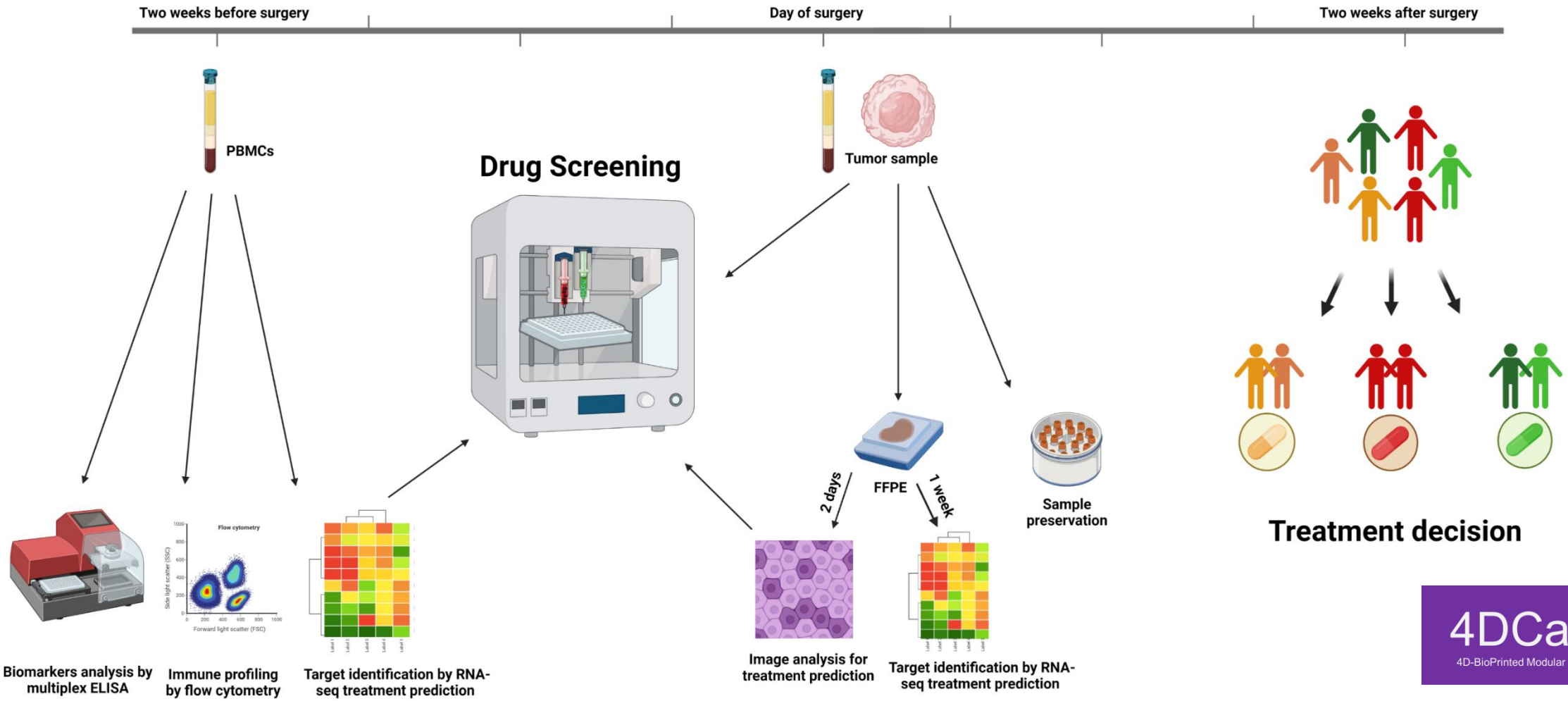
RSF Lab

TEL AVIV UNIVERSITY
Pursuing the Unknown

Clinical trial workflow



Anne Krinsky Anshika Katyal Opal Avramoff



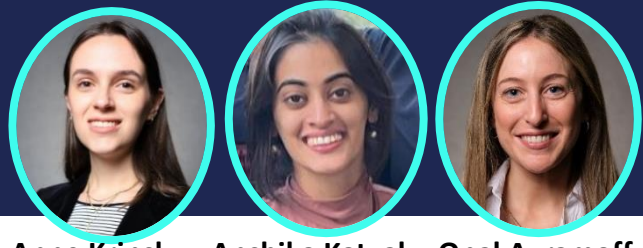
4DCanPredict
4D-BioPrinted Modular Drug Screening Platform for Cancer

With Ronnie Frommer-Shapira, Sheba Medical Center - Pangea

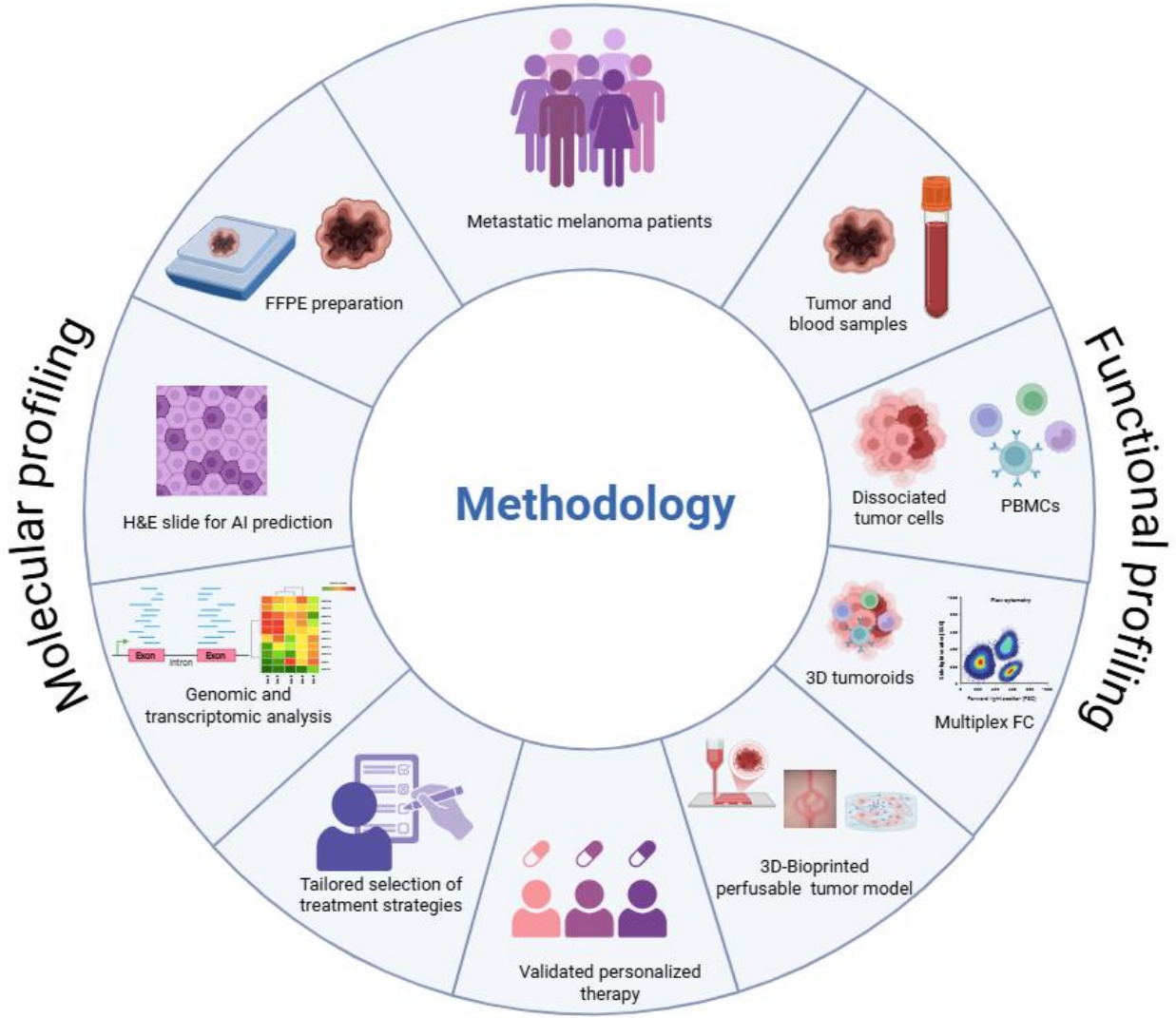
RSF Lab

TEL AVIV UNIVERSITY
Pursuing the Unknown

Clinical trial workflow



Anne Krinsky Anshika Katyal Opal Avramoff



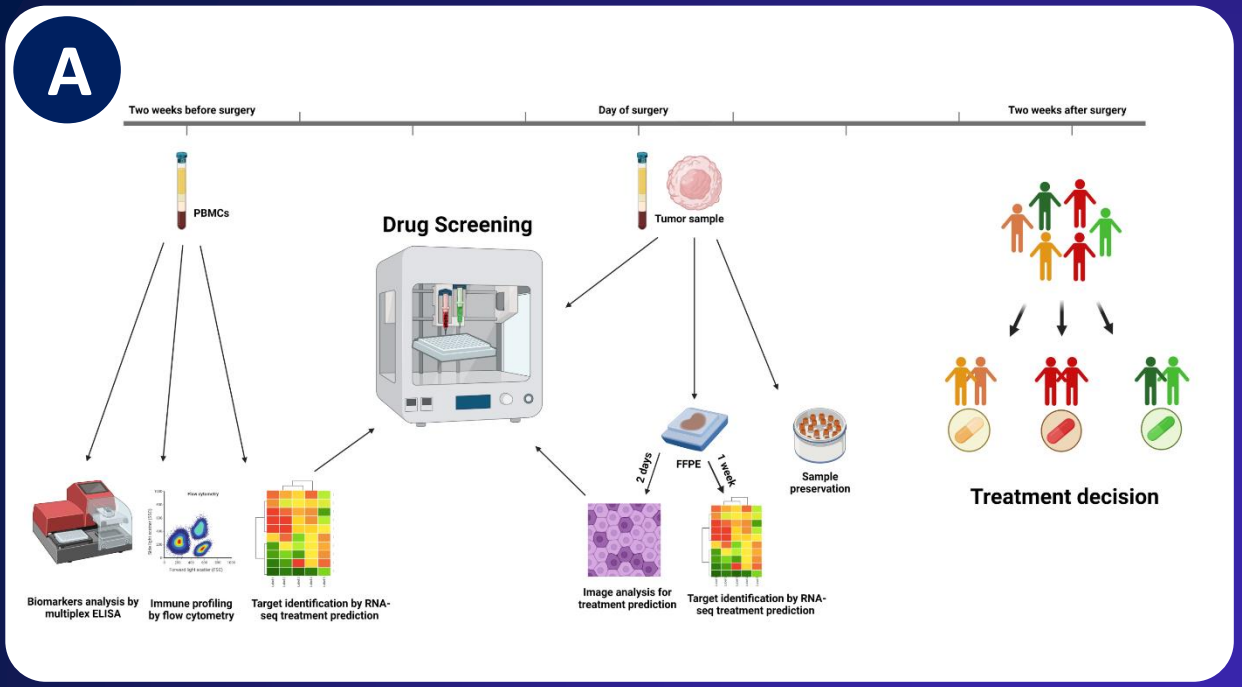
4DCanPredict

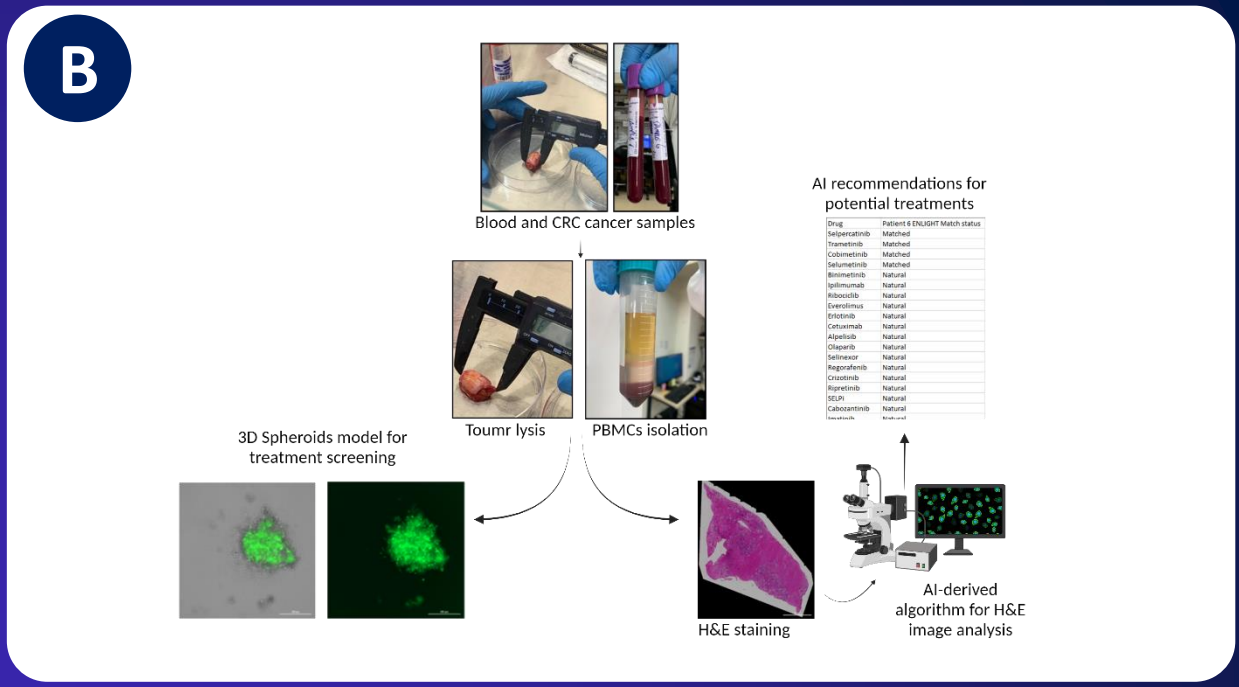
4D-BioPrinted Modular Drug Screening Platform for Cancer

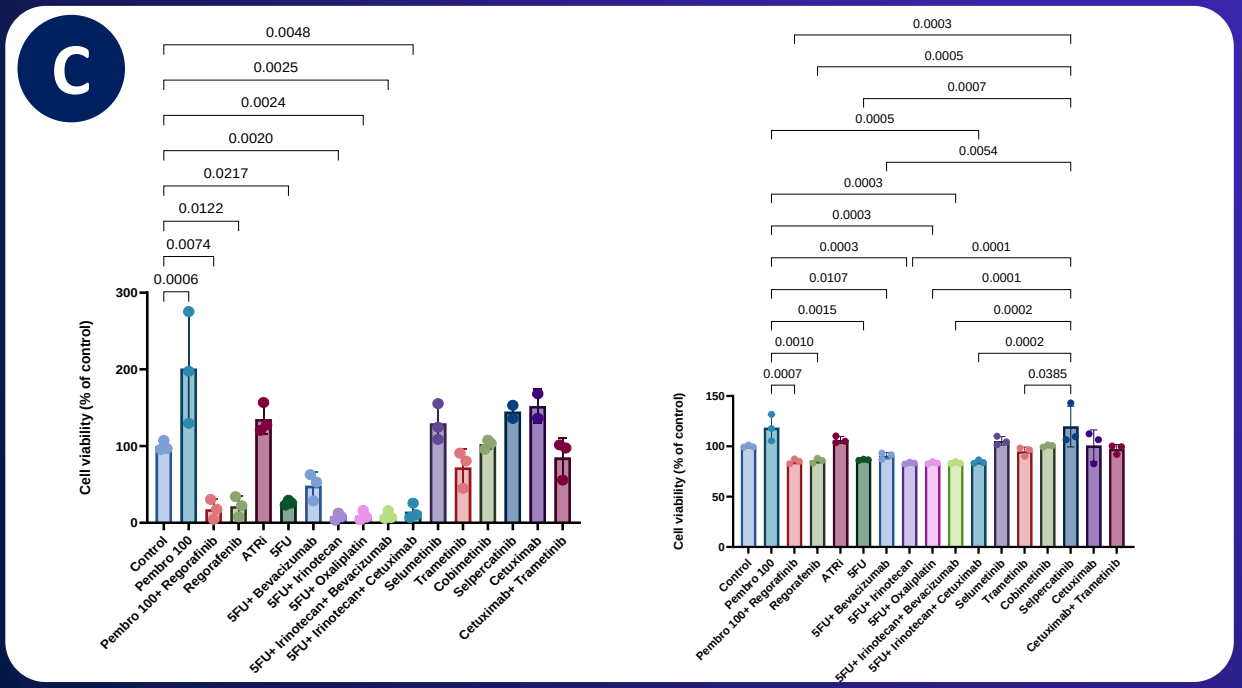
With Ronnie Frommer-Shapira, Sheba Medical Center - Pangea

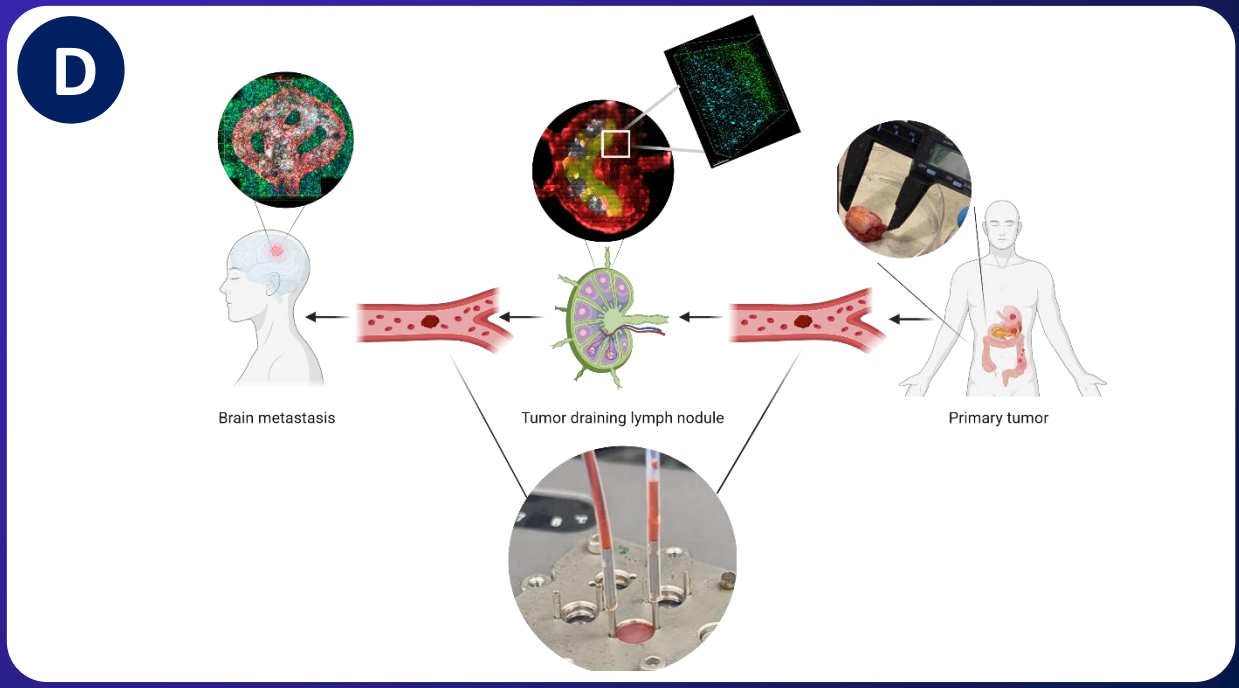
RSF Lab

TEL AVIV UNIVERSITY Pursuing the Unknown


A
Two weeks before surgery
Day of surgery
Two weeks after surgery
PBMCs
Drug Screening
Tumor sample
Biomarkers analysis by multiplex ELISA
Immune profiling by flow cytometry
Target identification by RNA-seq treatment prediction
2 days
FFPE
1 week
Sample preservation
Image analysis for treatment prediction
Target identification by RNA-seq treatment prediction
Treatment decision

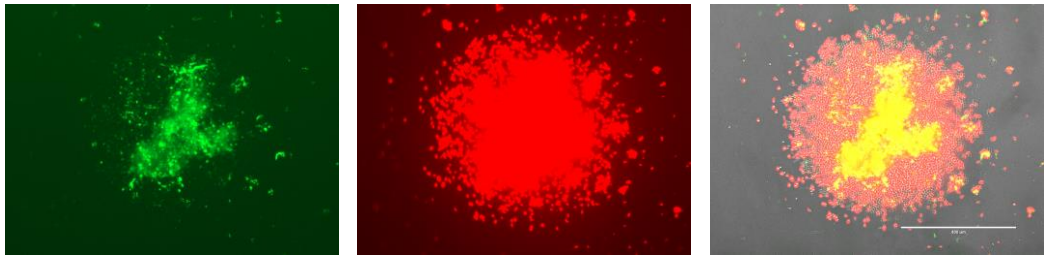

B
Blood and CRC cancer samples
AI recommendations for potential treatments
Toumr lysis
PBMCs isolation
3D Spheroids model for treatment screening
H&E staining
AI-derived algorithm for H&E image analysis

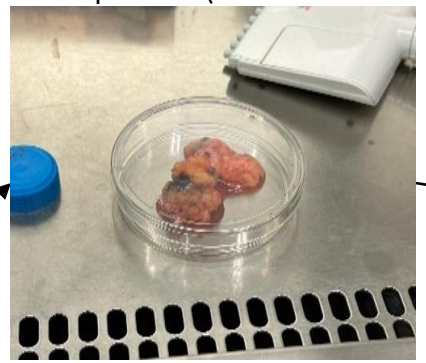

C
Cell viability (% of control)
Control
Pembro 100
Pembro 100+ Regorafinib
Regorafenib
ATRi
5FU
5FU+ Bevacizumab
5FU+ Irinotecan
5FU+ Oxaliplatin
5FU+ Irinotecan+ Bevacizumab
5FU+ Irinotecan+ Cetuximab
Selumetinib
Trametinib
Cobimetinib
Selpercatinib
Cetuximab
Cetuximab+ Trametinib

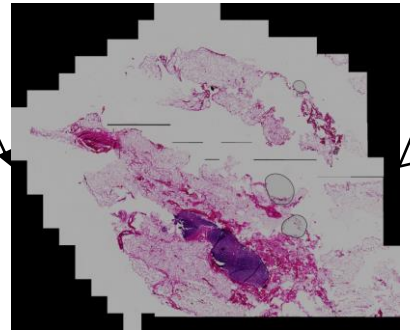

D
Brain metastasis
Tumor draining lymph nodule
Primary tumor

#9 Mucosal melanoma patient

Female, 58, malignant mucosal melanoma.
Tissue site: resected from the groin lymph node.
ECOG PS: 1
Neoadjuvant therapy: Ipilimumab + Nivolumab (4 cycles)
Adjuvant therapy: Nivo (since 5.12.23, 20.12.23, 3.1.24)
Clinical outcome: PD (evaluated in Jan 2024)- 9.1 PET CT
Residual frozen cell suspension or PBMCs: Cell suspension (10 vials * low viability) and PBMCs (1 vial)







U-shape spheroids with 15,000 cells/well.
Cells from the tumor tissue were stained with **CellBrite green** and the **PBMCs** were stained with **CellBrite red**
Cells from the tumor tissue: **PBMCs 2:1**

Drug	Patient 9 ENLIGHT Match status
Pembrolizumab	Matched
Ripretinib	Matched
Crizotinib	Matched
Pazopanib	Matched
Ramucirumab	Matched
Axitinib	Matched
Regorafenib	Matched
Tivozanib	Natural
Cabozantinib	Natural
Cobimetinib | Selumetinib	Natural
Lenvatinib	Natural
Sorafenib	Natural
Ipilimumab	Natural
Bevacizumab	Natural
Selinexor	Natural
Trametinib	Unmatched
Binimetinib	Unmatched
Olaparib	Unmatched
Alpelisib	Unmatched
Sunitinib	Unmatched
Everolimus	Unmatched
Ribociclib	Unmatched
Cetuximab | Erlotinib	Unmatched
Imatinib	Unmatched
Selpercatinib	Unmatched
SELPi	Unmatched

RSF Lab
TEL AVIV UNIVERSITY
Pursuing the Unknown

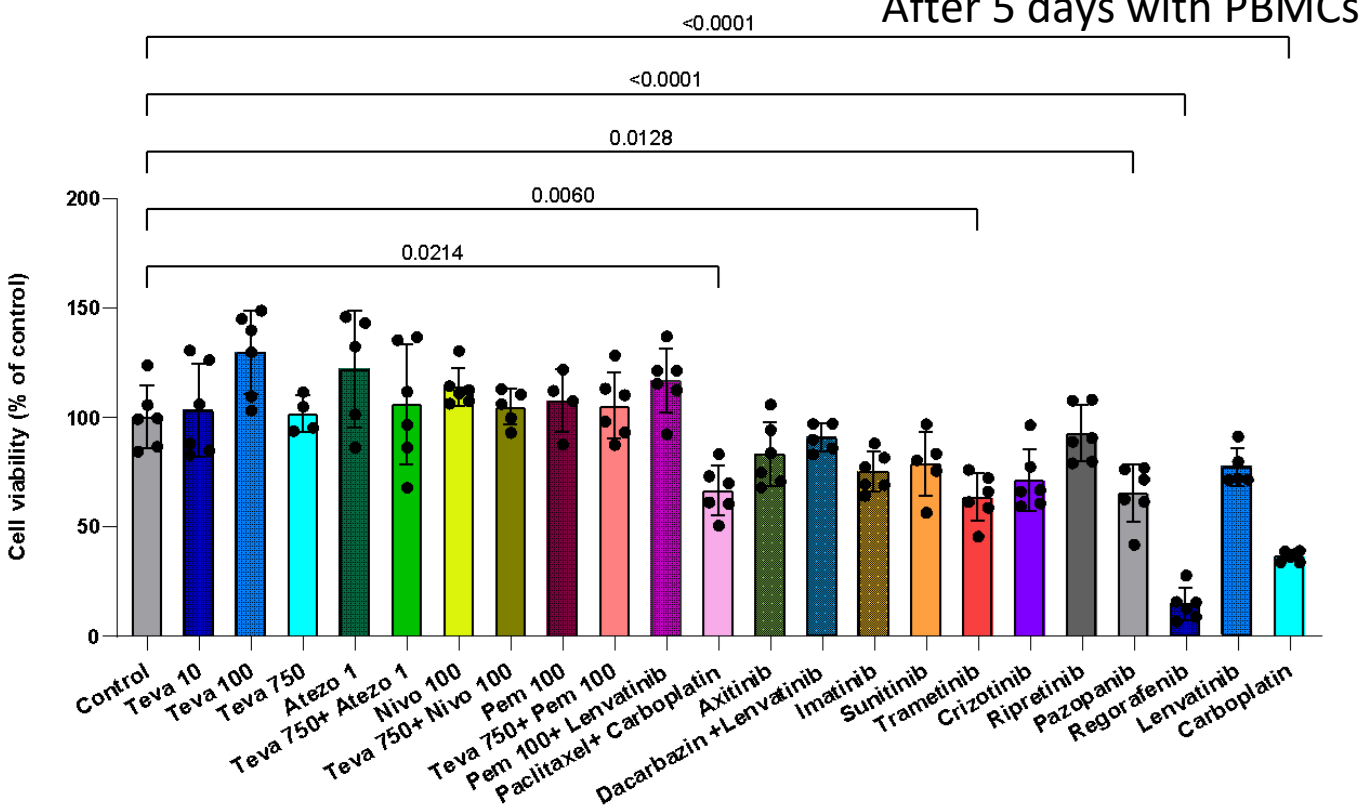
#9 Mucosal melanoma patient – Viability assay

Drug efficacy in 3D model (% Response)	Oncologists	H&E-based AI Algorithm
1. Regorafenib (93%)		Matched
2. Carboplatin (63%)	6	-
3. Trametinib (37%)	4	Unmatched
4. Pazopanib (35%)	2	Matched
5. Paclitaxel+ Carboplatin (33%)	6	-
6. Crizotinib (29%)		Matched
7. Imatinib (25%)	1	Unmatched
8. Lenvatinib (23%)	5	Neutral
9. Sunitinib (22%)	3	Unmatched
10. Axitinib (17%)		Matched
11. Dacarbazine+ Lenvatinib	7	-

All the other drugs (Teva, Atezolizumab, **Nivolumab**, Pembro, Teva+ Pembro, Pembro+ Lenvatinib) showed 0% response.- Also UNMATCHED by our H&E-based AI Algorithm

Cell viability (CellTiter-Glo®) according to the calibration curve

After 5 days with PBMCs



Clinical status- Progressive disease
Tx: 4 cycles Ipi-Nivo, surgery, 2 cycles of Nivolumab
Adjuvant- Regorafenib?

Axitinib VEGFR inhibitor

Crizotinib Tyrosine kinase inhibitor, targeting (EML4)-ALK fusion protein

Carboplatin antineoplastic alkylating agent

Dacarbazine Antineoplastic agent

Imatinib Tyrosine kinase inhibitor

Lenvatinib RTK inhibitor, targeting VEGFR, FGFR, PDGFRa, KIT, RET

Trametinib MEK inhibitor

Atezolizumab Anti-PD-L1 antibody immunotherapy

Paclitaxel taxoid chemotherapeutic agent

Pazopanib inhibitor of multiple protein tyrosine kinases with potential antineoplastic activity.

Pembrolizumab/ Nivolumab Anti PD-1 receptor

Regorafenib A kinase inhibitor (VEGFR)

Ripretinib kinase inhibitor targeting KIT and PDGFRA

Sunitinib targeting multiple RTK, including PDGFR, VEGFR, KIT, RET, FLT3

Teva Immunotherapy

PD-1/ PD-L1 small-molecule modulators versus mAbs


Rita Guedes


Helena Florindo

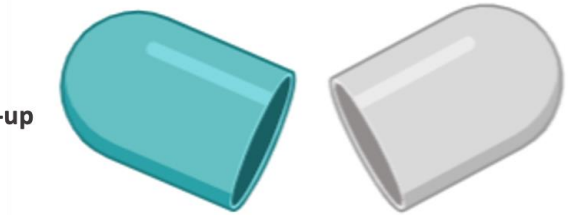

Rita Acúrcio

Discovery of new small-molecule immune system modulators targeting PD-1/PD-L1 interaction using computer-assisted drug design (CADD) approach

Offer the possibility of avoiding macrophage-induced PD-1 resistance

Possible oral bioavailability

Easier access to intracellular targets

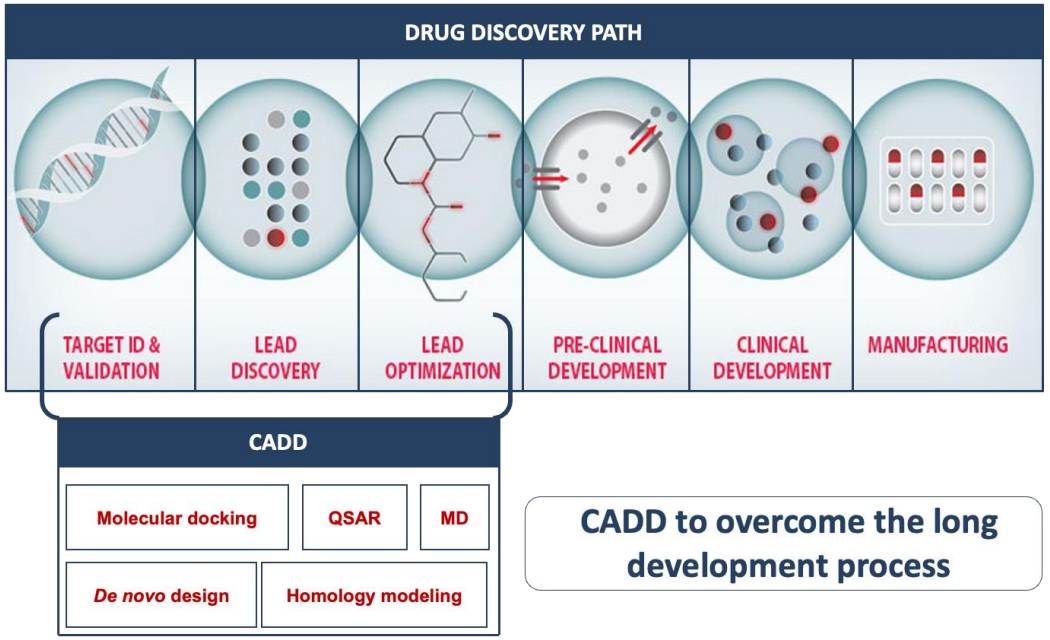


High manufacturing and scale-up feasibility

Improved pharmacokinetics and/or pharmacodynamics

Greater diffusion rate within the tumor microenvironment

More affordable and accessible than mAbs



CADD to overcome the long development process

No PD-1/PD-L1 small-molecule modulators have been ever approved

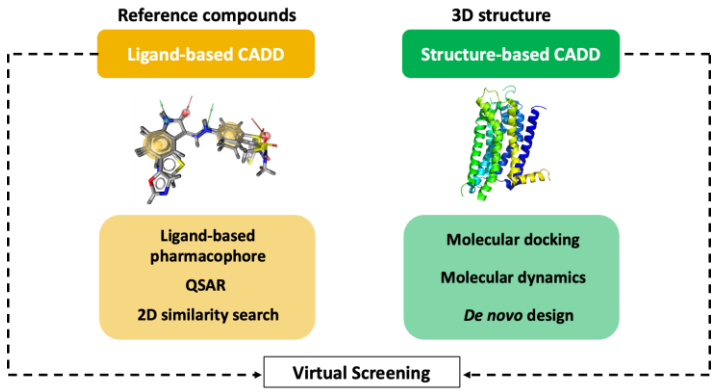
Acúrcio R. et al., Journal for Immunotherapy of Cancer, 2022

U LISBOA
imed Research Institute for Medicines
RSF Lab
TEL AVIV UNIVERSITY Pursuing the Unknown

PD-1/ PD-L1 small-molecule modulators: our strategy



Rita Guedes Helena Florindo Rita Acúrcio



Hit validation

- *In vitro* & *ex vivo* assessment of PD-1/PD-L1 inhibition.
- T-cell activation by PD-1/PD-L1 inhibition

- Anti-tumor efficacy
- Impact on tumor immune cell profiling

In silico

PD-1/PD-L1 binding assays (High Throughput Format, Differential Scanning Fluorometry, WaterLOGSY NMR)

In vitro & Ex

In vivo

Acúrcio R. et al., Journal for Immunotherapy of Cancer, 2022

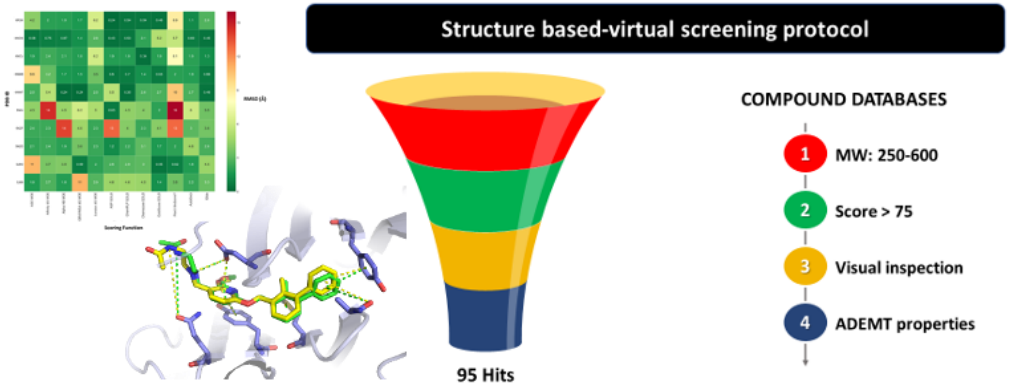
imed Research Institute for Medicines RSF Lab TEL AVIV UNIVERSITY Pursuing the Unknown

Discover and develop PD-1/PD-L1 small molecule modulators

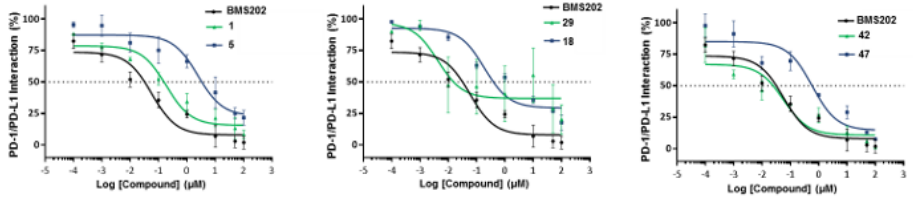


Rita Guedes Helena Florindo Rita Acúrcio

In silico



Hit validation

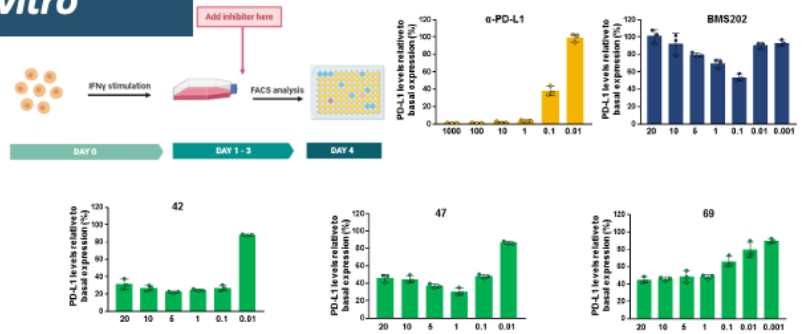


Inhibitor	IC_{50} (μM) ± SD	Docking score
1	0,186 ± 0,066	108
5	2,39 ± 1,037	79
BMS202	0,057 ± 0,022	102

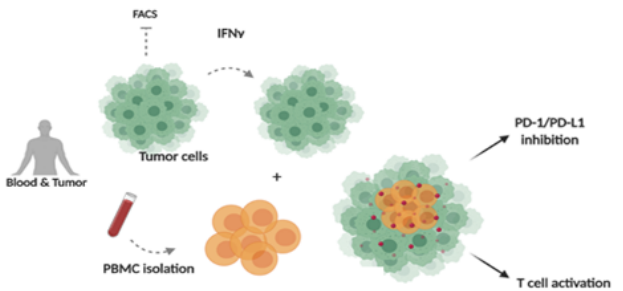
Inhibitor	IC_{50} (μM)	Docking score
18	0,190 ± 0,069	101
29	0,004 ± 0,004	106
BMS202	0,057 ± 0,022	102

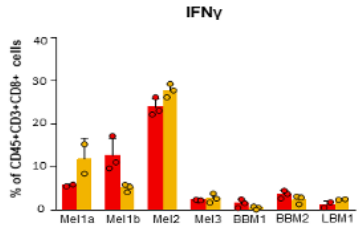
Inhibitor	IC_{50} (μM)	Docking score
42	0,057 ±0,031	91
47	0,596 ± 0,024	83
BMS202	0,057 ± 0,022	102

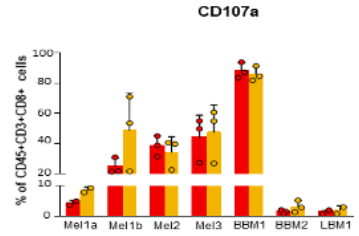
In vitro



Ex vivo







Acúrcio R. et al., Journal for Immunotherapy of Cancer, 2022

imed Research Institute for Medicines

RSF Lab

TEL AVIV UNIVERSITY Pursuing the Unknown

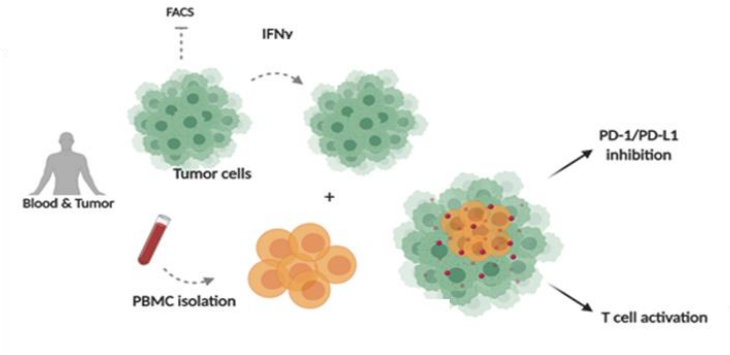
PD-1/ PD-L1 small-molecule modulators: our strategy



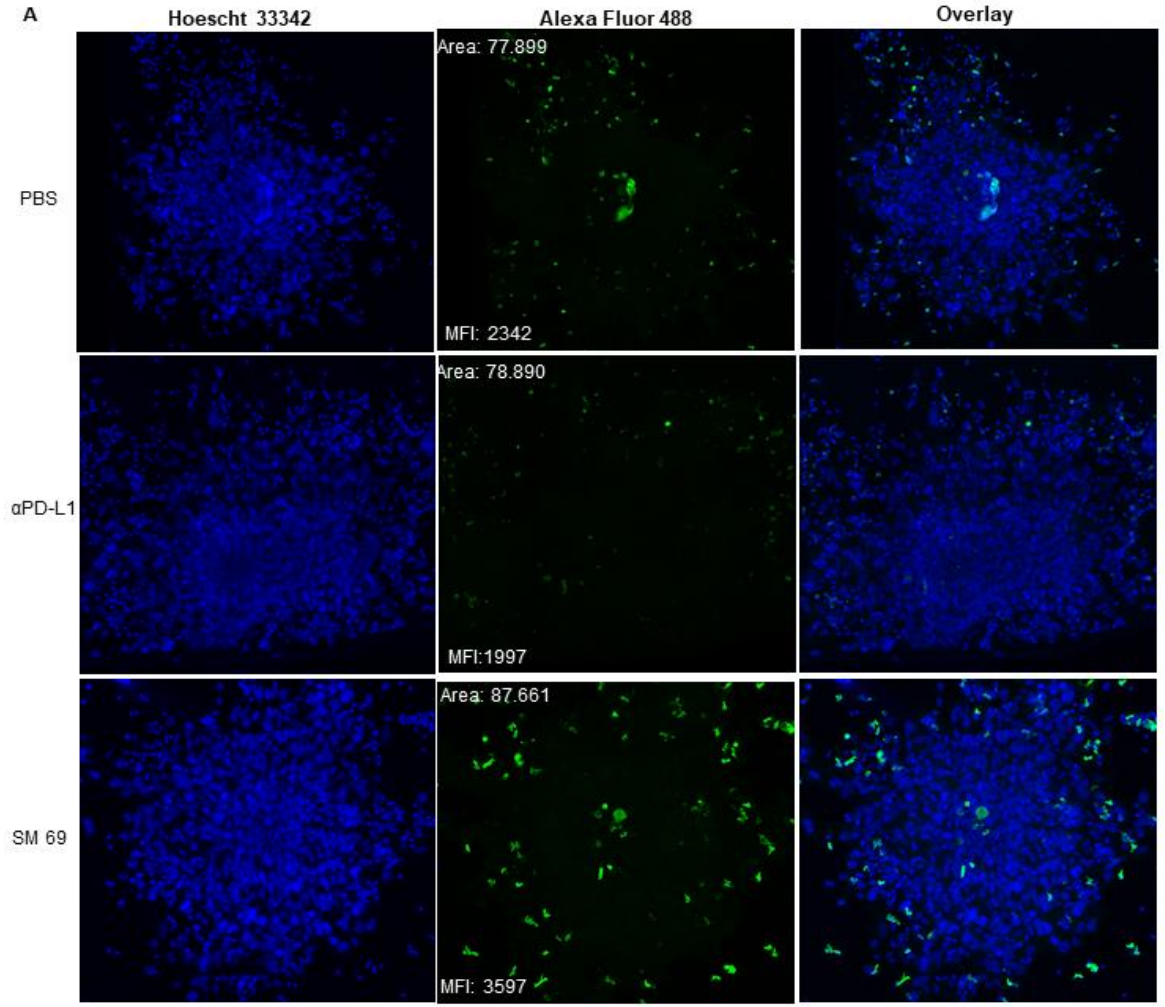
Rita Guedes Helena Florindo Rita Acúrcio

In vitro & Ex vivo

CD8⁺ T-cell infiltration on 3D spheroids of melanoma composed of patient-derived melanoma cells and autologous PBMC



PD-1/PD-L1 small molecule inhibitor promote T-cell infiltration and decrease tumor cell sprouting.



Mean ± SD, N = 3, from one independent experiment performed in triplicate or duplicate (limited amounts of patient tumor or blood available).

Acúrcio R. et al., Journal for Immunotherapy of Cancer, 2022

imed Research Institute for Medicines
RSF Lab
TEL AVIV UNIVERSITY Pursuing the Unknown

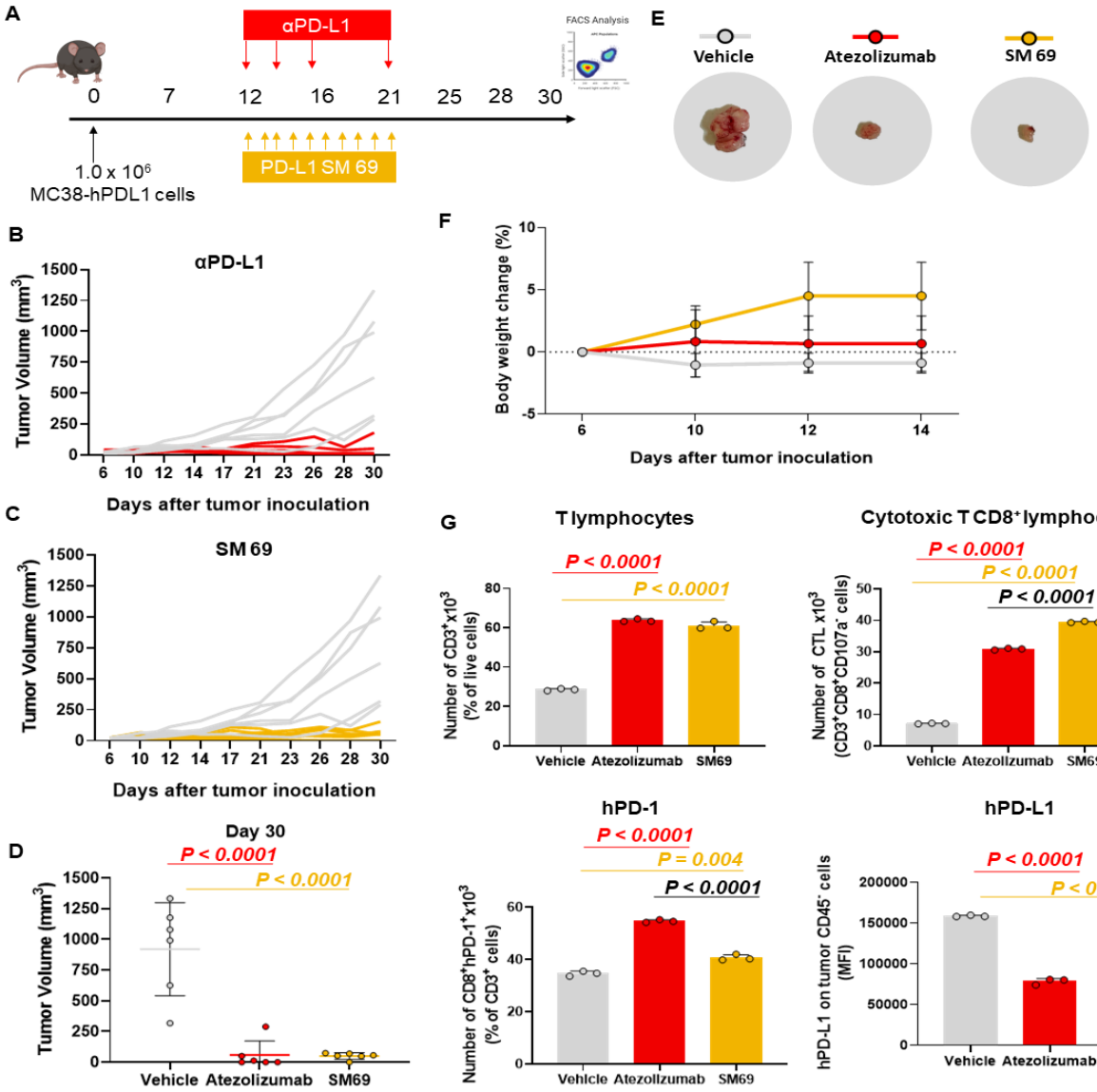
PD-1/ PD-L1 small-molecule modulators: our strategy



Rita Guedes Helena Florindo Rita Acúrcio

In vivo

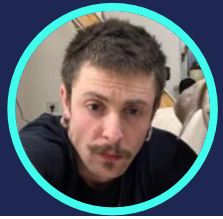
- We discovered small molecules that are effective alternatives to PD-L1 monoclonal antibodies:
  - Restores T-cell function
  - Control tumor growth
  - Suitable for different routes of administration



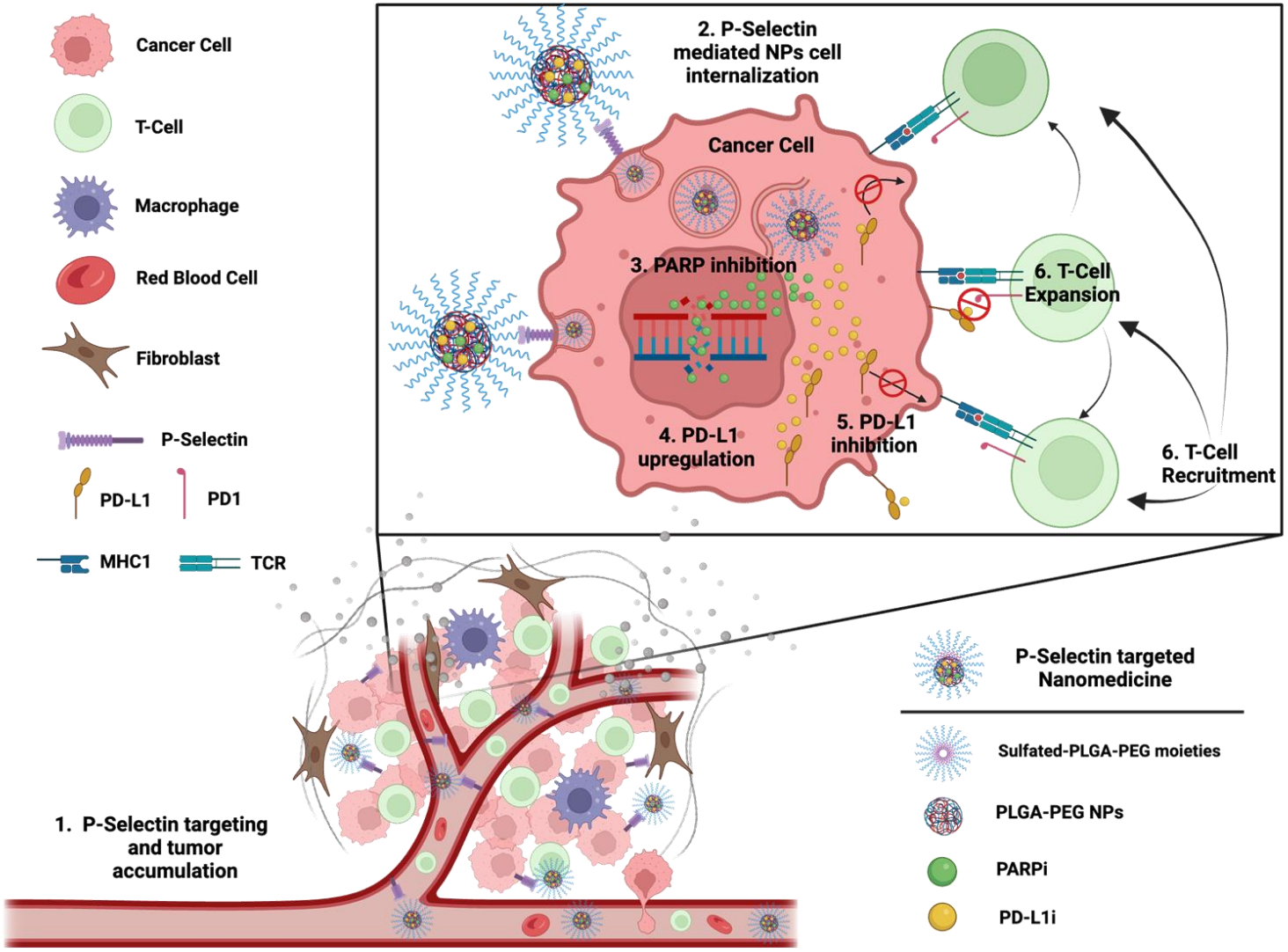
Acúrcio R. et al., Journal for Immunotherapy of Cancer, 2022

TEL AVIV UNIVERSITY
Pursuing the Unknown

P-Selectin-targeted Polymeric Nanomedicine for BRCA-mutated BC



Daniel Rodriguez Shani Koshrovski-Michael Pradip Dey



Selectin Therapeutics, Inc.
PRECISION NANOMEDICINE

RSF Lab

TEL AVIV UNIVERSITY
Pursuing the Unknown

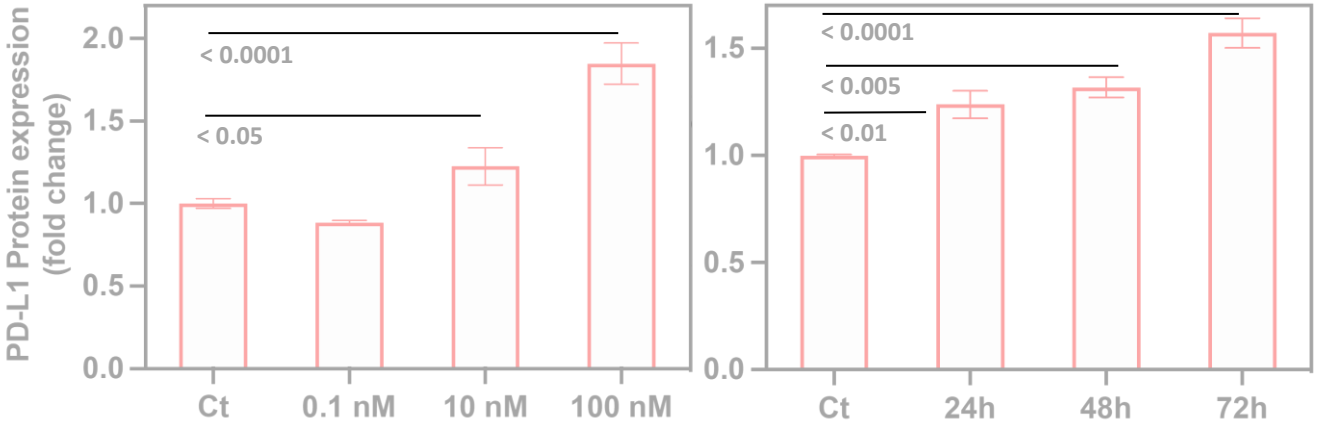
Koshrovski-Michael *et al.*, *Science Advances*, 2024

PARPi Treatment Induces PD-L1 Expression

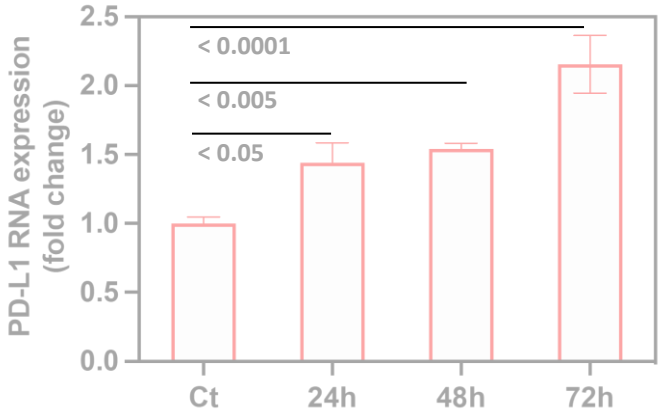


Daniel Rodriguez **Shani Koshrovski-Michael** **Pradip Dey**

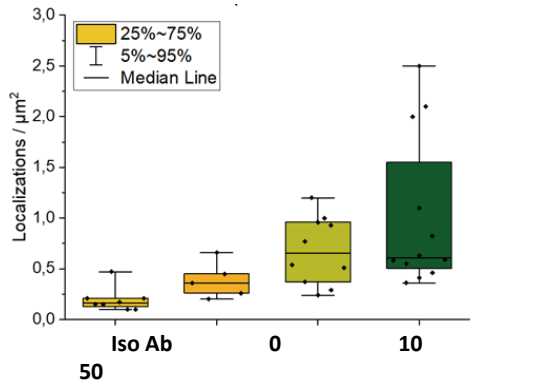
PARPi-induced PD-L1 **Protein** Expression in a Dose-(left) and Time-(right) Dependent Manner

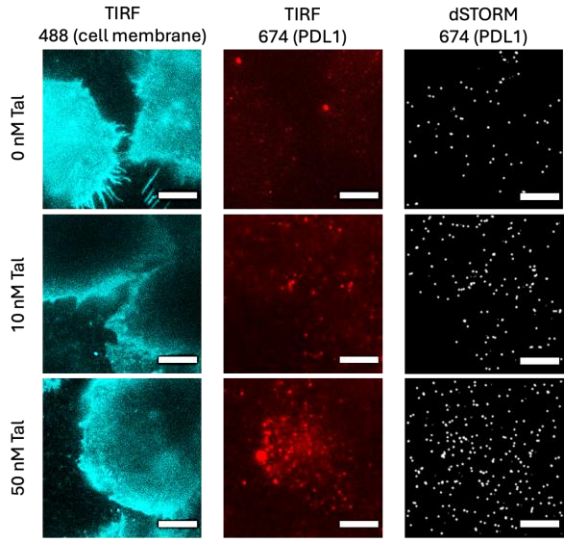


PARPi-induced PD-L1 **RNA** Expression in a Time-Dependent Manner



dSTORM localizations per cell after PARPi treatment





Koshrovski-Michael *et al.*, *Science Advances*, 2024

RSF Lab

TEL AVIV UNIVERSITY
Pursuing the Unknown

Computer-assisted drug designed PD-L1i Small Molecule Immunotherapy (SMi)


Adi Yona


Shir Shahar


America Garcia Alvarado

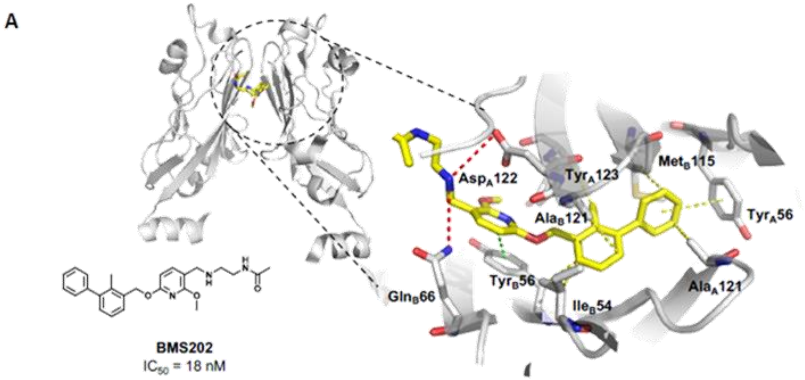

Marina Green Buzhor

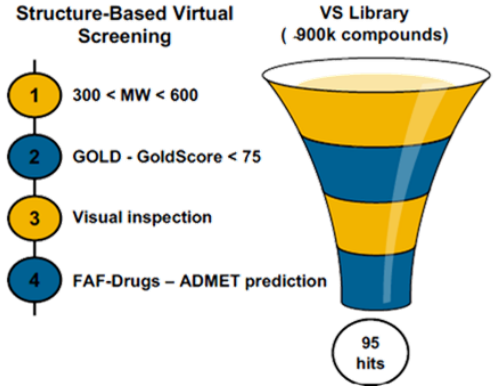
1. **BRCA mutation is associated with ↑ TILS**

2. **PARPi therapy might impact the TME**
   - Downregulate proinflammatory cytokines
   - Can recruit DC, NK and macrophages
   - Increase neoantigen production
   - Increase ICI's expression

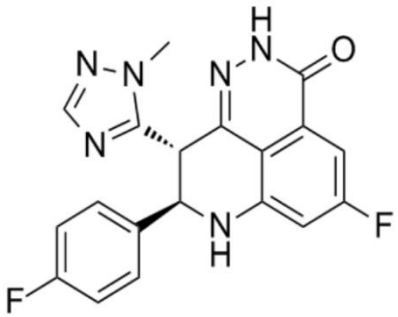
Identification of novel small molecules *in silico:*

- 3D protein modelling
- Molecular docking
- Chemical filtering





PARPi- Talazoparib

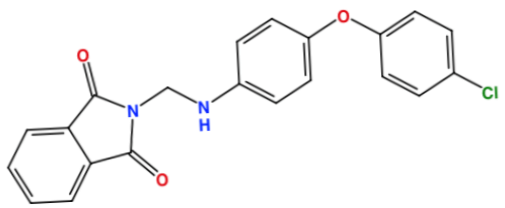


+

Atezolizumab

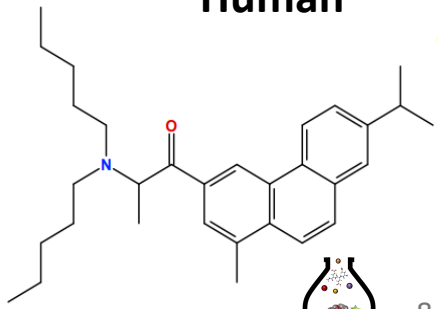
Koshrovski-Michael *et al.*, *Science Advances,* 2024

Murine



Acurcio *et al.*, JITC 2024

Human



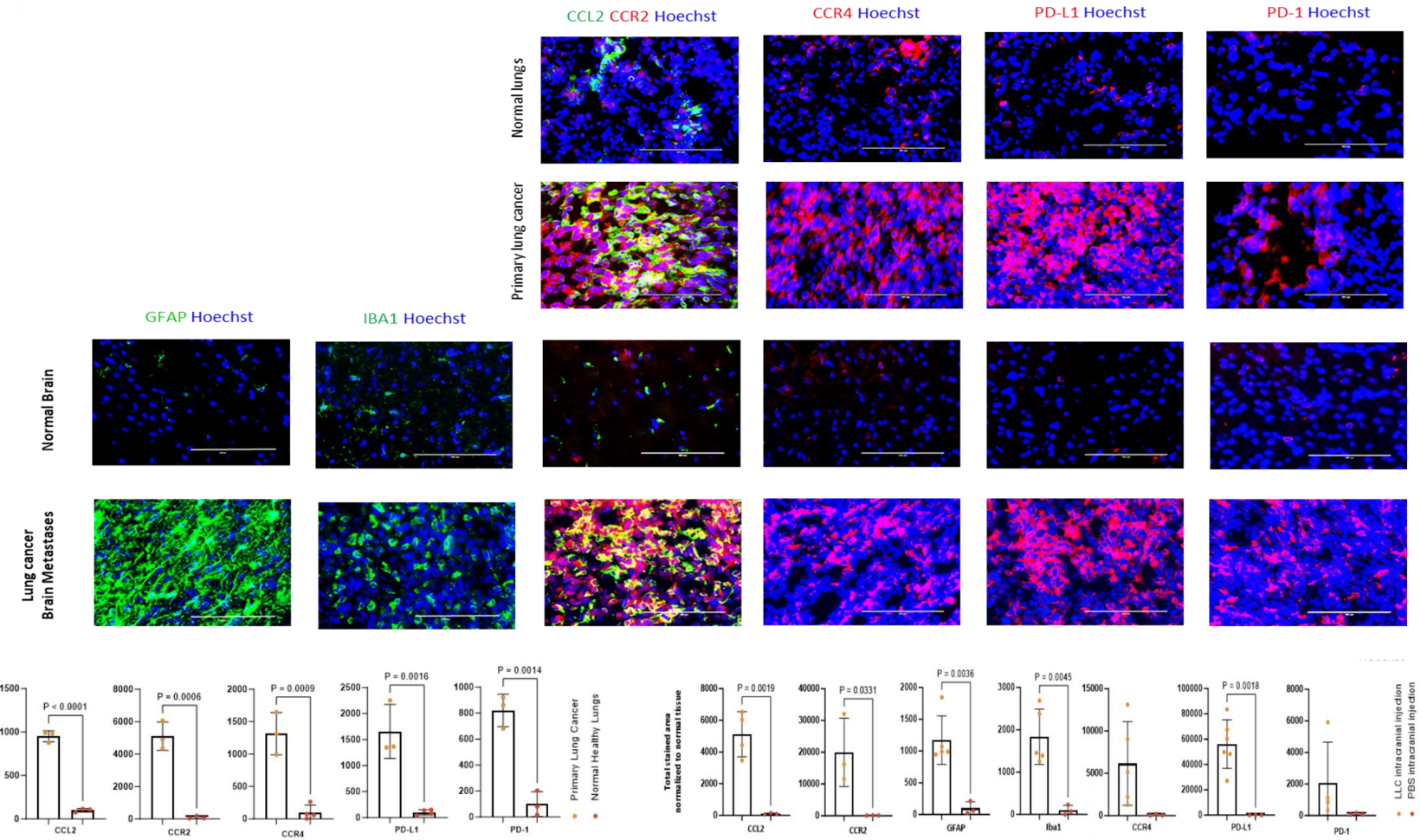
RSF Lab

TEL AVIV UNIVERSITY Pursuing the Unknown

P-selectin, CCL2, and PD-L1 are overexpressed in melanoma, breast and lung cancer brain metastases



Sabina Pozzi Sahar Israeli Dangoor Adan Miari



Yeini, *et al.,* Nature Communications 2021; Pozzi, *et al., JCII* 2022; Israeli Dangoor, *et al*., Brain, 2025

RSF Lab

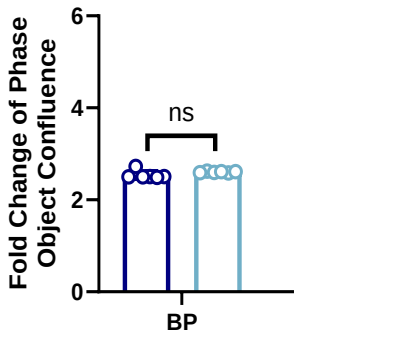
TEL AVIV UNIVERSITY
Pursuing the Unknown

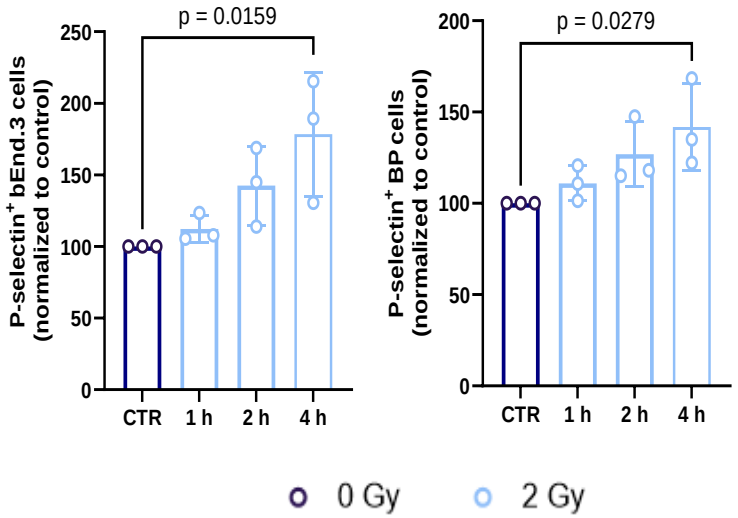
Tumor and endothelial cells upregulate P-selectin's expression upon low-dose irradiation



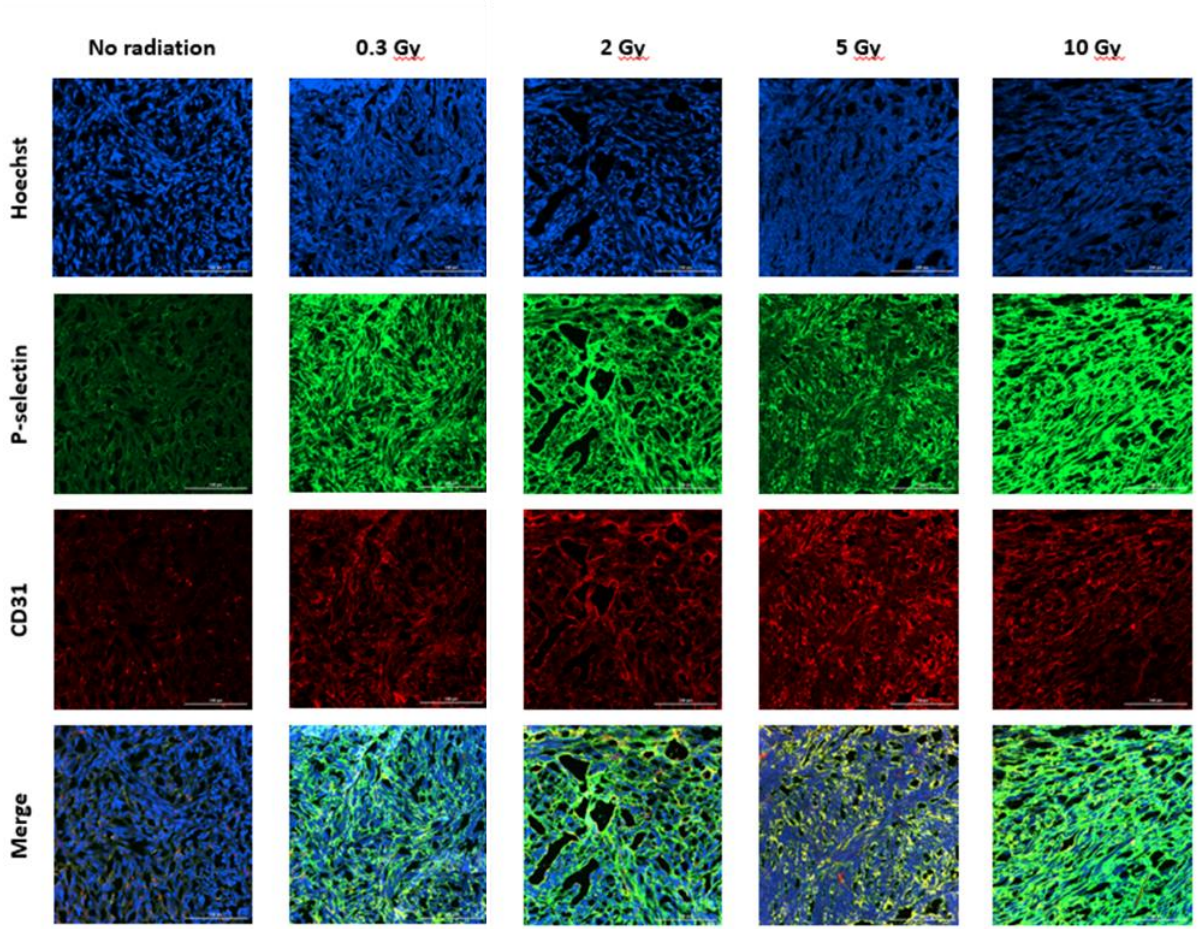
Tania Barnatan Giuseppe Longobardi Rami Khoury

in vitro





in vivo



Khoury, Longobardi, Barnatan *et al.*, JCR, 2025

RSF Lab

TEL AVIV UNIVERSITY
Pursuing the Unknown

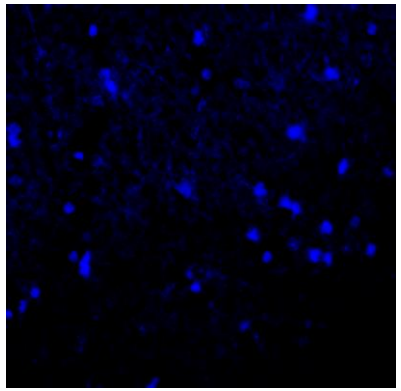
P-Selectin overexpression on tumor-adjacent blood vessels of pediatric brain tumors




Dana Venkert Tania Barnatan Giuseppe Longobardi Rami Khoury

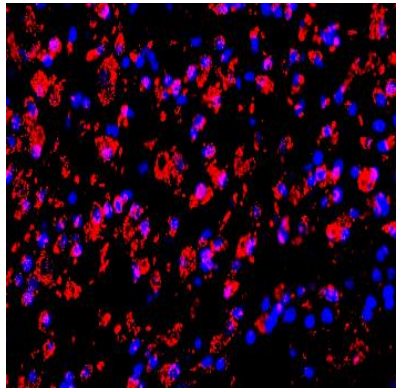
P-selectin in pediatric brain tumors

Normal brain



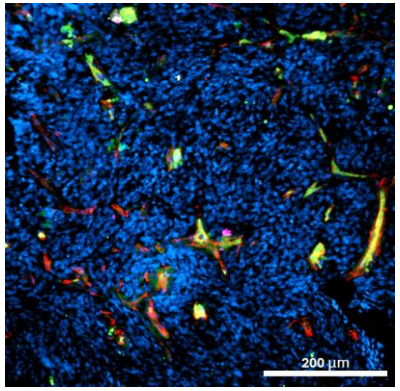
HOECHST P-Selectin

Pediatric DIPG



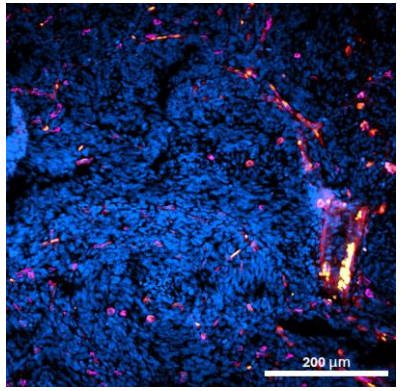
HOECHST P-Selectin

Pediatric LGG



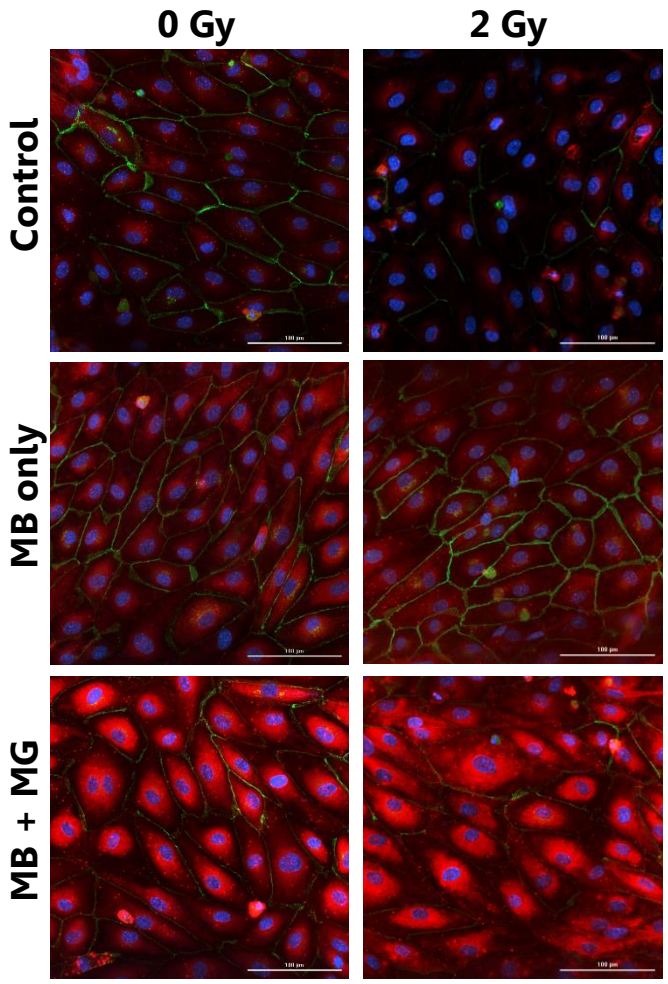
HOECHST CD31
P-Selectin PSGL-1

Pediatric MB

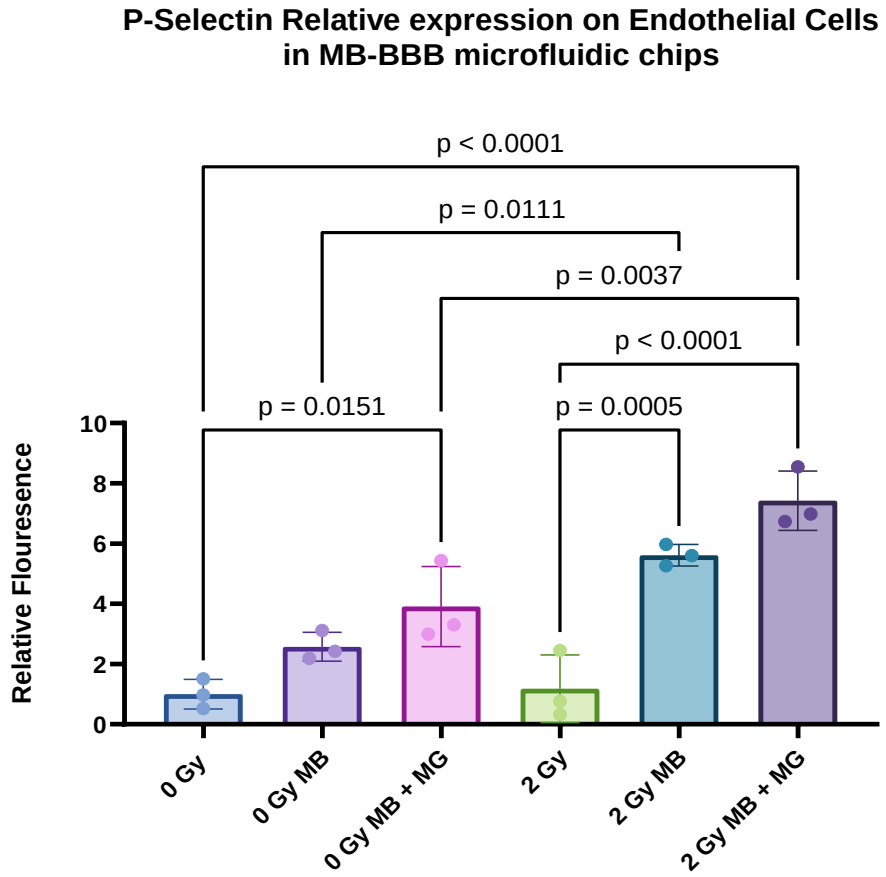


HOECHST CD31
P-Selectin PSGL-1

In vitro 3D microfluidic tumor-on-a-chip model



DAPI P-Selectin VE-CAD



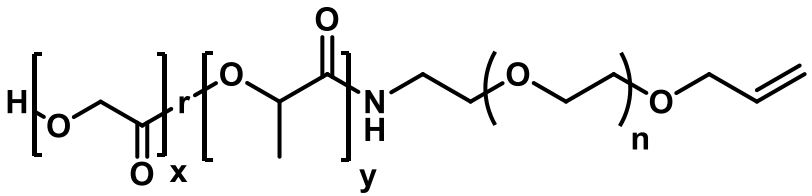
RSF Lab

TEL AVIV UNIVERSITY
Pursuing the Unknown

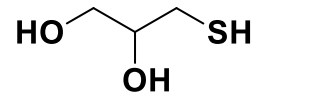
Mimicking the natural endogenous P-selectin ligand-1 by synthesizing sulfated polymers



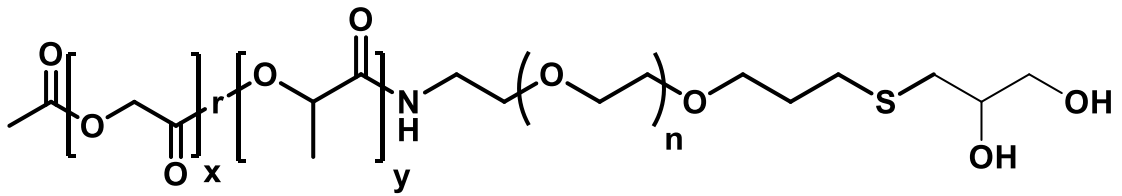
Ohad Hasin
Adi Yona
Marina Green Buzhor

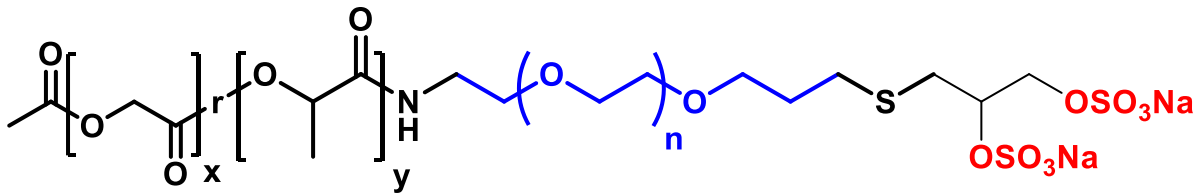


quantitative yield



quantitative yield



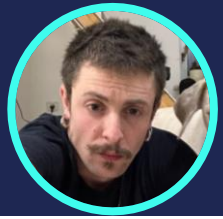


PLGA-PEG-GLY-$(OSO_3Na)_2$

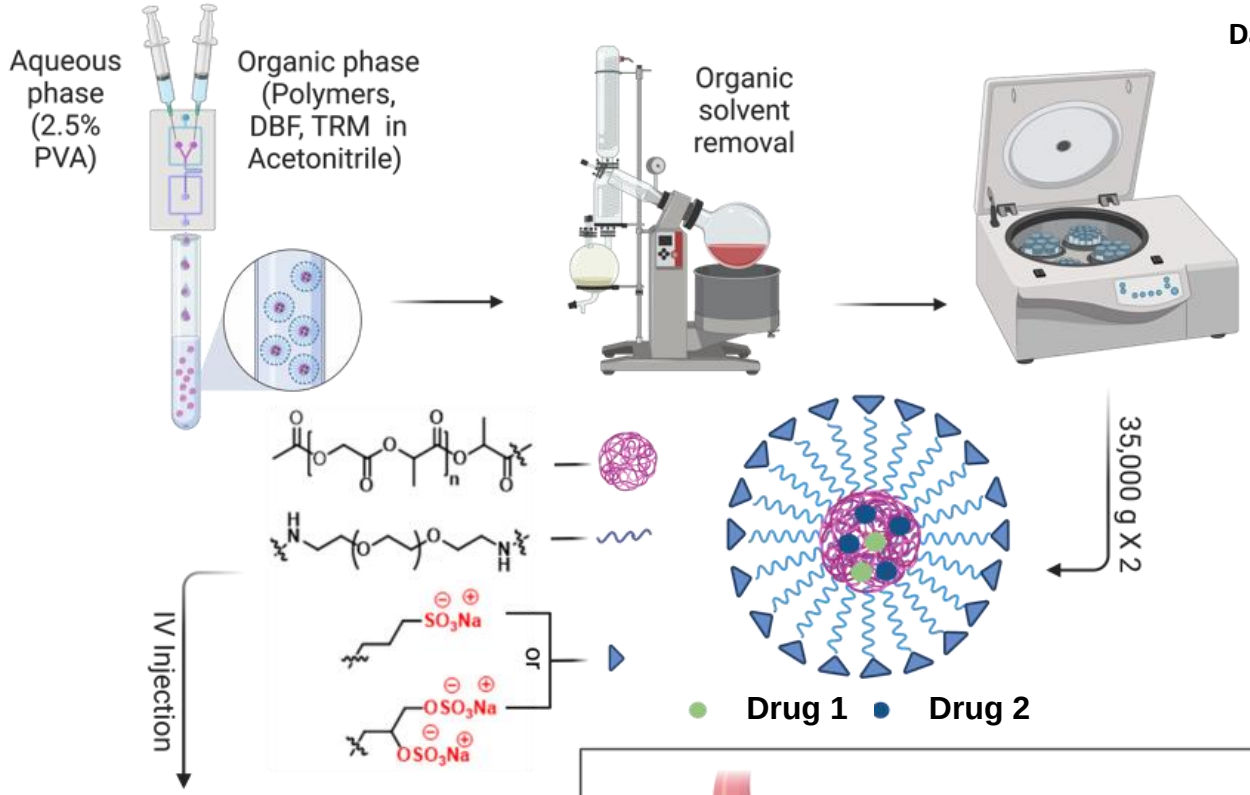
RSF Lab

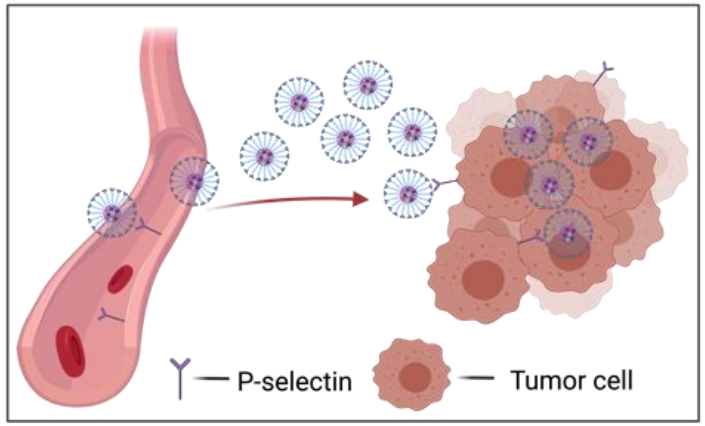
TEL AVIV UNIVERSITY
Pursuing the Unknown

Altering the PK profile of PARP and PD-L1 inhibitors with P-selectin-targeted NPs leads to better and safer therapy



Daniel Rodriguez Shani Koshrovski-Michael Pradip Dey





Koshrovski-Michael *et al.*, *Science Advances*, 2024

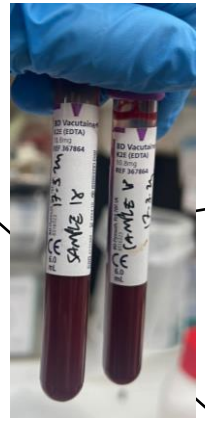
Selectin Therapeutics, Inc.
PRECISION NANOMEDICINE

RSF Lab

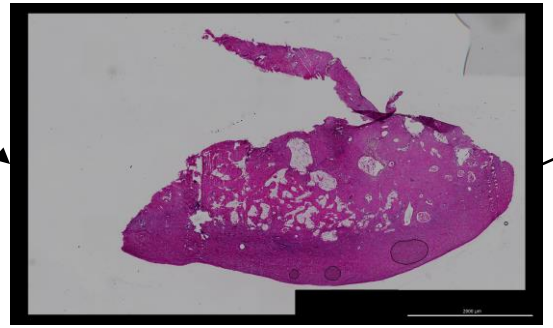
TEL AVIV UNIVERSITY
Pursuing the Unknown

18 CRC 17/3/24 Summary

Female, 48, Moderately differentiated adenocarcinoma
Hemicolectomy, Stroke
The mass shows moderately differentiated adenocarcinoma, mucinous carcinoma, extending to serosa. Focal vascular invasion.
MSS, TMB 7 (intermediate), BRAF V600E, **TP53** c.844C>T p.Arg282Trp, **SMAD4** c.1324C>T p.Gln442Ter, **CHEK2** c.1283C>T p.Ser428Phe
Tissue site: Ovary
ECOG PS: 0
Neoadjuvant therapy: Folfox (4 cycles), Folfiri (1-cycles) (5FU- 2 doses of 3700mg)
Adjuvant therapy: Irinotecan (514mg)+ Encorafenib+ Cetuximab (400mg) -> Irinotecan+ Cetuximab (suffered from side effects of Myalgia)
Clinical outcome: Pet CT from 22.6.24 showed NED. Next scan in September 2024
Residual frozen cell suspension or PBMCs: only PBMCs (1 vial)



U-shape spheroids with 15,000 cells/well.
Cells from the tumor tissue were not stained while the **PBMCs were** stained with **CellBrite orange**
Cells from the tumor tissue: PBMCs 2:1



Drug	ENLIGHT Match status	Score
SELPi	Strong matched	0.76
Trametinib	Strong matched	0.66
Cobimetinib | Selumetinib	Strong matched	0.66
Crizotinib	Strong matched	0.65
Imatinib	Strong matched	0.64
Cabozantinib	Strong matched	0.63
Sorafenib	Matched	0.6
Sunitinib	Matched	0.6
Everolimus	Matched	0.6
Cetuximab | Erlotinib	Matched	0.6
Axitinib	Matched	0.58
Tivozanib	Matched	0.58
Ramucirumab	Matched	0.56
Pazopanib	Matched	0.56
Pembrolizumab	Neutral	0.55
Selpercatinib	Matched	0.54
Vemurafenib	Matched	0.54

18 CRC 17/3/24 - Recommendations

RSF Lab

SHEBA Tel HaShomer

The oncologists' recommendations

1. **Braf+ Cetuximab**
2. **Braf+ MEK+ Cetuximab**
3. **Irinotecan+** Vemurafenib**+ Cetuximab**
4. **Braf+ MEK**
5. Everolimus

pangea biomed

Pangea's recommendations

1. **SELPi**
2. **Trametinib**
3. Cobimetinib | Selumetinib
4. **Crizotinib**
5. Imatinib
6. **Cabozantinib**
7. Sorafenib
8. **Sunitinib**
9. Everolimus
10. **Cetuximab** | Erlotinib
11. Axitinib
12. Tivozanib
13. Ramucirumab
14. **Pazopanib**
15. Pembrolizumab
16. Selpercatinib
17. Vemurafenib

Investigational drugs

Teva

Crizanlizumab

Dabrafenib+ Trametinib NPs

Crizalizumab a P-selectin inhibitor

Dabrafenib/ Vemurafenib BRAF inhibitor

Teva Immunotherapy

Trametinib MEK inhibitor

Axitinib VEGFR and kinase inhibitor

Sunitinib RTK inhibitor

Crizotinib Receptor tyrosine kinase inhibitor

Cetuximab IgG1 monoclonal antibody against EGFR

Pembrolizumab Anti-PD-1 antibody immunotherapy

Irinotecan antineoplastic enzyme inhibitor

Regorafenib a kinase inhibitor

Crizanlizumab Anti P-selectin

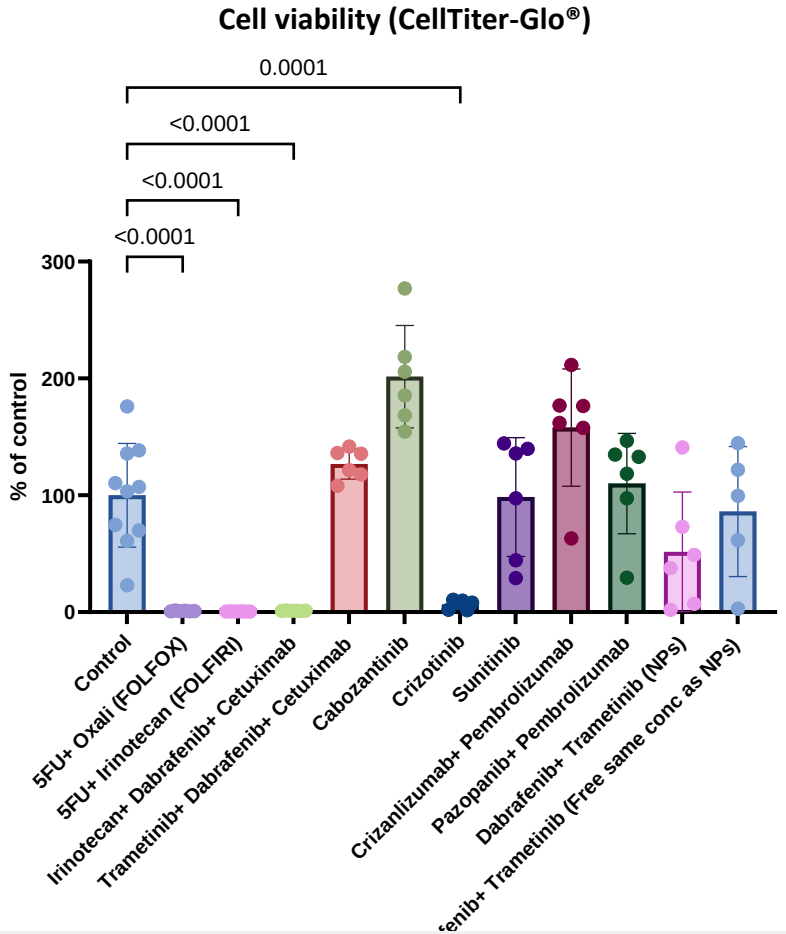
Cabozantinib TKI

Pazopanib small molecule inhibitor of multiple protein tyrosine kinases with potential antineoplastic activity

18 CRC 17/3/24 Summary- Viability assay

After 5 days
With PBMCs

Drug efficacy in 3D model (% Response)	Oncologists	Pangea
5FU+ Oxaliplatin (99%)		
5FU+ Irinotecan (99%)		
Irinotecan+ Dabrafenib+ Cetuximab (99%)		Cetuximab 10
Crizotinib (92%)		4
Dabrafenib+ Trametinib as NPs (49%)		
Dabrafenib+ Trametinib as free drug (14%)		
Sunitinib (2%)		8



Crizalizumab 2.6 µg/mL
a P-selectin inhibitor

Dabrafenib 10nM (NPs)/ 10ng/mL/ Vemurafenib
BRAF inhibitor

Teva
Immunotherapy

Trametinib 1nM (NPs)/12 ng/mL
MEK inhibitor

5FU 25µg/mL
Pyrimidine analog

Crizotinib 2.32 ug/mL
Receptor tyrosine kinase inhibitor

Sunitinib 31.8 ng/mL
RTK inhibitor

Cetuximab 0.3mg/ml
IgG1 monoclonal antibody against EGFR

Pembrolizumab pem 100ug/mL
Anti-PD-1 antibody immunotherapy

Irinotecan 9µg/mL
antineoplastic enzyme inhibitor

Cabozantinib 2.5 ng/mL
TKI

Oxaliplatin 385µg/mL
Platinum-based chemotherapy agent

Pazopanib 175 ng/mL
small molecule inhibitor of multiple protein tyrosine kinases with potential antineoplastic activity

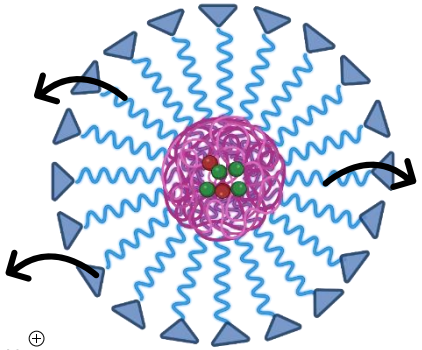
Cabozantinib, Teva, Crizanlizumab, and Pazopanib showed 0% response.

Sulfated-PLGA-PARPi/PD-L1i NPs are highly monodisperse, reproducible and scalable

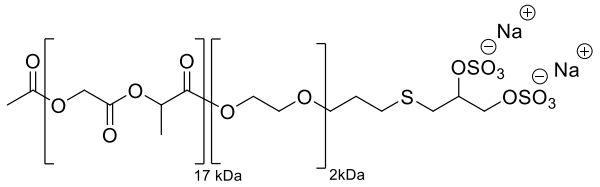
Shir Shahar

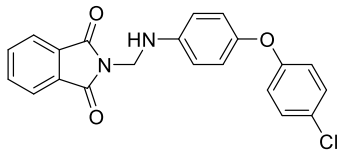
America Garcia Alvarado

Poly(Lactide-co-glycolide) – PLGA (85:15) 70 kDa

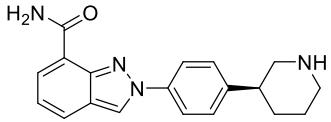


AcO-PLGA-*b*-PEG-$(SO_3)_2$

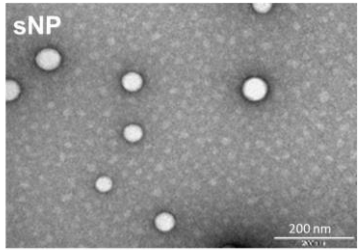


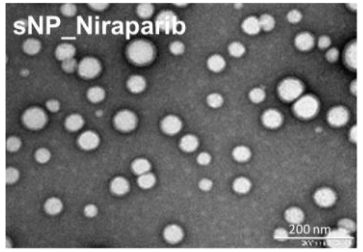


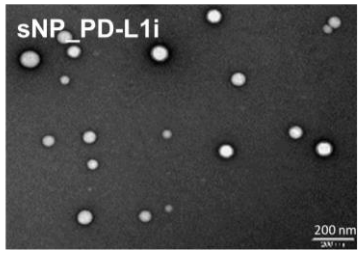
PD-L1i

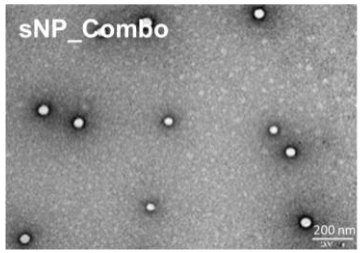


Niraparib

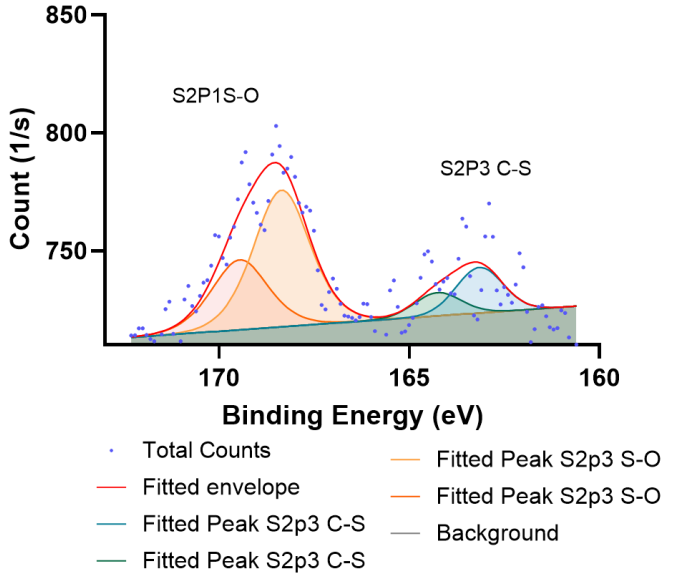








	Size by DLS (nm)		ζ (mV)		PDI		DLC (wt %)		DLE (%)		
Sample name	Size by TEM (nm)	Before lyophilization	After lyophilization	Before lyophilization	After lyophilization	Before lyophilization	After lyophilization	Niraparib	PD-L1i	Niraparib	PD-L1i	Yield [%]
sNP	42 ± 8.0	110 ± 1.5	119 ± 1.5	-33 ± 9.0	-26 ± 0.8	0.16 ± 0.01	0.19 ± 0.01	-	-	-	-	55 ± 4.8
sNP_Nir	52 ± 14.0	108 ± 6.0	124 ± 0.9	-30 ± 5.0	-20 ± 0.4	0.20 ± 0.01	0.20 ± 0.01	4 ± 0.5	-	59 ± 3.2	-	55 ± 10
sNP_PD-L1i	45 ± 8.0	113 ± 2.0	118 ± 1.8	-29 ± 4.0	-23 ± 4.5	0.19 ± 0.01	0.20 ± 0.01	-	16.9 ± 2.9	-	84 ± 7.2	60 ± 5.7
sNP_Combo	42 ± 8.0	110 ± 1.5	119 ± 1.5	-33 ± 9.0	-26 ± 0.8	0.16 ±0.01	0.19 ± 0.01	4.5 ± 0.4	17 ± 0.8	53 ± 4.8	87 ± 1.3	55 ± 4.8



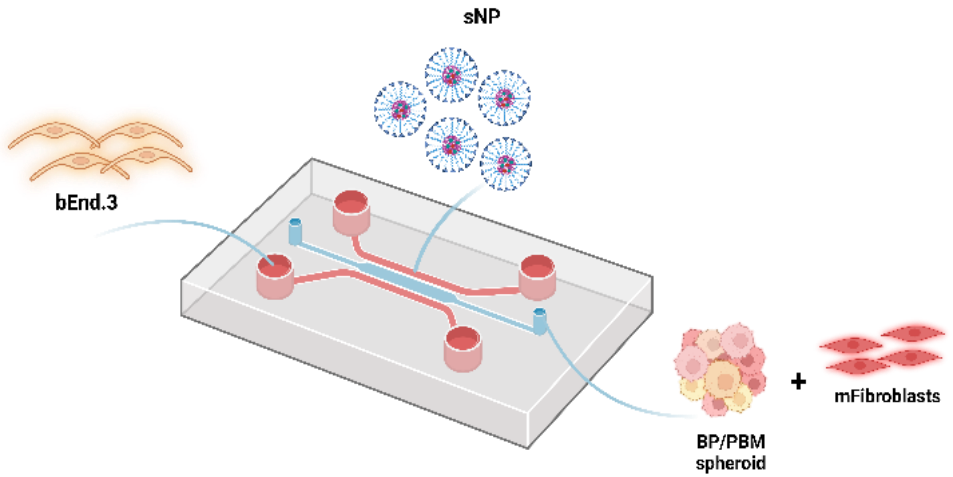
Khoury, Longobardi, Barnatan *et al.*, JCR, 2025

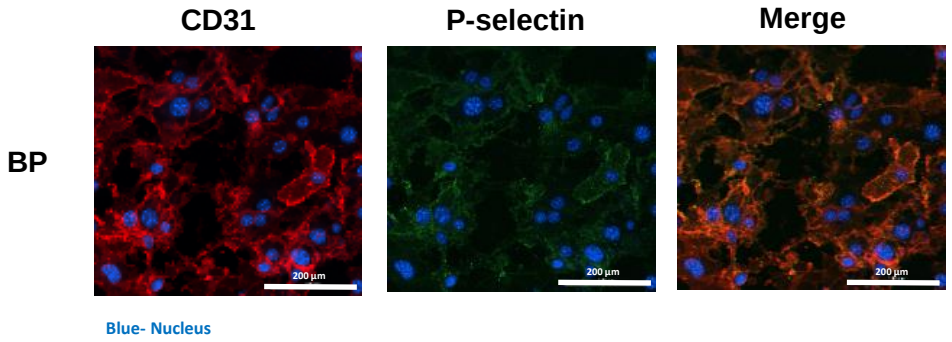
Radiation enhances the accumulation of sNPs in advanced tumor-on-a-chip model



Tania Barnatan Giuseppe Longobardi Rami Khoury

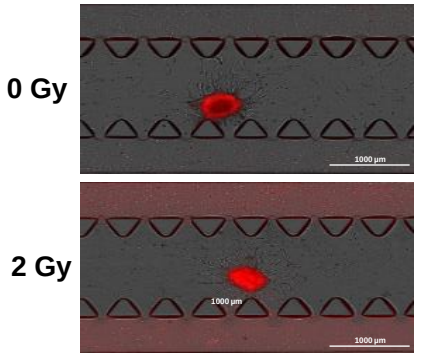
Development of a tumor-on-a-chip model

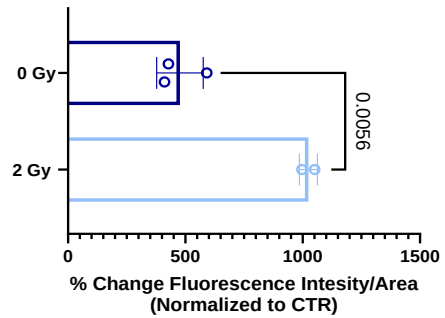




Blue- Nucleus

sNP-Cy5 internalization in the tumor-on-a-chip model





Khoury, Longobardi, Barnatan *et al*., JCR, 2025

RSF Lab

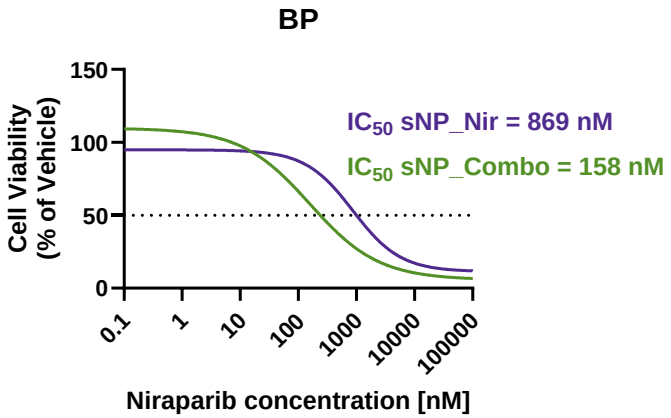
TEL AVIV UNIVERSITY
Pursuing the Unknown

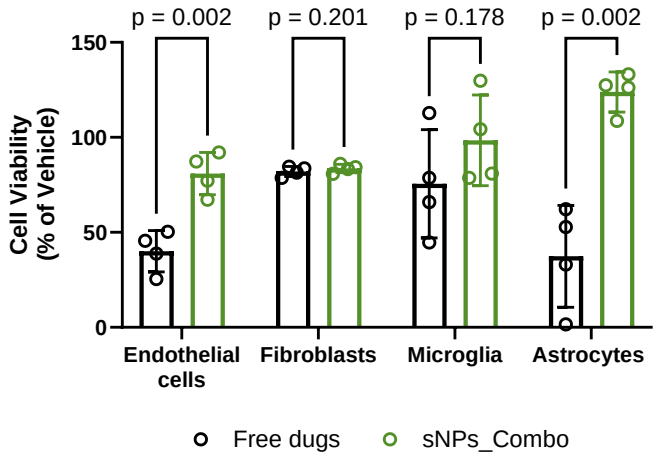
sNPs enhance Niraparib sensitivity when combined with PD-L1 inhibitors in both 2D and 3D models



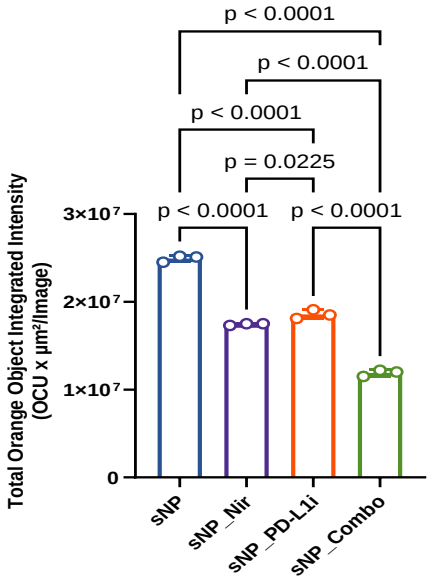
Tania Barnatan Giuseppe Longobardi Rami Khoury

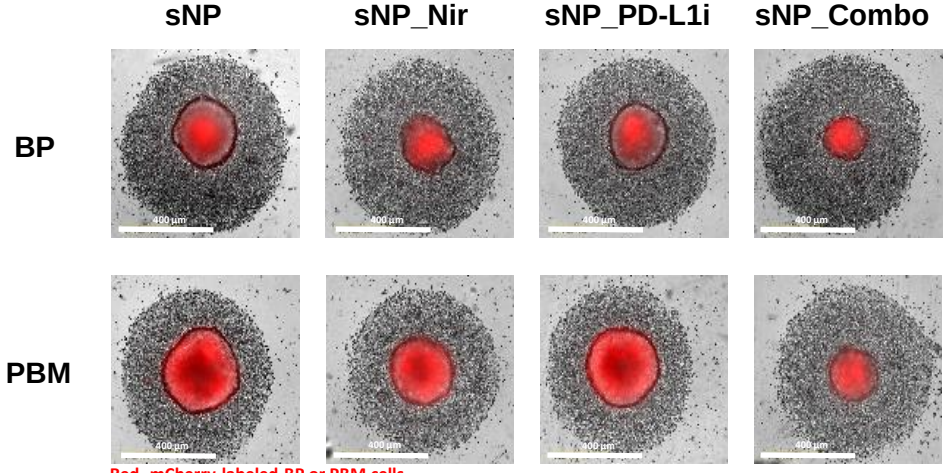
2D





3D





Red- mCherry-labeled BP or PBM cells
Gray- Splenocytes

Khoury, Longobardi, Barnatan *et al.*, JCR, 2025

RSF Lab

TEL AVIV UNIVERSITY
Pursuing the Unknown

Intracranial, Intracardiac, and Spontaneous BRCA-mut/null breast cancer brain metastases models

Rami Khoury

- **Intracranial injection of BP and BPB cell lines, after primary tumor resection**

- **Intracardiac injection of brain tropic BP or BPB cell lines (termed BP- or BPB-BrM)**
  Pros: A good model to study interactions between cells and TME immunophenotyping.
  Cons: Not a good model for intervention, due to other organ metastasis.

BP

In vivo selection round	Cell line injected	Number of cells injected/ mouse	% BrM formation
1	Parental BP	1×10^6	20%
2	BP-BrM1	1×10^6	40%
3	BP-BrM2	1×10^6	60%
4	BP-BrM3	1×10^6	70%
5	BP-BrM4	1×10^5	80%
6	BP-BrM4	1×10^5	ongoing

BPB

In vivo selection round	Cell line injected	Number of cells injected/ mouse	% BrM formation
1	Parental BPB	1×10^6	20%
2	BPB-BrM1	1×10^6	30%
3	BPB-BrM2	1×10^6	ongoing
4			
5			
6			

- **Intracranial injection of brain tropic BP or BPB cell lines (termed BP- or BPB-BrM)**
  Pros: Enables interventional studies on brain-tropic cells that are already enriched with BrM-specific traits.
  Cons: Bypasses the natural metastatic steps.

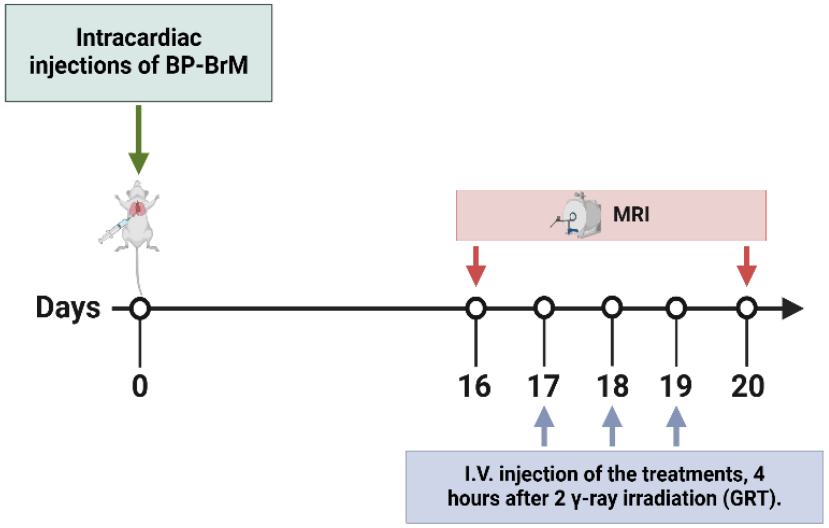
RSF Lab

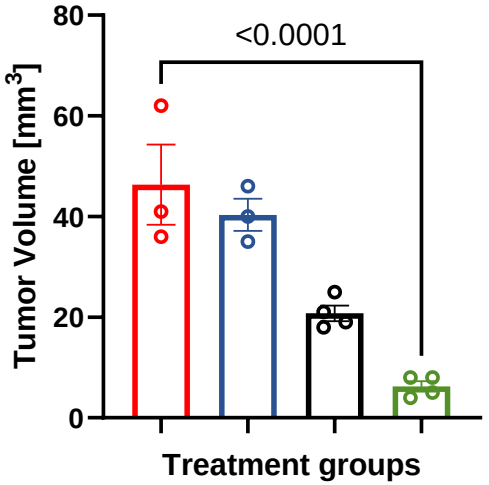
TEL AVIV UNIVERSITY
Pursuing the Unknown

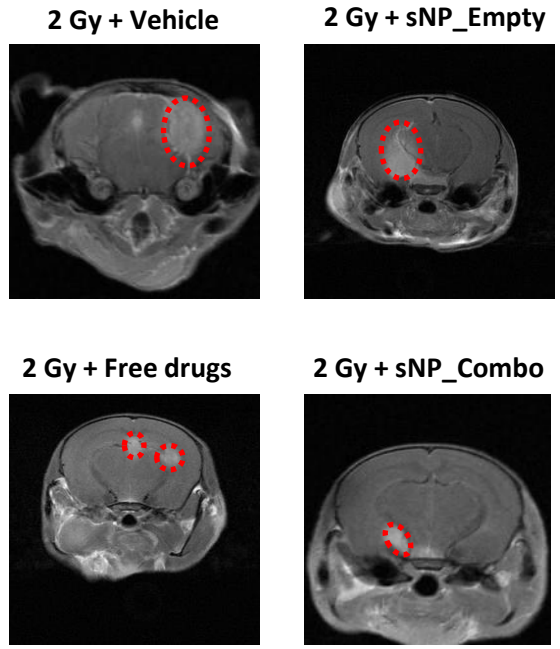
sNP_Combo has a stronger anti-tumor effect on BRCA1-deficient breast cancer BrM, in comparison to free drugs



Tania Barnatan Giuseppe Longobardi Rami Khoury







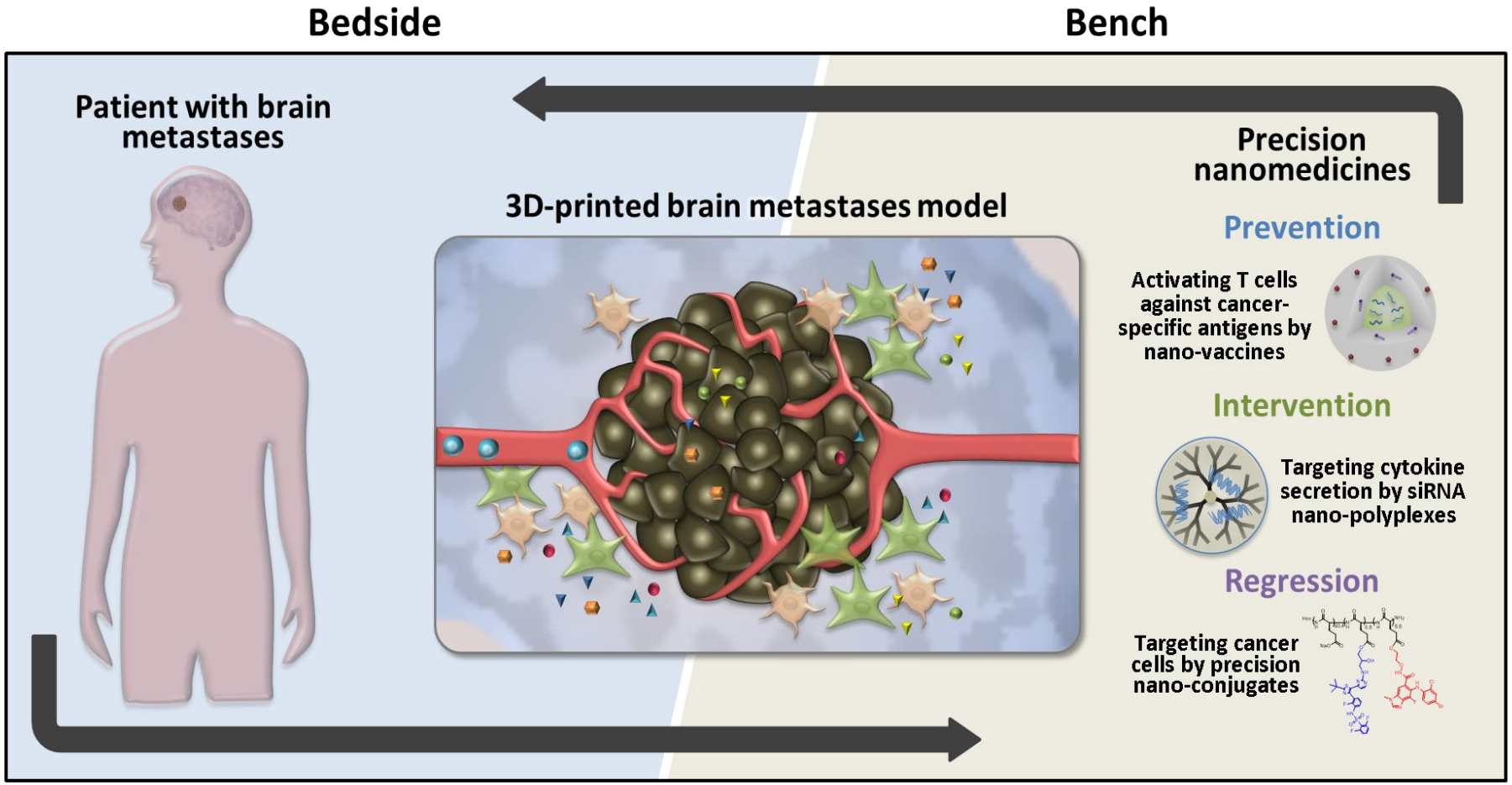
2 Gy + Vehicle 2 Gy + sNP 2 Gy + Free drugs 2 Gy + sNP_combo

Khoury, Longobardi, Barnatan *et al.*, JCR, 2025

RSF Lab

TEL AVIV UNIVERSITY
Pursuing the Unknown

From Bench to bedside and back



3DBrainStrom: Bridging the translational gap - bedside to bench and back

erc Advanced Grant

RSF Lab

TEL AVIV UNIVERSITY
Pursuing the Unknown

RSF's Multidisciplinary research team

The whole is greater than the sum of its parts …

RSF Lab

TEL AVIV UNIVERSITY אוניברסיטת תל אביב

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

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

Yulia Liubomirski, PhD
Opal Avramoff
Koren Salomon
Adan Miari
Shir Shahar
Tania Barnatan
Shahar Greenberg
Sahar Israeli Dangoor, PhD
Paula Ofek, PhD
Keren Miller, PhD
Anat Eldar-Boock, PhD
Eilam Yeini , PhD
Sabina Pozzi, PhD
Galia Tiram, PhD
Shiran Ferber, PhD
Hadas Gibori, PhD
Hagit Mann-Steinberg, PhD
Dikla Ben-Shushan, PhD
Christian Burgos
Noa Reisman
Sapir Golan
Roni Blatt
Liron Stern
Nitzan Albeck
Audrey Slupowski

Patient-derived tumor models

Daniella Vaskovich-Koubi
Anne Krinsky
Yair Roth
Rami Khoury
Neta Frommer
Saeed Sirhan, MD
Lidar Fridrich, MD
Miki Goldenfeld, MD
Shelly Sofer, MD
Rony Shreberk-Hassidim, MD
Ilanit Shetzigovski-Meller, MD
Gal Bachar, MD
Yael Shtilerman, MD
Ori Hadad, MD

3D-Bioprinted tumor models

Ron Kleiner
Dana Venkert
Anshika Katyal
Giuseppe Longobardi, PhD
Maya Elbaz
Ehud Segal, PhD
Lena Neufeld, PhD
Gal Shenbach-Koltin
Tal Zur
Zohar Shatsberg
Liora Omer
Shlomit Levy

Design, synthesis and characterization of novel nanomedicines

Marina Green Buzhor, PhD
Rina Sevostianov
Adi Yona
America Garcia Alvarado
Ohad Hasin, PhD
Or Kandli
Daniel Ajamil Rodriguez, PhD
Yana Epshtein, PhD
Shani Koshrovski-Michael, PhD
Pradip Dey, PhD
Alexis Wolfel, PhD
Shlomi Lazar, PhD
Anna Scomparin, PhD
Shay Eliyahu, PhD
Hemda Baabur-Cohen , PhD
Ela Markovsky, PhD
Dina Polyak, PhD
Adva Krivitsky, PhD
Racheli Blau, PhD
Evgeny Pisarevsky, PhD
Joao Conniot, PhD
Alessio Malfanti, PhD
Ruri Ruperti

Administration

Ayelet Hashdi

Collaborators:

University of Lisbon
Helena Florindo, PhD
Rita Guedes, PhD
Tel Aviv University:
Asaf Madi, PhD
Dinorah Friedmann-Morvinski , PhD
Adi Barzel, PhD
Doron Shabat, PhD
Roey Amir, PhD
Ben Maoz, PhD
Lihi Adler-Abramovich, PhD
MSKCC/Selectin Therapeutics
Dan Heller, PhD
UCSD/Selectin Therapeutics
Praveen Raju, MD
PreciseBio, Claro3D:
Aryeh Batt
Rotem Golan

Clinical Collaborators:

MSKCC
Richard White, MD, PhD
Praveen Raju, MD, PhD
Tel Aviv Sourasky Medical Center:
Zvi Ram, MD
Rachel Grossman, MD
Dov Hershkovitz, MD
Sheba Medical Center:
Ronnie Shapira, MD
Alicia Talianski, MD
Iris Barshack, MD
Jair Bar, MD
Johns Hopkins University:
Henry Brem, MD
Thomas Hyde, MD
Rambam Medical Center:
Irit Ben-Aharon, MD
Tal Goshen, PhD

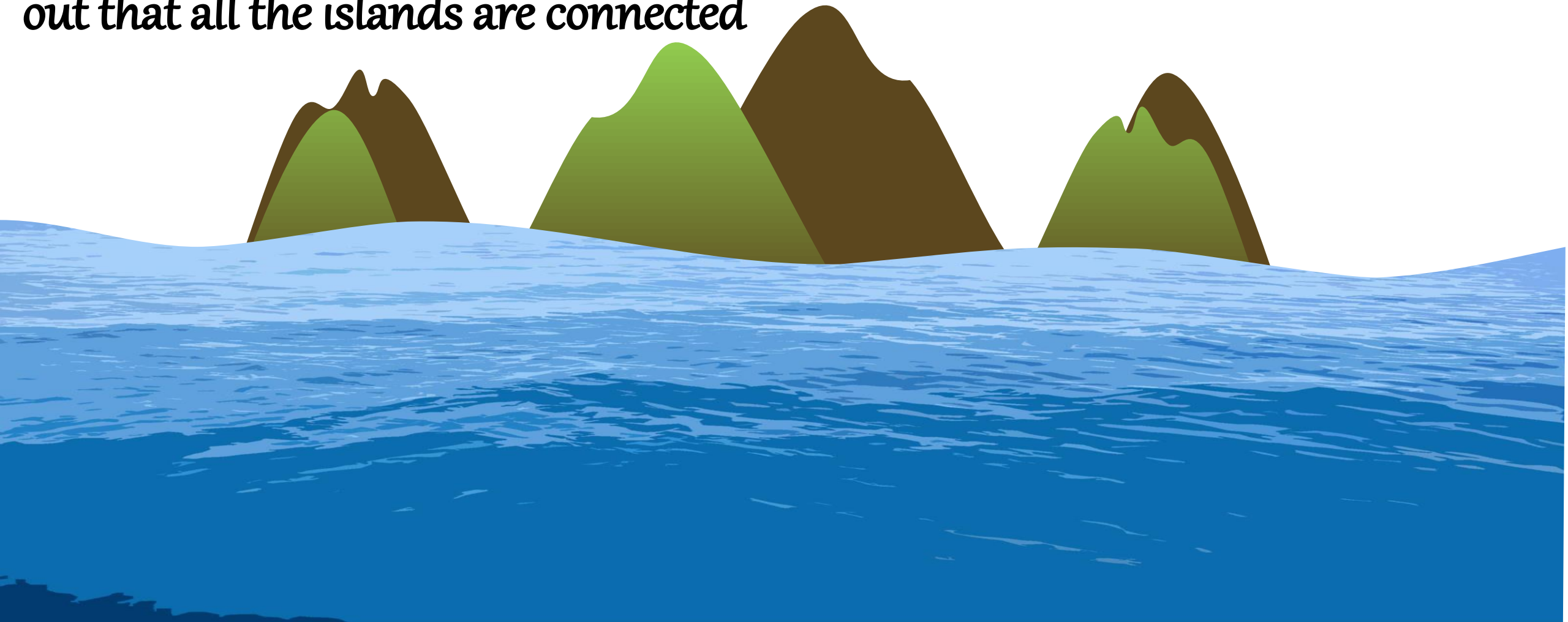
erc

רשות החדשנות Israel Innovation Authority | European Innovation Council | Melanoma Research Alliance | MERCK | teva | Kahn Foundation | ICRF Israel Cancer Research Fund | EuroNanoMed2 | European Training Network THERACAT | HORIZON 2020 | "la Caixa"


CHRISTIANITY
BUDDISM
ISLAM
SHINTO
TAOISM
HINDUISM
JUDAISM
SIKHISM

Multidisciplinary Bioconvergent Research Team-
The whole is greater than the sum of its parts …

When you drain the water from the ocean you will find out that all the islands are connected



TEL AVIV UNIVERSITY
אוניברסיטת תל אביב

RSF Lab

www.SatchiFainaroLab.com @RSFLab

רשות החדשנות
Israel Innovation Authority

erc European Research Council

ISRAEL SCIENCE FOUNDATION

"la Caixa"

HORIZON 2020

האגודה למלחמה בסרטן

The Azrieli Foundation

European Innovation Council

BSF

YORAN INSTITUTE FOR HUMAN GENOME RESEARCH

MERCK

Kahn Foundation

CBRC Cancer Biology Research Center

Melanoma Research Alliance

Gray School of Medical Sciences
Gray Faculty of Medical & Health Sciences
Tel Aviv University

teva

EuroNanoMed2

ICRF Israel Cancer Research Fund

Kadar Award

Marian Gertner Institute
Faculty of Engineering and Faculty of Medicine
Tel Aviv University

European Training Network THERACAT