



Hilton Orlando
6001 Destination Pkwy, Orlando, FL
March 6, 2025

Innovation in the Non-Surgical Treatment of Cutaneous Malignancy by Local Delivery

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Innovation in the Non-Surgical Treatment of Cutaneous Malignancy by Local Delivery



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NON-MELANOMA (BCC, SCC)



MERKEL CELL CARCINOMA



MELANOMA



CUTANEOUS T CELL LYMPHOMA



Engineering the Optimization of Locoregional Treatment of Skin Malignancy

1. OPTIMIZE TUMOR CELL DEATH

- Necroptosis
- Ferroptosis
- Pyroptosis

3. IMMUNE CONDITION THE DLN

- Increase DC activation
- Optimize T_{E/M} T cells (CD8, TH1)
- Decrease Treg

*Optimize Tumor Cell Death
+ Immune Condition the Tumor DLN*

*Skin
Tumor*

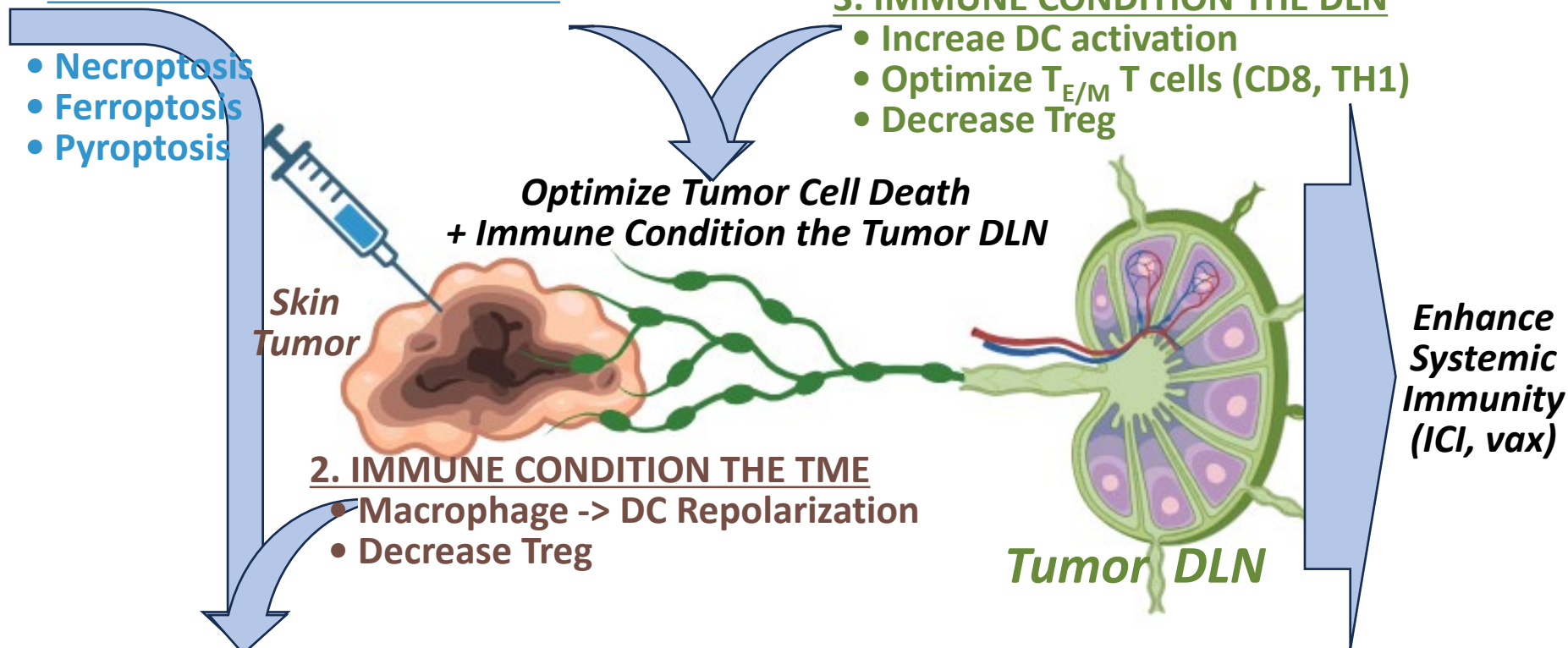
2. IMMUNE CONDITION THE TME

- Macrophage -> DC Repolarization
- Decrease Treg

*Optimize Tumor Cell Death
+ Immune Condition the TME*

Tumor DLN

*Enhance
Systemic
Immunity
(ICI, vax)*



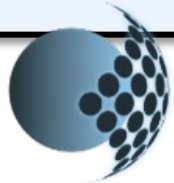
~ Dermatology Innovation Forum 2025 ~ Orlando, FL ~

Bioadhesive Drug Carriers (BDCs)



Yale University
School of Medicine

New Haven, Connecticut, USA



STRADEFY BIOSCIENCES

ELM STREET
VENTURES



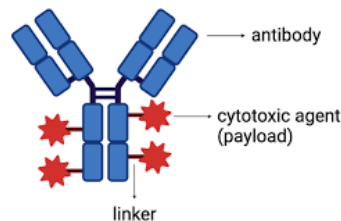
biohaven®
Yale



Mark Saltzman, Yale School of BME
Michael Girardi, Yale School of Med
Jeff Goldberg, Exec. Chair, Stradefy
Brian Dixon, Elm Street Ventures

BDC Mechanism of Action - localized and differentiated

ADC



Delivery

Systemic

Localization

Cell surface

Internalization

**Endocytosis
(requires tumor Ag)**

**Release/
Tumor Kill**

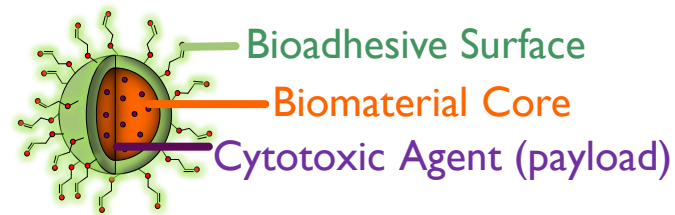
**Linker cleavage
(**<10 actives**/ADC)**

Manufacturing

Biologic synthesis

BDC  STRADEFY

Biodegradable Drug Carriers™



Local

Cell surface & **TME**

**Endocytosis
(tumor Ag agnostic)**

**Diffusion, long residence
(**>10,000 actives**/BDC)**

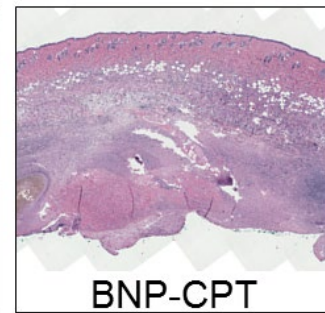
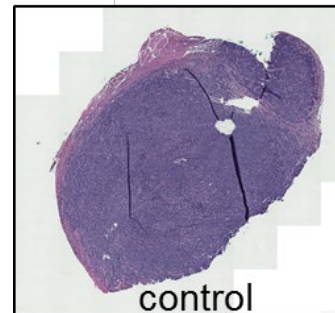
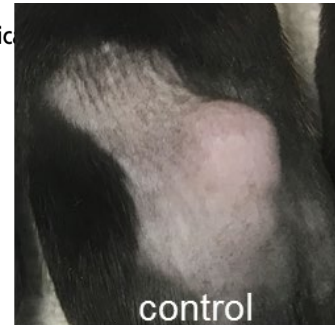
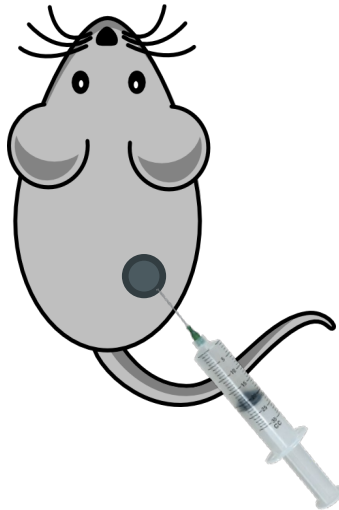
Chemical synthesis

Nonsurgical treatment of skin cancer with local delivery of bioadhesive nanoparticles

Jamie K. Hu^a, Hee-Won Suh^b, Munibah Qureshi^a, Julia M. Lewis^a, Sharon Yaqoob^a, Zoe M. Moscato^b, Sofia Griff^b, Alison K. Lee^a, Emily S. Yin^a, W. Mark Saltzman^b, and Michael Girardi^{a,1}

^aDepartment of Dermatology, School of Medicine, Yale University, New Haven, CT 06520; and ^bDepartment of Biomedical Engineering and Applied Science, Yale University, New Haven, CT 06511

Intratumoral injection
of BNP-CPT (20mg/kg)



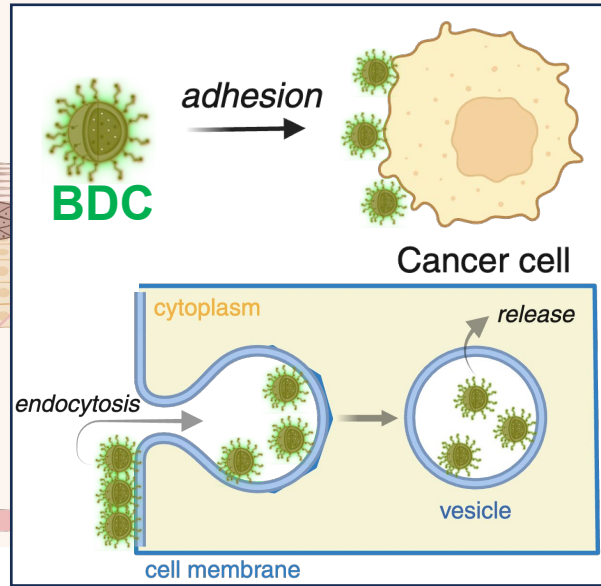
BDC Mechanism of Action

malignant skin tumor

*intra*tumoral delivery
of **BDCs**

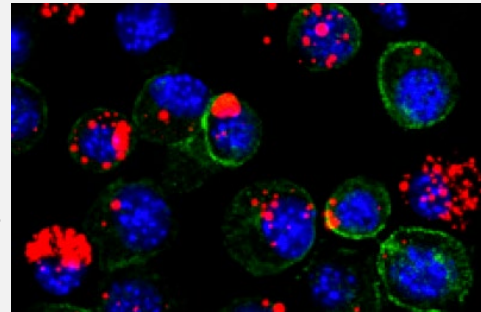
Lymph node

Blood vessel



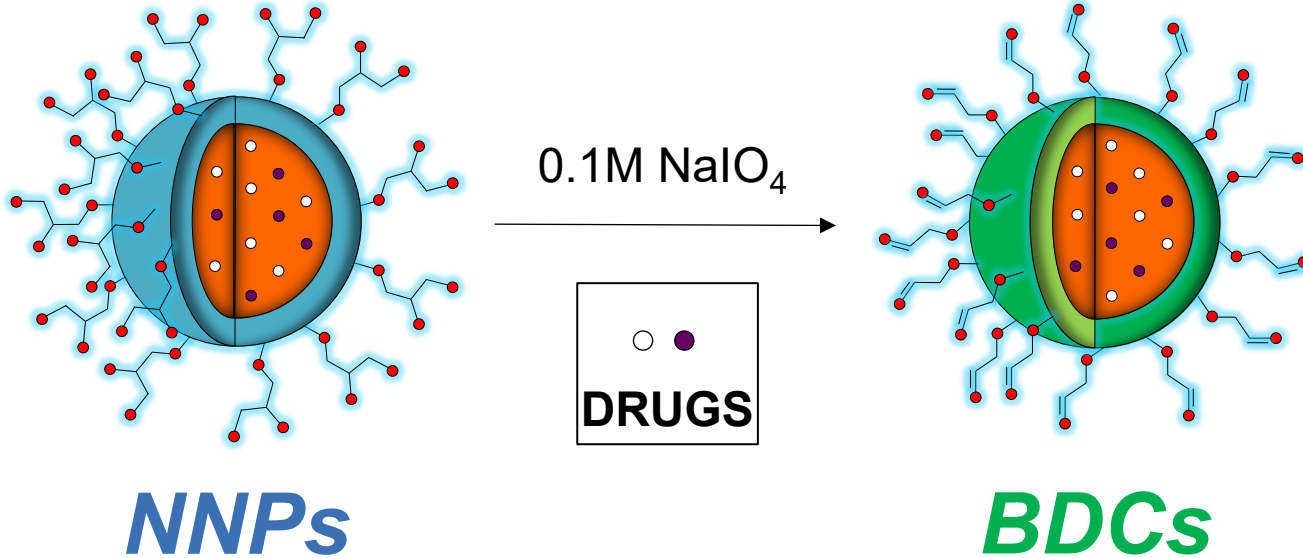
tumor resolution

Confocal images of SCC
cells after 24hr exposure
with red dye-loaded BDCs



**Non-Adhesive Nanoparticle
(PLA-HPG-vicinyol diol)**

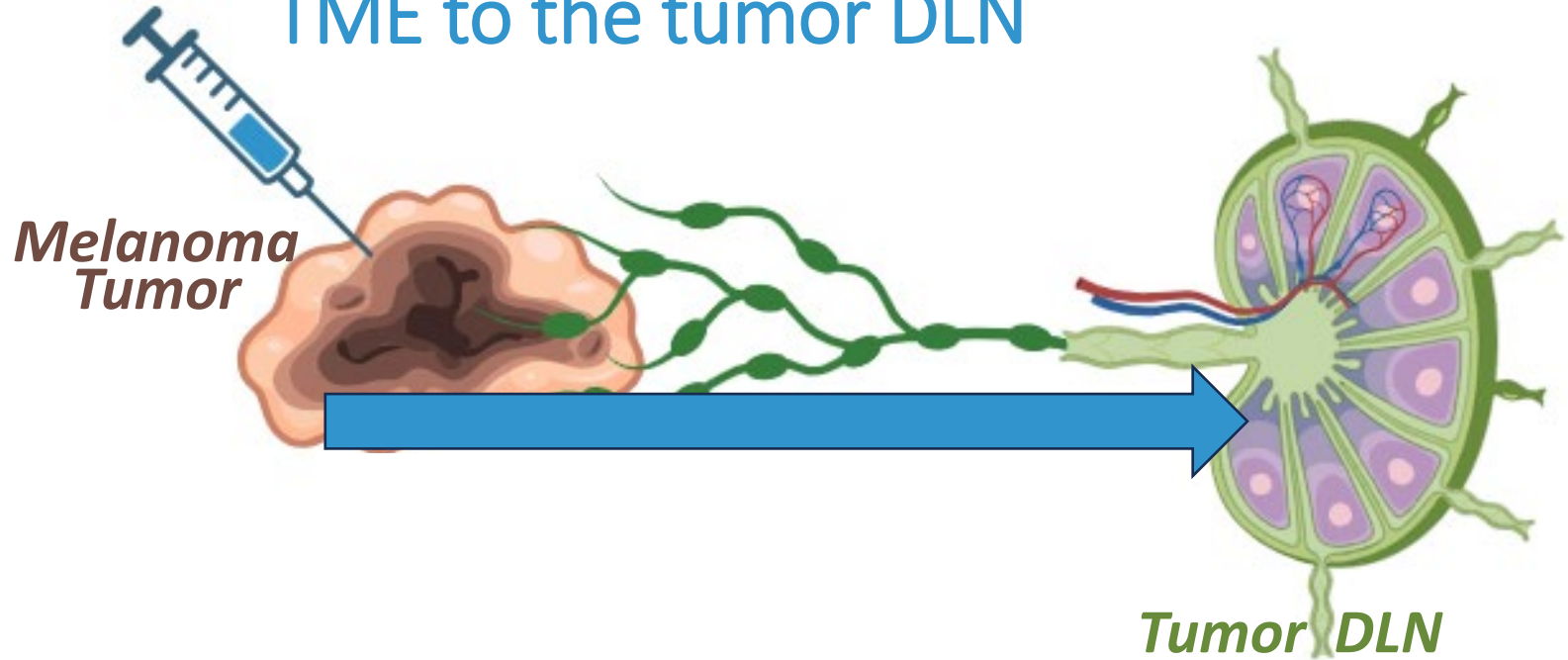
**Biodegradable Drug Carriers (BDCs)
(PLA-HPG-aldehyde)**



NNP or BDC use depends on the indication and desired properties.

NNP = Non-Adherent NP of HPG-PLA

Engineered to release agent from the
TME to the tumor DLN





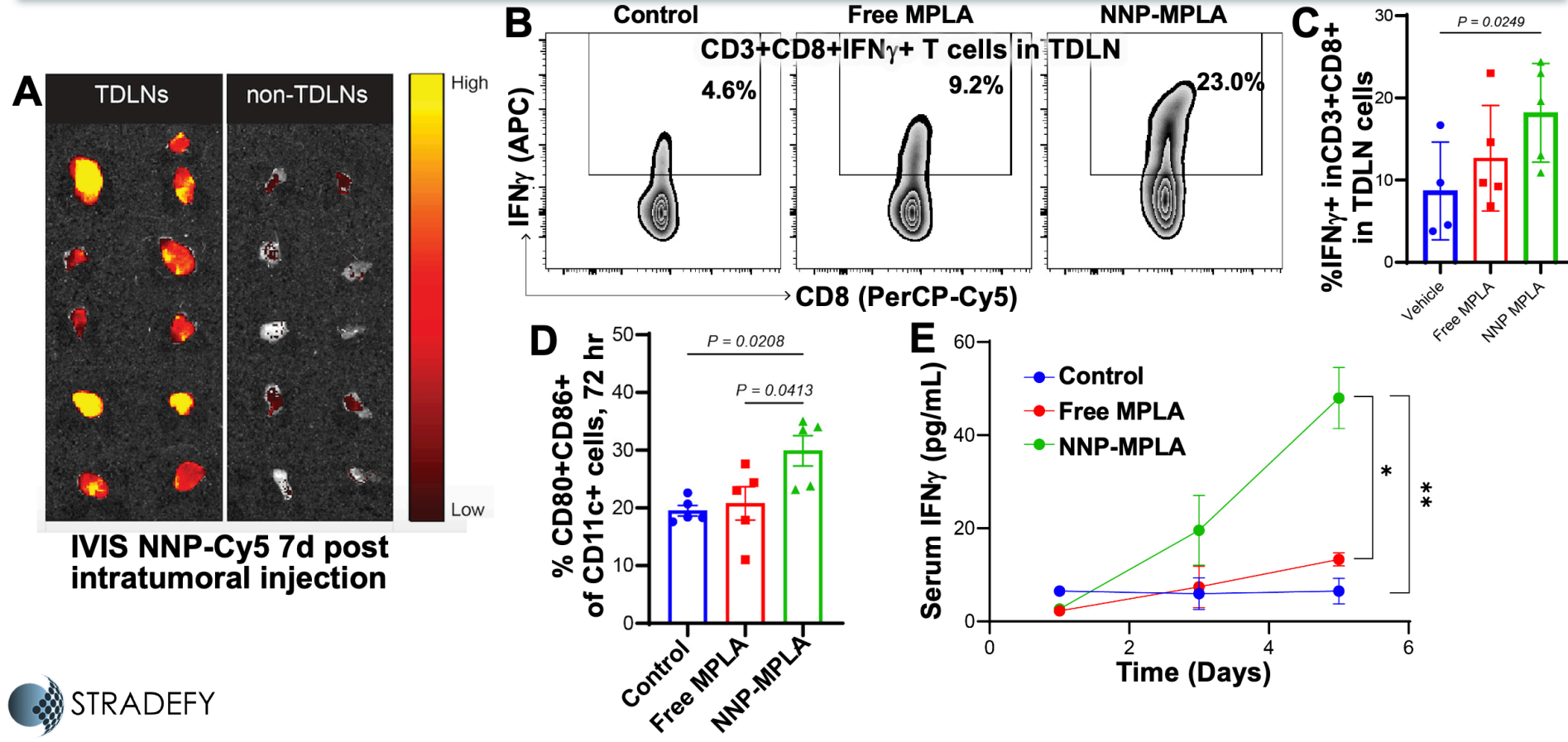
Enhanced Intratumoral Delivery of Immunomodulator Monophosphoryl Lipid A through Hyperbranched Polyglycerol–Coated Biodegradable Nanoparticles

Jungsoo Chang^{1,2,10}, Kwangsoo Shin^{2,10}, Julia M. Lewis¹, Hee Won Suh², Joohyung Lee¹, William Damsky¹, Suzanne Xu¹, Marcus Bosenberg^{1,3,4,5,6,7}, W. Mark Saltzman^{1,2,6,8,9} and Michael Girardi^{1,6}



NNP-MPLA for Locoregional Melanoma

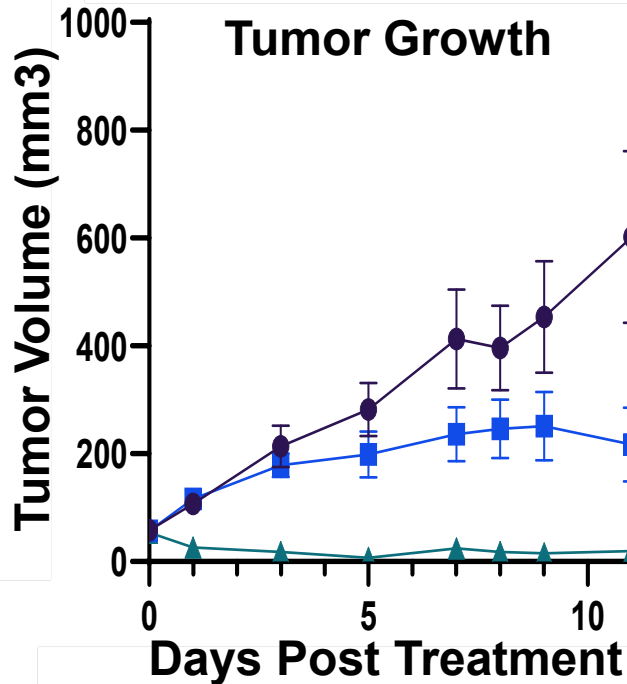
From the TME → to the TDLN



Enhancing Melanoma Local Immunotherapy

Intralesional CHEMO + NNP-MPLA

- YUMMER-1.7 model of established melanoma.
- MPLA is a TLR-4 agonist.



Vehicle
EXA + free MPLA
EXA + NNP-MPLA

Day 0

Day 11



Stradefy Bio: Innovative Site-Directed Therapeutics



Core technology - Bioadhesive Drug Carriers (BDCs)

- Like ADCs, but higher drug load, better retention & cell internalization

Complimented by NNP that drive agents from TME→DLN

- Ideal for packaging immunostimulatory agents like MPLA

First Indication is Non-Melanoma Skin Cancer.

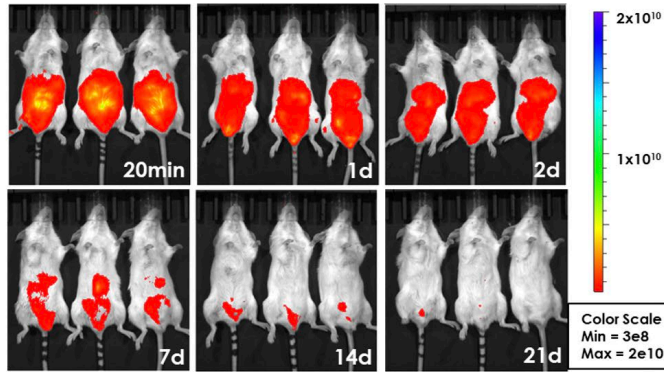
- BCC, SCC, Melanoma, MCC, ovarian cancer

BNP-EXA Intraperitoneal Delivery

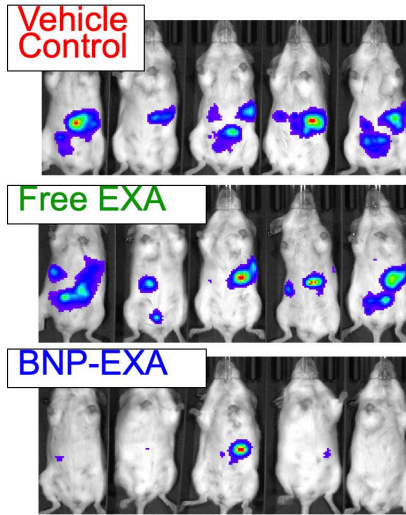
Ovarian cancer metastasized to the peritoneum....

- Ovarian cancer cell line w/ luciferase reporter for imaging (ID8 Luc)
- Stradefy BNPs with fluorescent label for location tracking

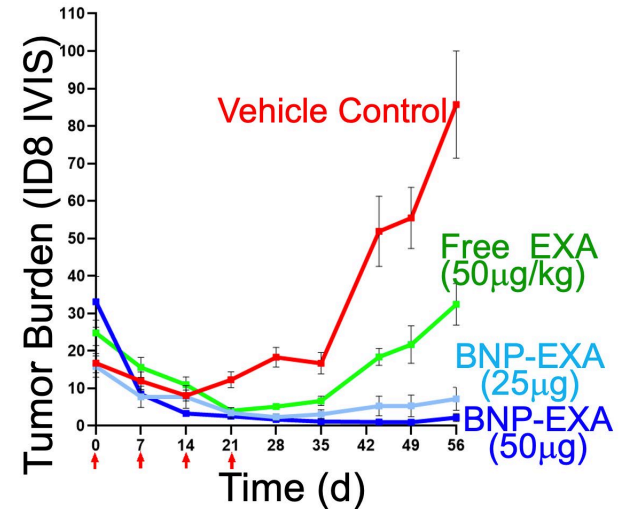
BNP Retention Signal



Tumor Imaging Day 49



Tumor Signal





Thank you!

W. Mark Saltzman, PhD

Yale Biomedical Engineering

*Jeffrey Goldberg
Executive Chair*

jgoldberg@stradefybio.com



**STRADEFY
BIOSCIENCES**



BLAVATNIK FUND



Yale Innovation

**ELM STREET
VENTURES**



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Yale

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INSTITUTE**

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CANCER CENTER
SKIN SPORE

**SKIN
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FOUNDATION**

**R.S. Evans
Charitable
Foundation**

DF

American Skin Association™

**Spatz Family
Charitable
Foundation**

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