AGENDA

University of Connecticut
Board of Trustees

Committee for Research, Entrepreneurship and Innovation
April 25, 2024, at 1:00 p.m.

Virtual Meeting

Public Streaming Link (with live captioning upon request): https://ait.uconn.edu/bot

(A recording of the meeting will be posted on the Board website https://boardoftrustees.uconn.edu/ within seven days of the meeting.)

Call to order at **1:00 p.m.**

1. Public Participation*
   *Individuals who wish to speak during the Public Participation portion of the Thursday, April 25, meeting must do so 24 hours in advance of the meeting's start time (i.e., 1:00 p.m. on Wednesday, April 24) by emailing BoardCommittees@uconn.edu. Speaking requests must include a name, telephone number, topic, and affiliation with the University (i.e., student, employee, member of the public). The Committee may limit the entirety of the public comment to a maximum of 30 minutes. As an alternative, individuals may submit written comments via BoardCommittees@uconn.edu, and all comments will be transmitted to the Committee.

2. Minutes from the December 7, 2023, Meeting

3. Early Results from Revised SPARK Technology Commercialization Fund Program
   - Presentation by:
     Dr. Matthew Mroz, Manager, Research Development Services
     Dr. Vivek Ramakrishnan, Director, Venture Development
     Dr. Lindsay DeStefano, Associate Vice President for Research Development

4. Presentation by SPARK Grant Awardee: Dr. Raman Bahal, Pharmaceutical Sciences

5. Presentation by SPARK Grant Awardee: Dr. Ali Tamayol, Biomedical Engineering

6. Other Business

7. Executive Session (as needed)

8. Adjournment

PLEASE NOTE: *If you are an individual with a disability and require accommodations, please e-mail the Board of Trustees Office at boardoftrustees@uconn.edu prior to the meeting.*

TRANSFORMING
KNOWLEDGE, LIVES AND COMMUNITIES

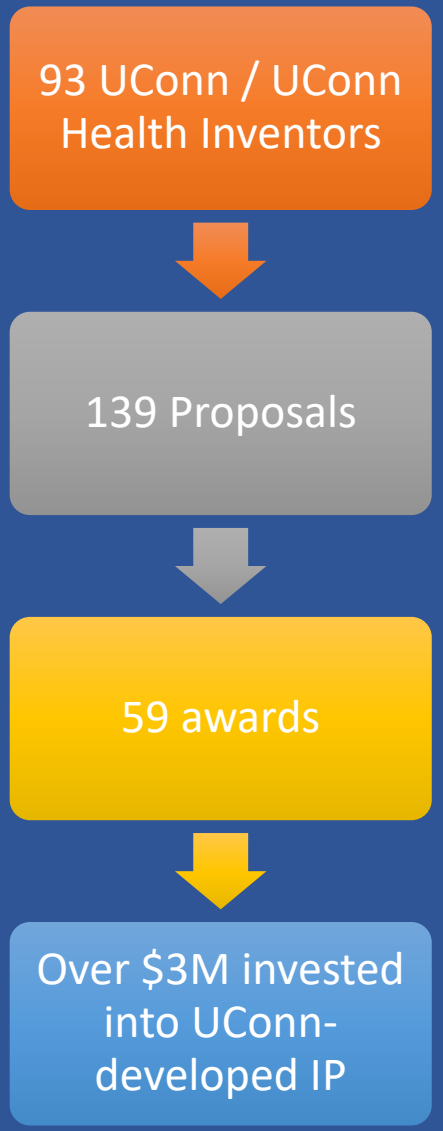
Revised Spark Program Early Results

Technology Commercialization Services
Research Development Services
UConn Office of Research

April 25, 2024

UCONN RESEARCH

SPARK Technology Commercialization Fund (FY 2015-2024)



UCONN RESEARCH

Overview – SPARK Technology Commercialization Fund

Analysis of awards given from FY18-FY21

25 Awards

- 19 invention disclosures (76%)
- 12 new companies formed: Early stage or pre-seed only
- 9 licenses/option agreements

More is needed to drive real world impact

UCONN RESEARCH

FY22 SPARK Program Revision

Key needs

- Differentiate from research funding
- Invest in ideas that lead to commercialization
- Build momentum towards translation

Program revisions

- Rigorous, and commercialization focused application process
- Reviews by Entrepreneurs-in-Residence with business experience
- Fewer awards (100,000$ for two years)
- Expectation of startup or new IP
- Extensive guidance and 1-1 coaching by UConn TCS

UCONN RESEARCH

From Researcher to Entrepreneur

Developing translational mindset and know-how

TCS Coaching and feedback during application process

TCS Engagement with Awardees

- **1:1 Check-ins**
- **6-month progress checks, with pitch-style presentations**
- **Regulatory, business development feedback**

UCONN RESEARCH

Highlights of Revised SPARK Program (FY 22-23)

- 9 projects – 100% invention disclosures
- 5 startups. 1 new startup being incorporated
- 2 technologies licensed to 3rd parties
- $3.4 M in new federal funding to SPARK awardees (DOD, NASA, SBIR)
- Two industry-funded projects $250,000
- Successful pilot scale up in production facility in MA.
- FDA breakthrough designation for startup

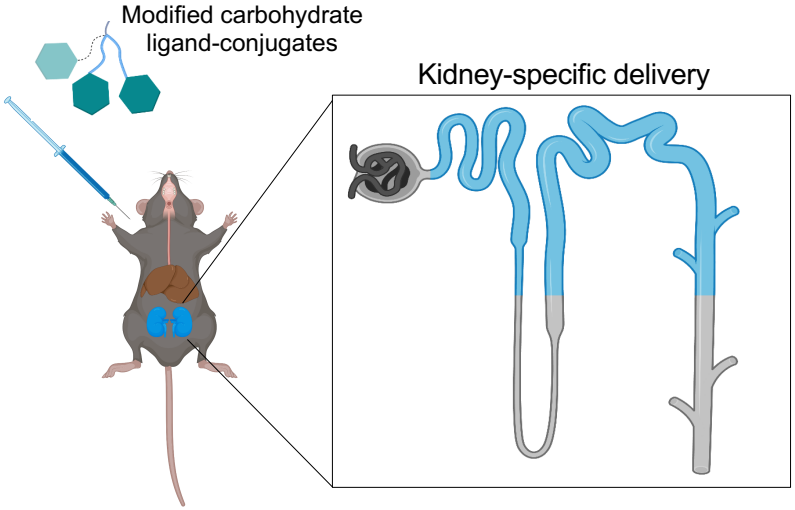
UCONN RESEARCH

Thank you

Questions?

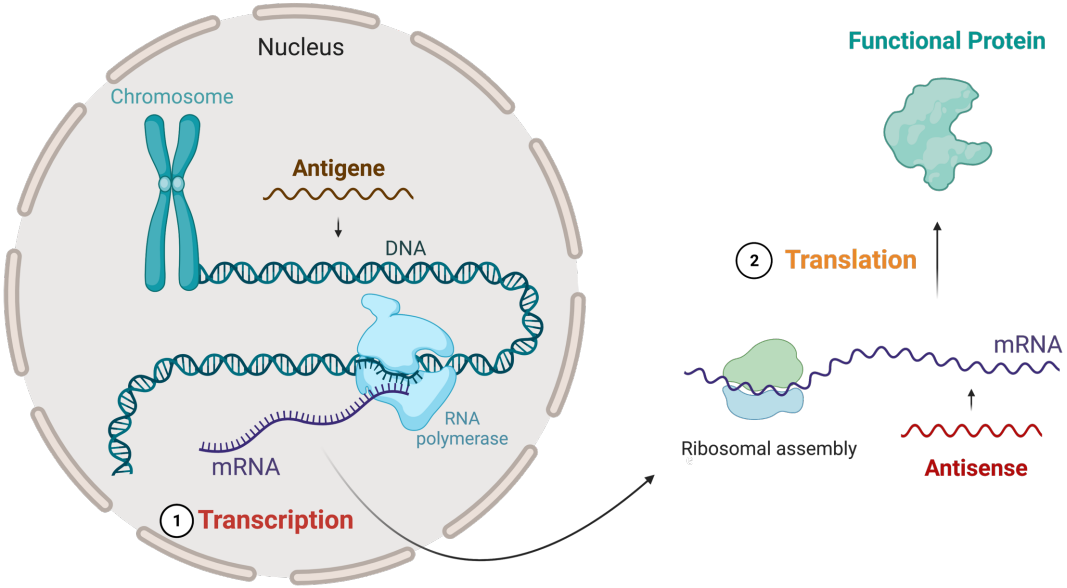
UCONN
RESEARCH

Developing next-generation kidney-targeted therapeutics



Raman Bahal, Ph.D.
Associate Professor
Department of Pharmaceutical Sciences, UConn.

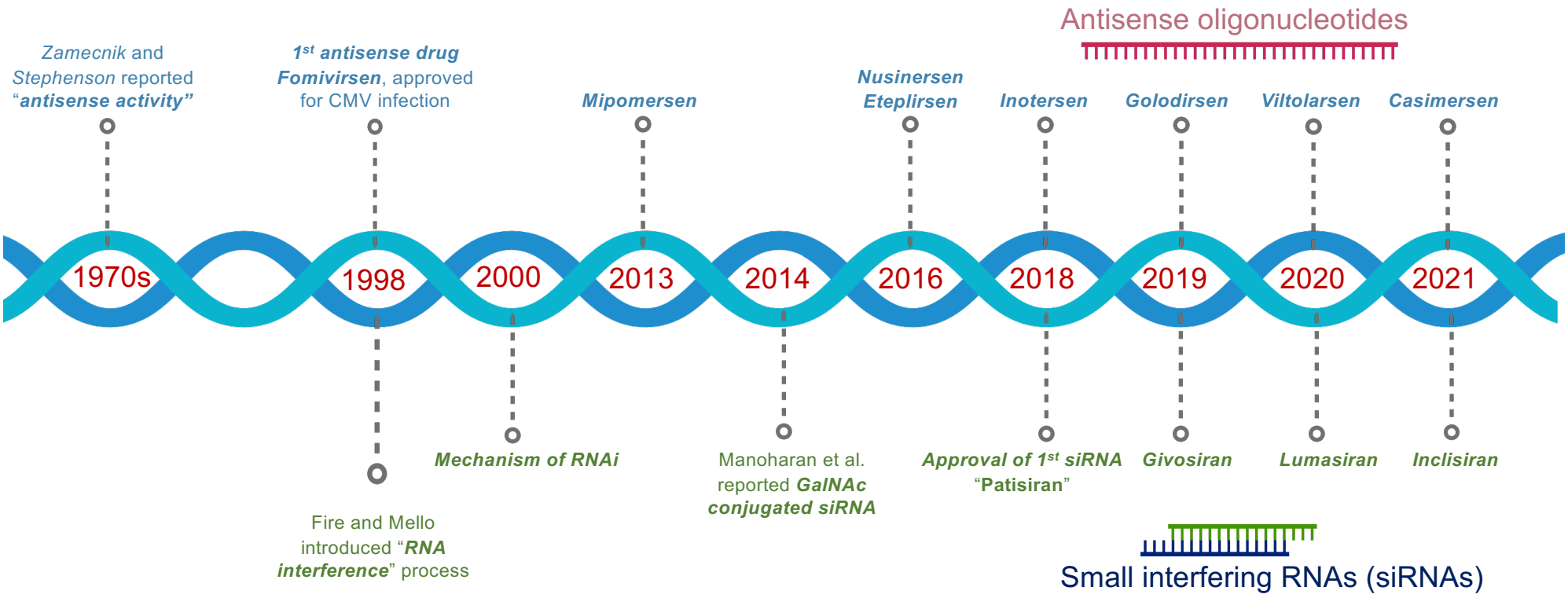
Research platform and mission



Integrating nucleic acids chemistry and gene delivery to illuminate biology and develop novel therapeutics

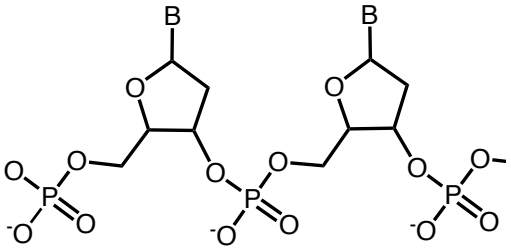
Rise of RNA therapeutics

mRNA-targeted ASOs drugs

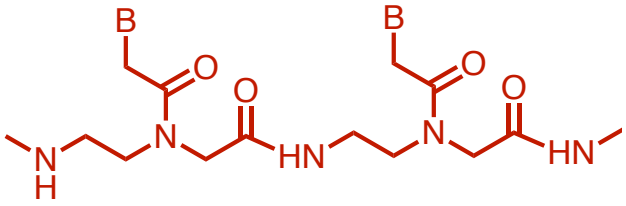


Peptide Nucleic Acid (PNA)

B: A, T, G, C

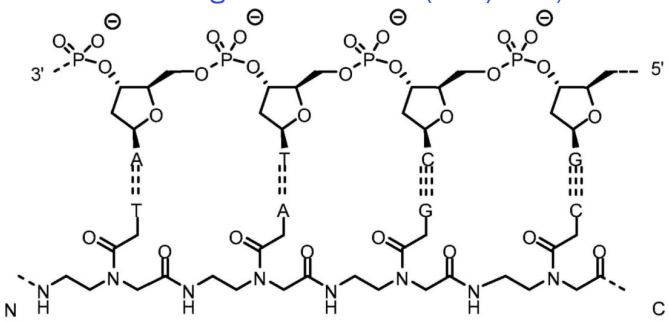


DNA



PNA

Negative backbone (DNA/RNA)



Neutral backbone (PNA)

Properties

- Enzymatic stability
- Neutral backbone
- High Binding affinity
- Specificity

Challenges

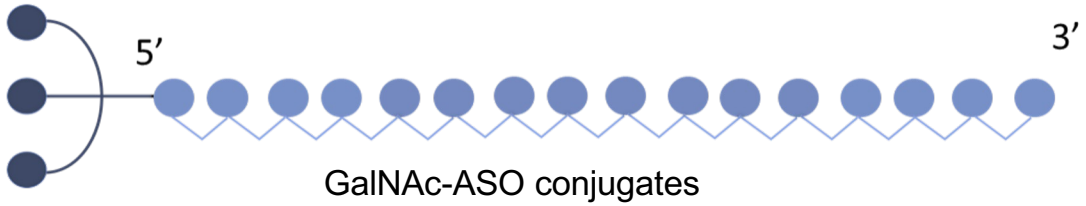
- Hydrophobicity
- Poor solubility
- Limited cellular permeability
- Rapid clearance

Nielsen PE, et al. Science, 1991 | Malik S et al, Cell Mol Life Sci, 2018

Liver targeted platforms

IONIS Pharma.

Ligand conjugated antisense (LICA)



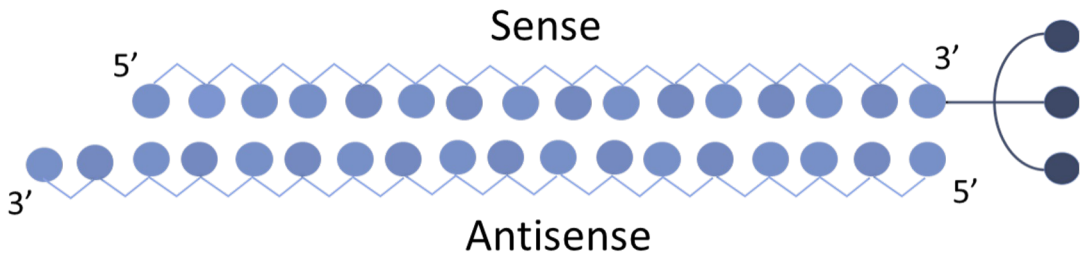
GalNAc-ASO conjugates

LICA – product pipeline

- Pelacarsen
- Eplontersen
- Olezarsen
- ION839
- ION224
- ION547
- IONIS-FB-LRx
- Fesomersen
- Cimdelirsen
- Sapablursen
- Donidalorsen

ALNYLAM Pharma.

Enhanced stabilization chemistry



GalNAc-siRNA conjugates

Alnylam ESC-GalNAc- Product pipeline

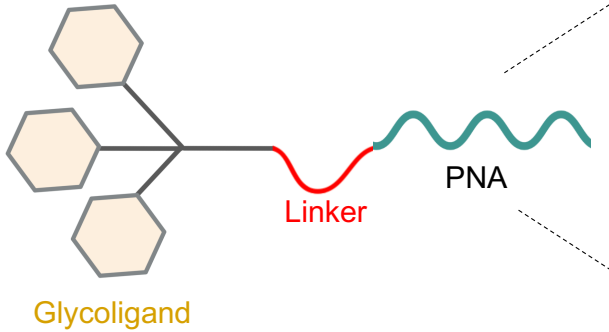
- Fitusiran
- Inclisiran
- Lumasiran
- Cemdisiran
- ALN-AAT02
- ALN-HBV02
- Zilebesiran
- ALN-HSD

Carbohydrate conjugates for liver-targeted delivery

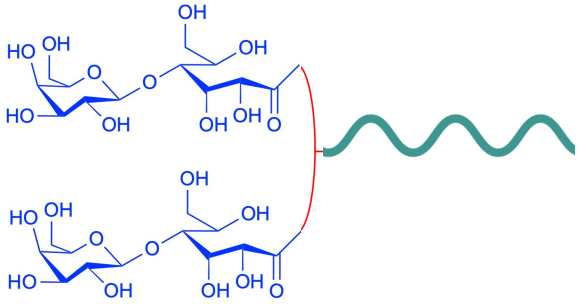
Multivalent Lactobionic Acid and N-Acetylgalactosamine-Conjugated Peptide Nucleic Acids for Efficient In Vivo Targeting of Hepatocytes

*Vikas Kumar, Aniket Wahane, Anisha Gupta, José E. Manautou, and Raman Bahal**

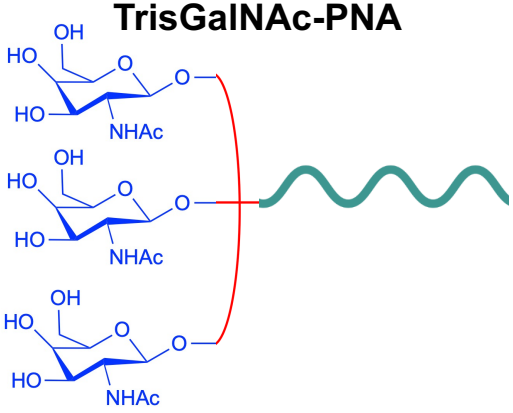
Advanced Healthcare Materials, 2023

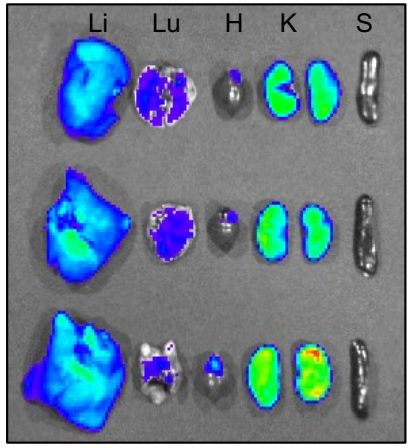


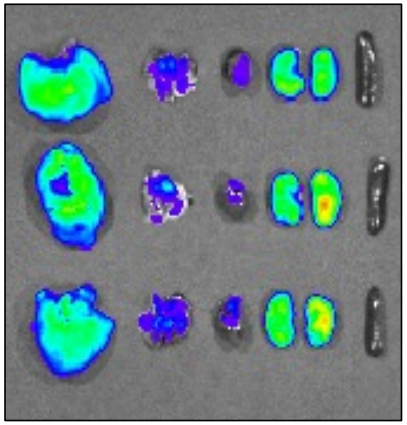
diLactobionic acid-PNA



TrisGalNAc-PNA

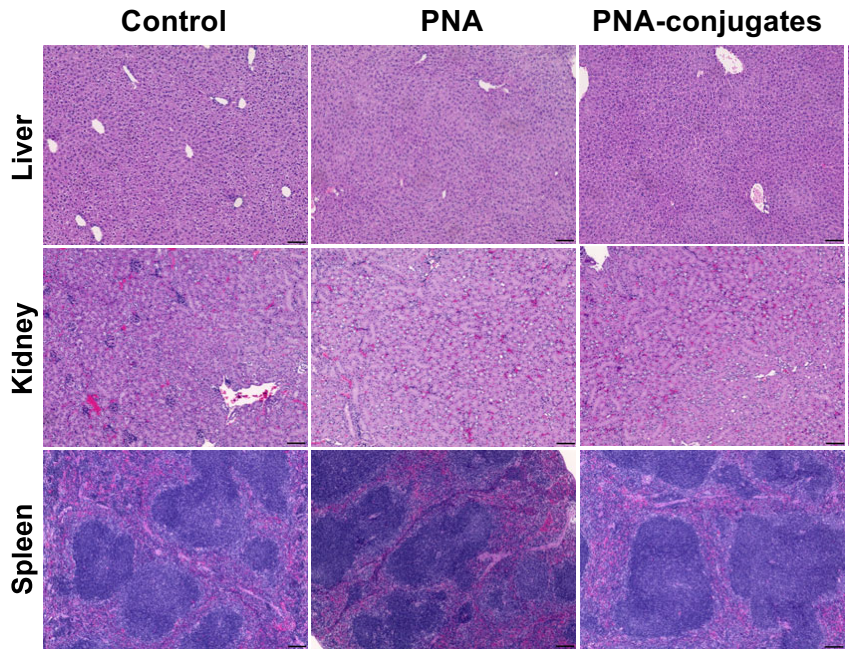




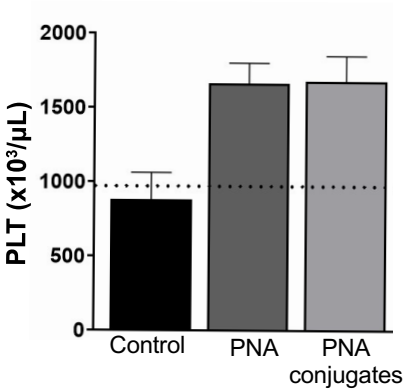


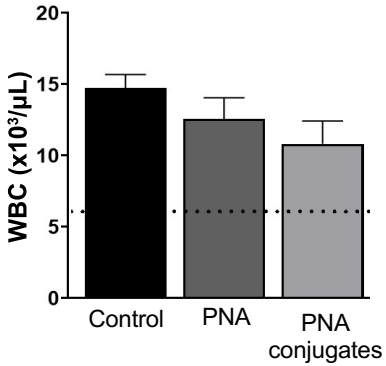
Safety analysis

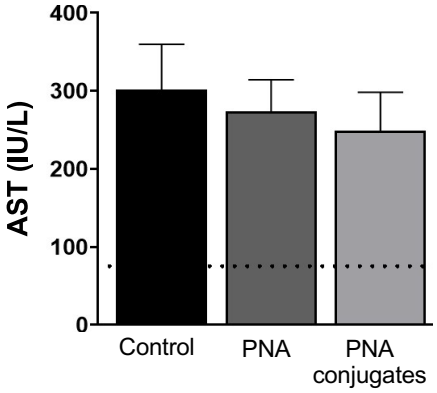
Histology

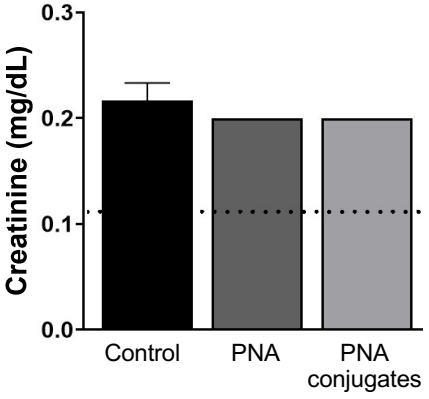


Metabolic panel analysis





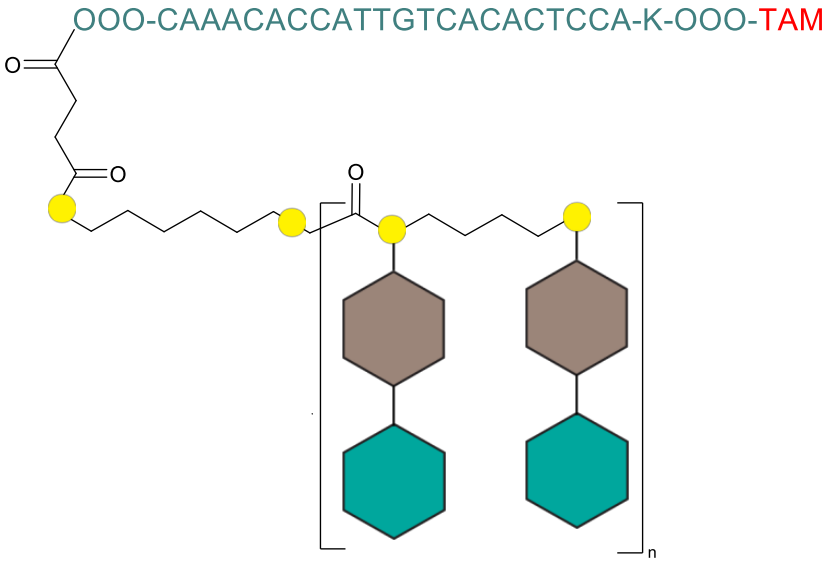


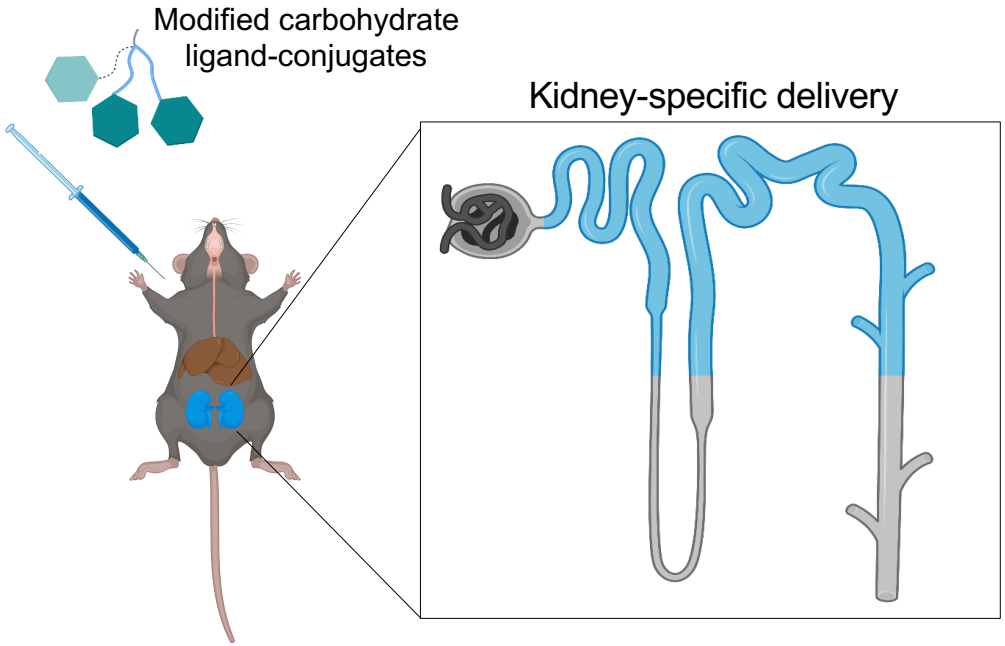


Kumar V et al. *Advanced Healthcare Material,* 2023

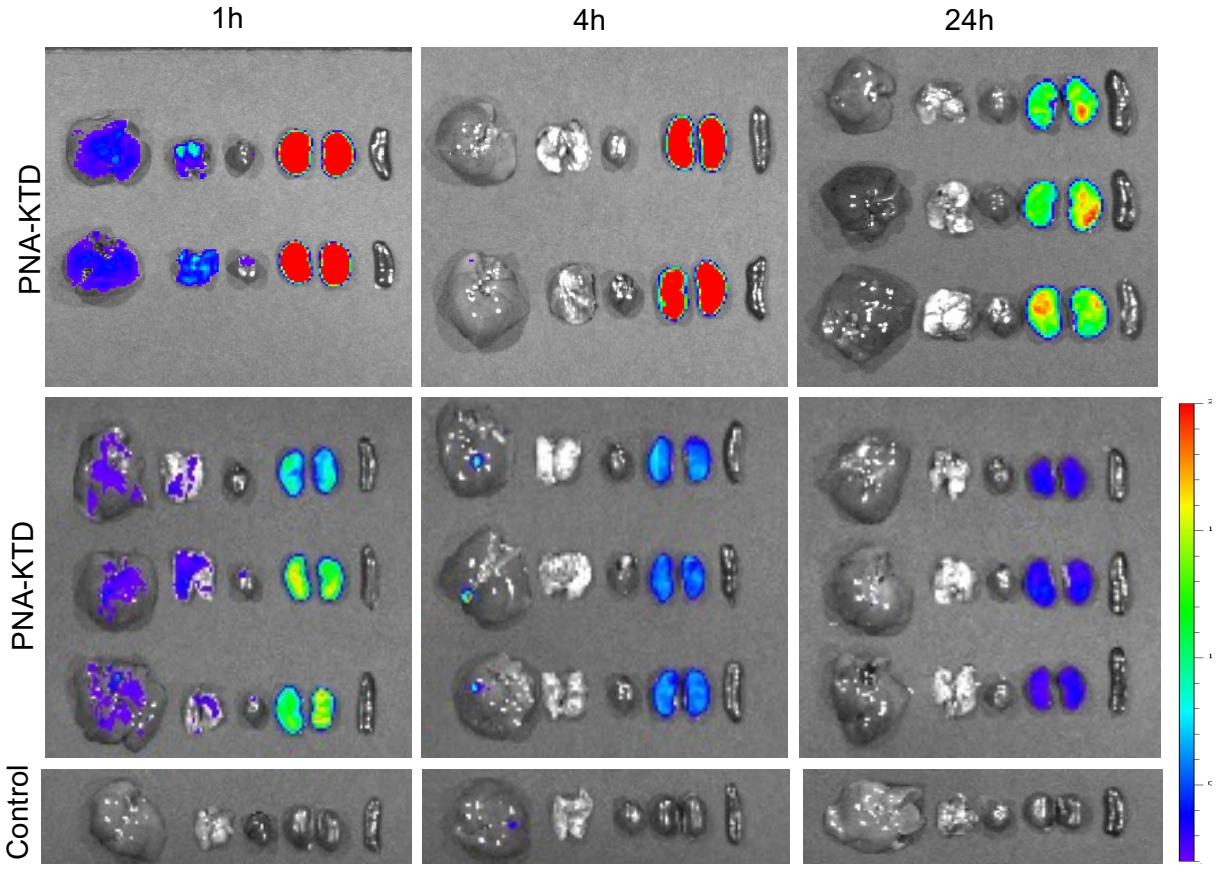
Kidney targeting with modified carbohydrate conjugates

Kidney-targeted modality (PNA-KTD or RENTAC)

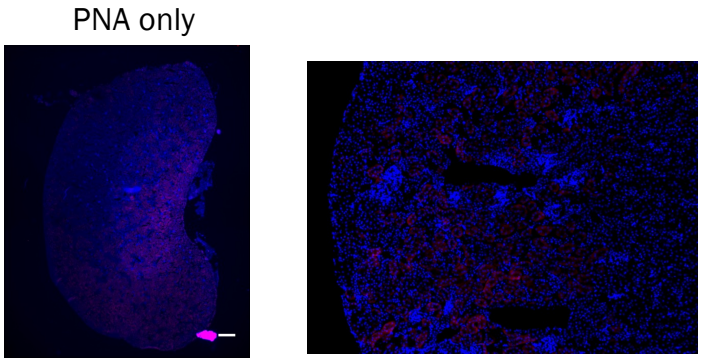


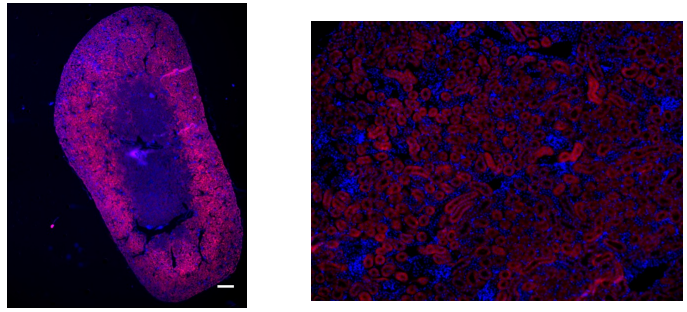


In vivo biodistribution of PNA-KTD conjugates



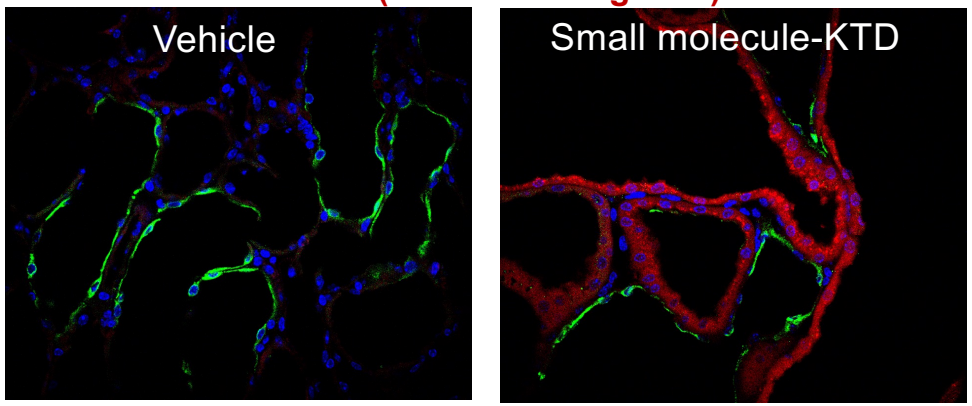
Organs L to R: liver, lungs, heart, kidney, spleen



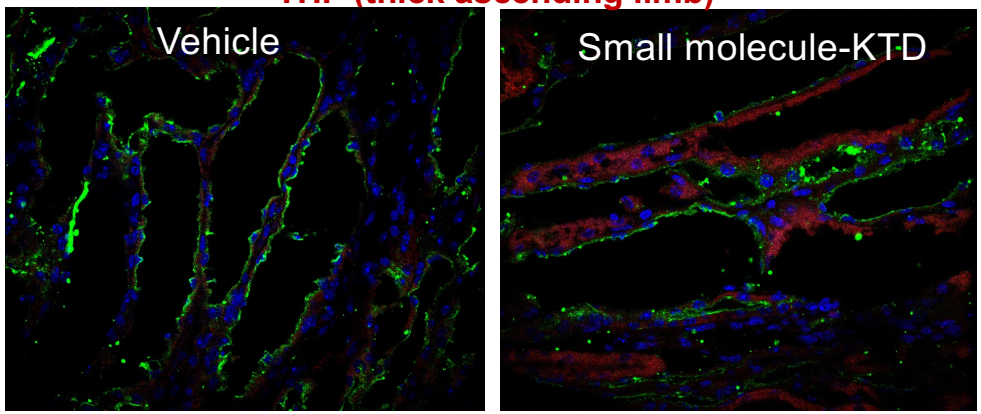


Cell-specific targeting of KTD glycoconjugates

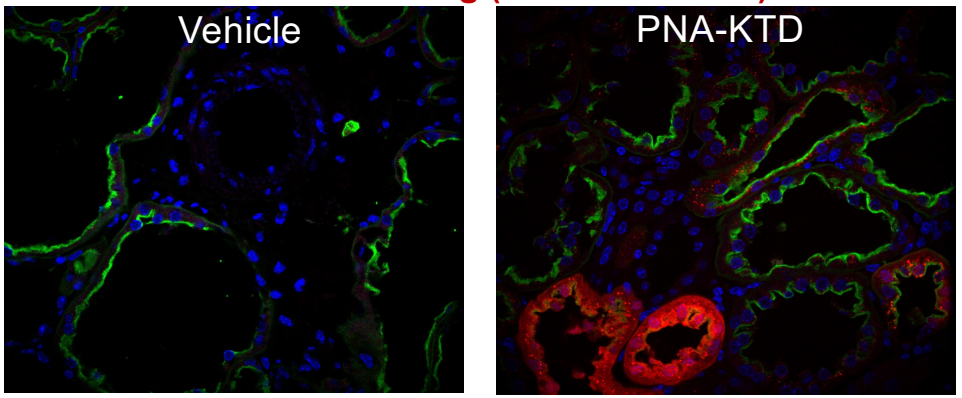
CLC-K (thin ascending limb)



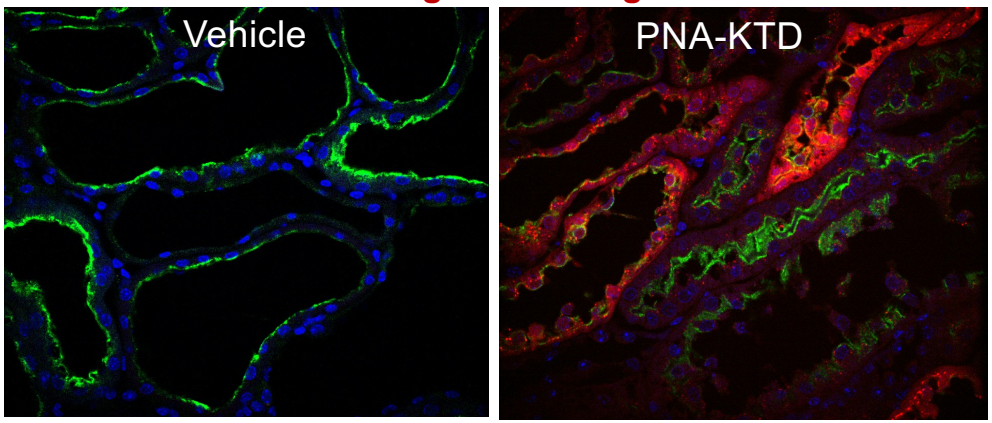
THP (thick ascending limb)



LTL staining (Proximal tubule)



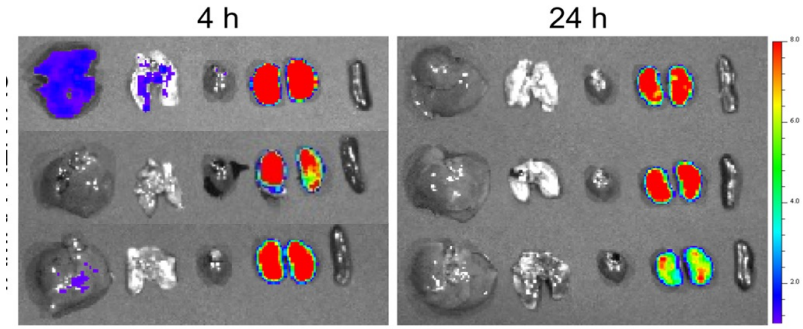
Megalin staining



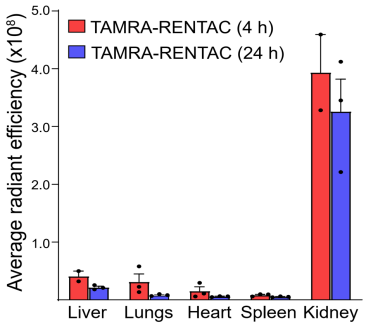
Dr. Tham (Somlo's lab, Yale)

RENTAC conjugates target the fibrosis pre-clinical model

TAMRA- RENTAC

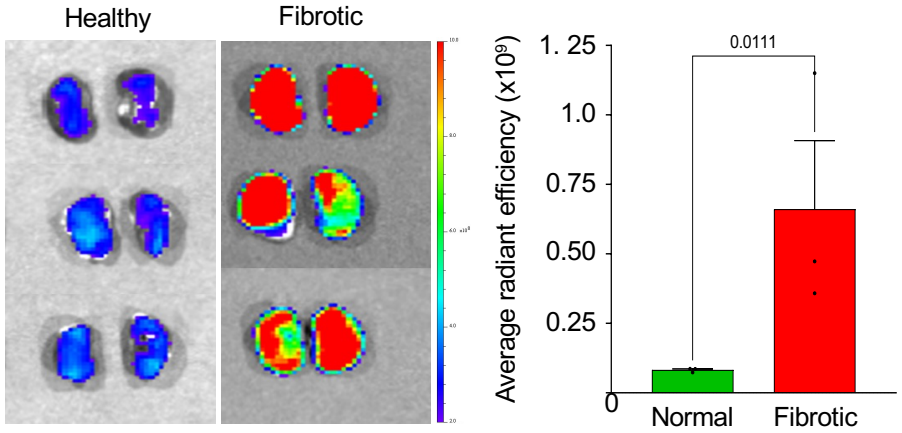


Organ distribution



Dose: 10 mg/kg (s.c.)
Folic acid kidney fibrosis model

Normal vs fibrotic kidney distribution



Unpublished data; in collaboration

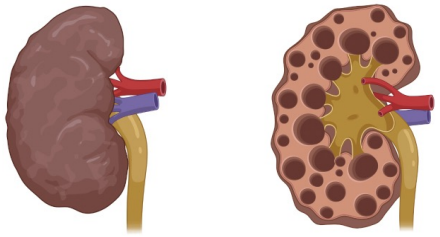
Ongoing work

Dr. S. Somlo
(Yale)

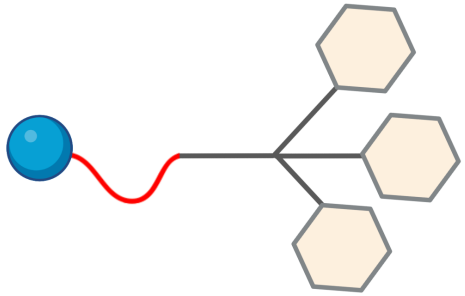
***PKD2*, a Gene for Polycystic Kidney Disease That Encodes an Integral Membrane Protein**

Toshio Mochizuki, Guanqing Wu,* Tomohito Hayashi,* Stavroulla L. Xenophontos, Barbera Veldhuisen, Jasper J. Saris, David M. Reynolds, Yiqiang Cai, Patricia A. Gabow, Alkis Pierides, William J. Kimberling, Martijn H. Breuning, C. Constantinou Deltas, Dorien J. M. Peters, Stefan Somlo†

Science, 1996



- Establishing the efficacy and pharmacokinetic studies in diseased mice
- Comprehensive safety assessment with cytokine panel analysis



Startup for kidney-targeted technology
Zeal Therapeutics

INITIATIVE FOR RNA MEDICINE
HARVARD MEDICAL SCHOOL

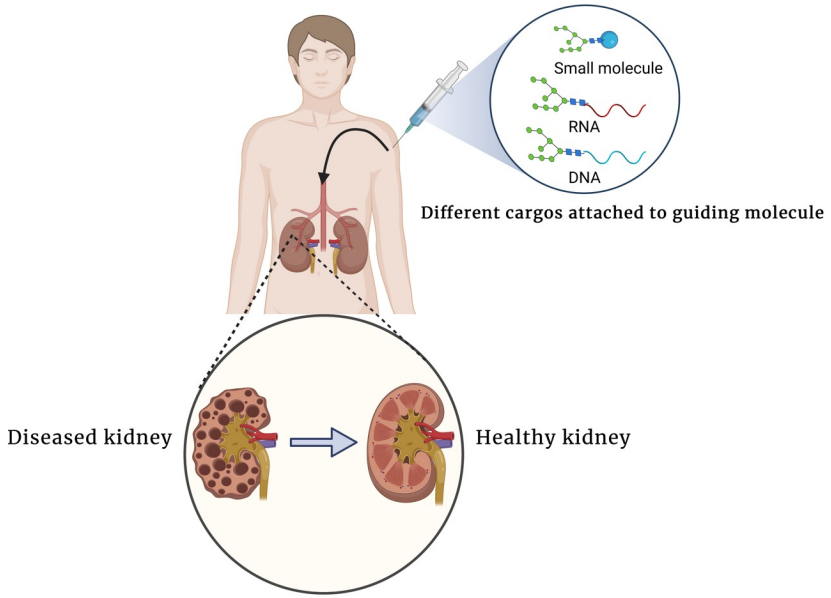
Frank J Slack, PhD, Co-Founder

- Director, HMS Initiative for RNA Medicine
- Co-discoverer of microRNA
- Over 25 years developing miRNA biology
- Co-founder, Mira Dx, 28/7 Tx, Impilo Tx

Iva Toudjarska, PhD, MBA Co-Founder, CEO

- Biotech executive, R&D to commercial, >20 years
- Company builder- investor, operator, CBO/COO, founder
- Platform development expertise
- Kidney drug discovery and development expertise

Alnylam PHARMACEUTICALS · PUTNAM ASSOCIATES · xontogeny · evotec · AUTOBAHN LABS



Other Collaborative Projects

Lung Fibrosis Treatment

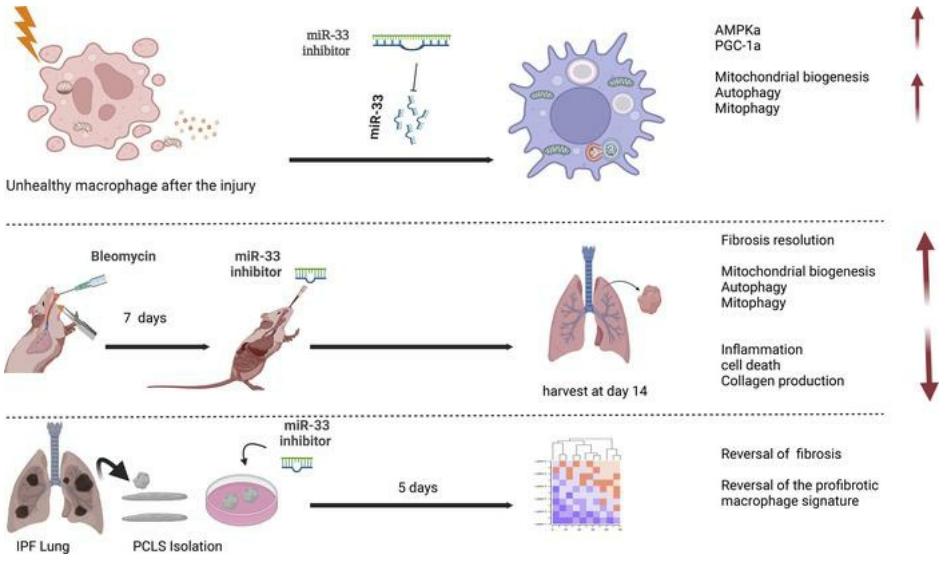
Dr. Farida Ahangari (Yale)

Dr. Naftali Kaminski (Yale)

JCI insight

microRNA-33 deficiency in macrophages enhances autophagy, improves mitochondrial homeostasis, and protects against lung fibrosis

Farida Ahangari, … , Carlos Fernández-Hernando, Naftali Kaminski



Patent filed

Brain Cancer Treatment

Dr. Mark Saltzman (Yale)

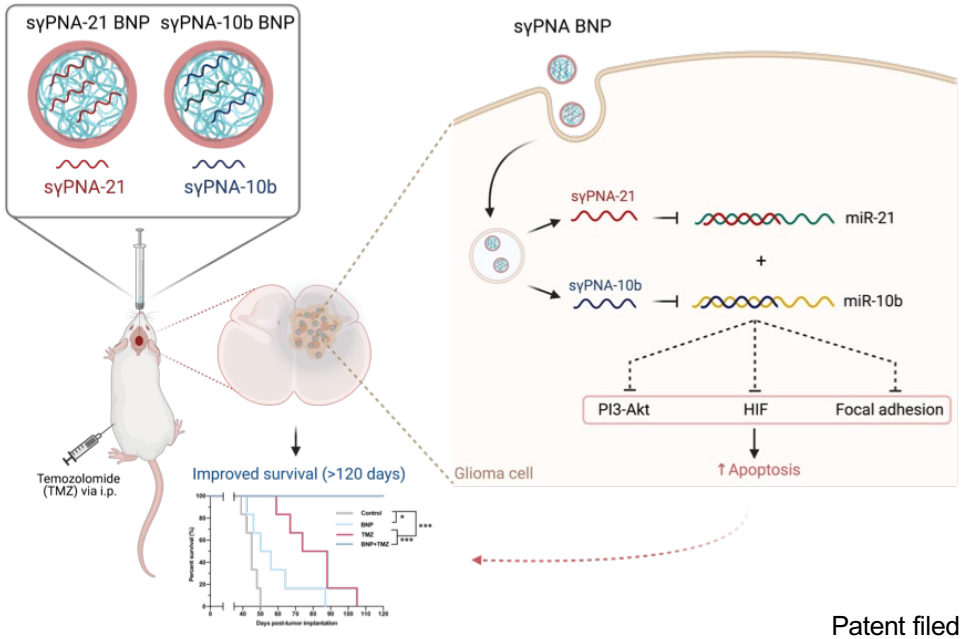
Dr. Ranjit Bindra (Yale)

SCIENCE ADVANCES | RESEARCH ARTICLE

CANCER

Anti-seed PNAs targeting multiple oncomiRs for brain tumor therapy

Yazhe Wang[1†], Shipra Malik[2†], Hee-Won Suh[1], Yong Xiao[1], Yanxiang Deng[1], Rong Fan[1], Anita Huttner[3], Ranjit S. Bindra[4], Vijender Singh[5], W. Mark Saltzman[1*], Raman Bahal[2*]

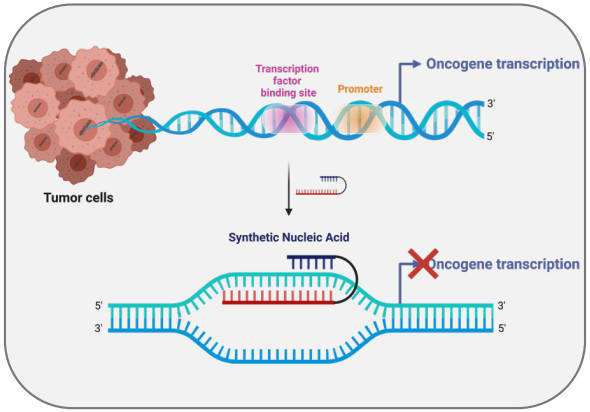


Patent filed

Unmet need-Targeting chromosomal DNA

DNA → mRNA → Protein

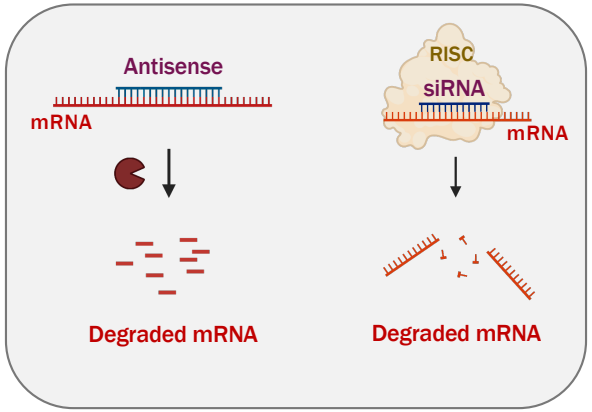
Anti-transcription
(Oncocript Therapeutics)



- ✓ Targeting the oncogenes at their origin
- ✓ Nucleic acid invades the chromosomal DNA
- ✓ Inhibits oncogene transcription

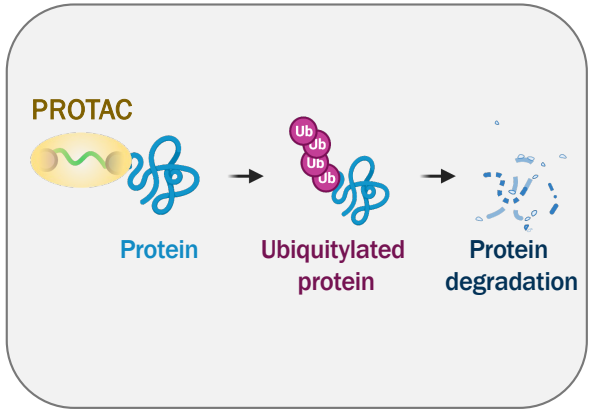
Antisense
(Ionis, Sarepta)

siRNA
(Alnylam)



- ➢ Targets mRNA in the cytoplasm
- ➢ Prevents mRNA translation
- ➢ mRNA still continues to be transcribed from the genome

Proteolysis Targeting Chimera (PROTAC)
(Arvinas)



- ➢ Targets protein and trigger degradation
- ➢ Cannot target “undruggable” proteins
- ➢ Off-target accumulation

Malik S, Pallavi SP et al. 2024, Cell Report Medicine

Acknowledgements

Lab members

Dr. Vikas Kumar

Aniket Wahane

Shipra Malik

Karishma Dhuri

Vishal Kasina

Sai Pallavi Pradeep

UConn technology commercialization service

Dr. Amit Kumar

Dr. Vivek Ramakrishnan

Dr. Ana Fidantsef

Collaborators

Dr. Stefan Somlo (Yale)

Dr. Tham Ming Shen (Yale)

Dr. Frank Slack (Harvard)

Dr. Gyongyi Szabo (Harvard)

National Institutes of Health

UConn Start PPOC

UConn SPARK Funding

Charles H. Hood Foundation

St. Baldrick's Foundation — Conquer Childhood Cancers

connecticut innovations

Dane O. Kildsig Center for Pharmaceutical Processing Research (CPPR)

Cooley's Anemia Foundation — Leading the Fight Against Thalassemia

Translational Research at

the Laboratory for Innovative Microtechnologies & Biomechanics (LIMB)

Ali Tamayol

LIMB

UNIVERSITY OF CONNECTICUT HEALTH CENTER

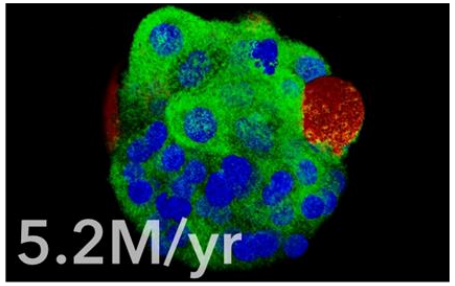
Musculoskeletal Injuries

Musculoskeletal disorders are frequent and account for $400 billion in annual healthcare costs in the United States

Motor vehicle traumas

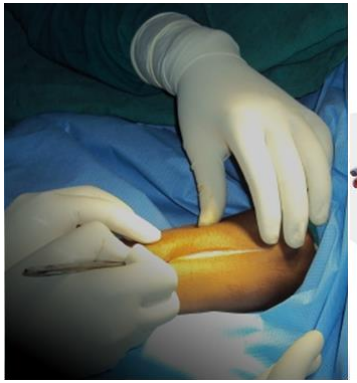
Blast injuries

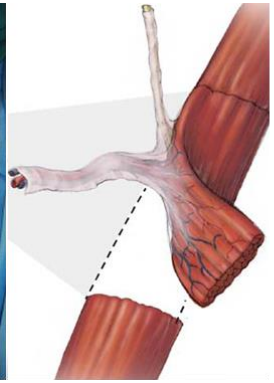
Tumor resection



Open fractures

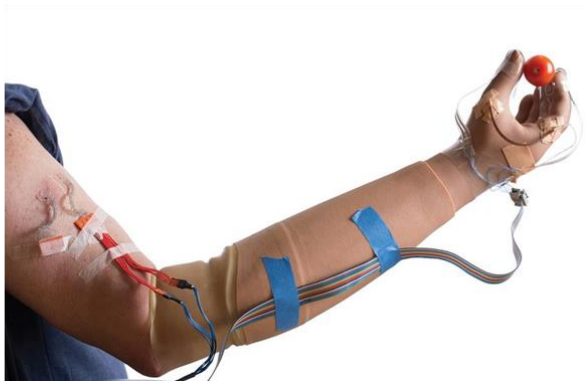
Muscle transplantation



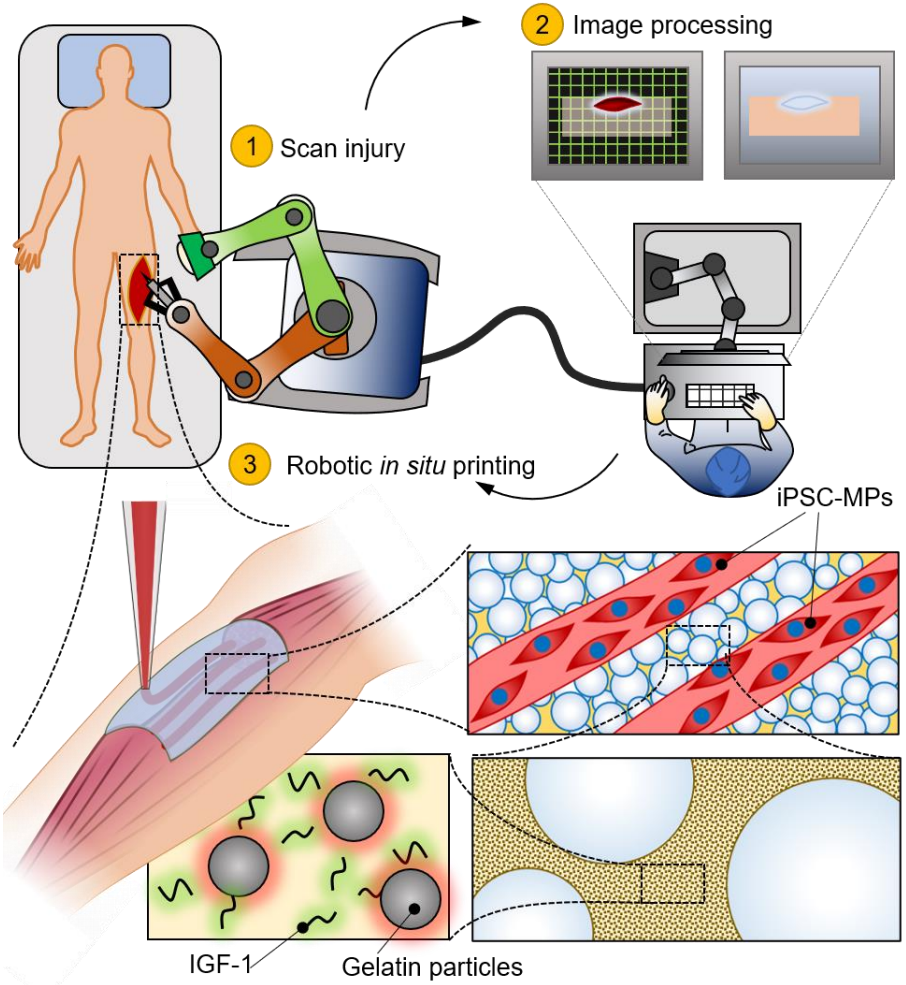


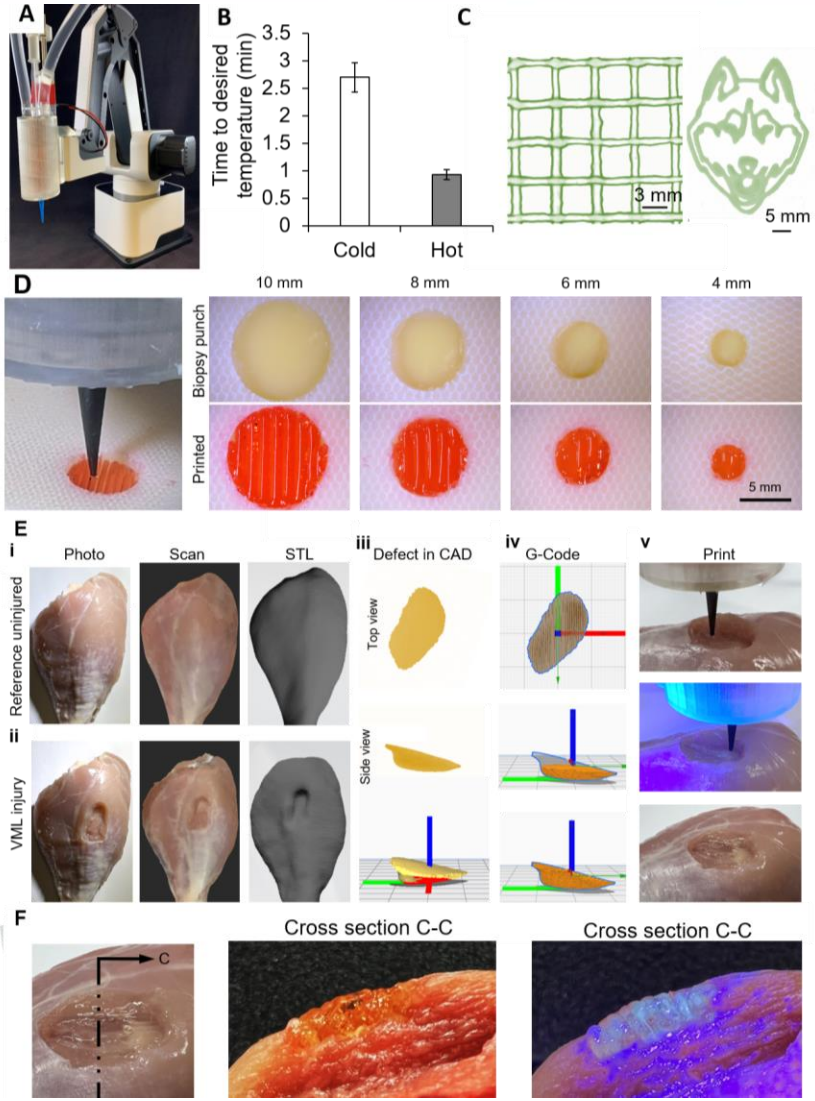
Physical therapy

Amputation and prosthetics

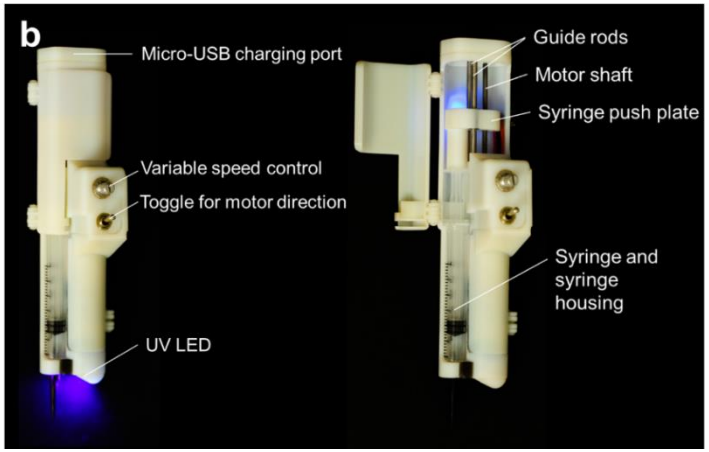


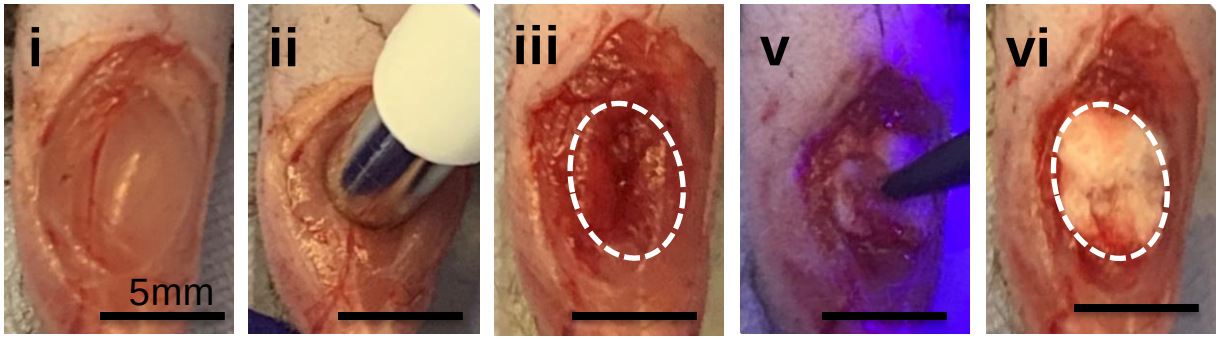
Intraoperative bioprinting

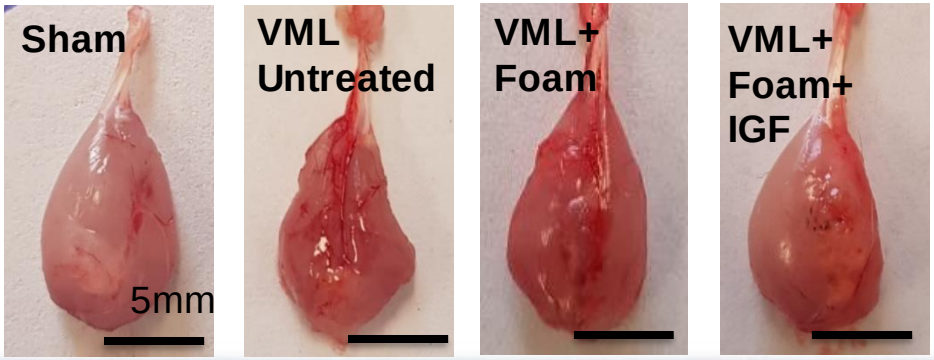


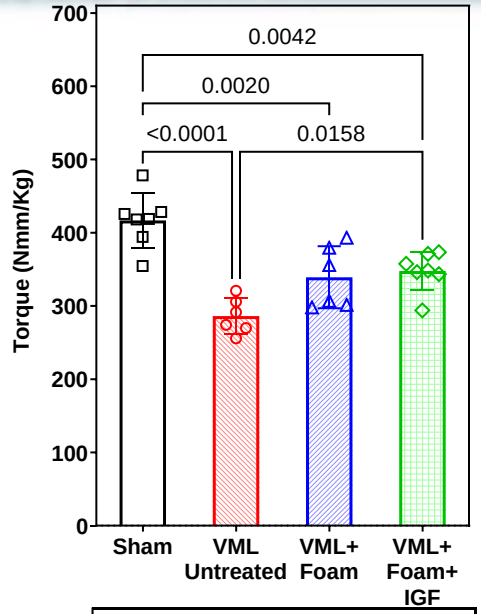


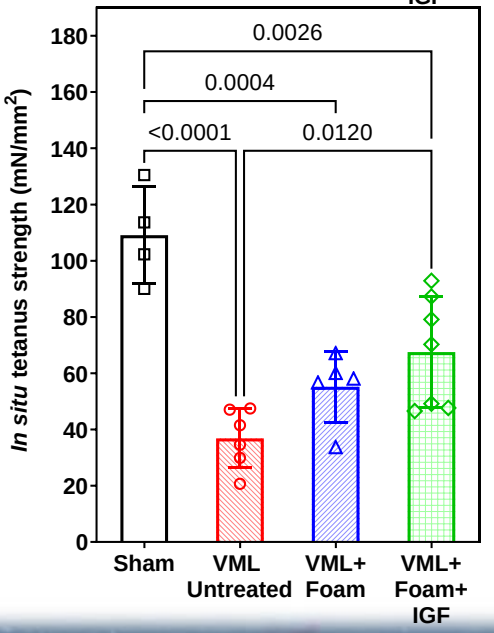
Porous bioinks



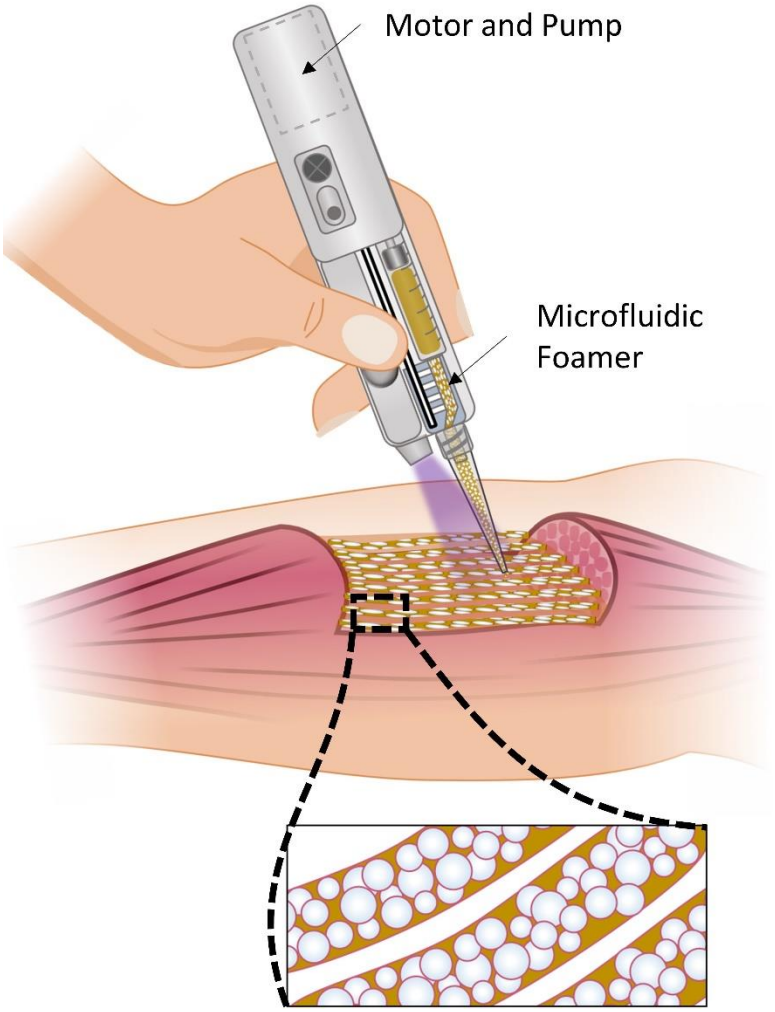








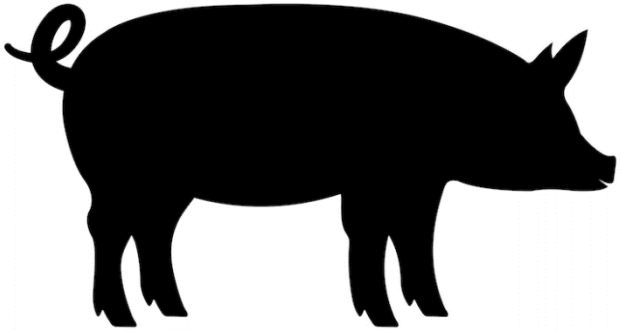
Value Proposition



- ☑ **SHORTEN** surgery from 10 to 1 hour
- ☑ **ELIMINATE** the need to **SACRIFICE** donor tissue
- ☑ **INCREASE** range of treatable injuries and profits
- ☑ **IMMEDIATELY** begin functional regeneration
- ☑ **REDUCES** hospital and rehab admission by 21 days
- ☑ **ENABLES** reconstruction at non-specialized centers

Accomplishments from Spark Grant

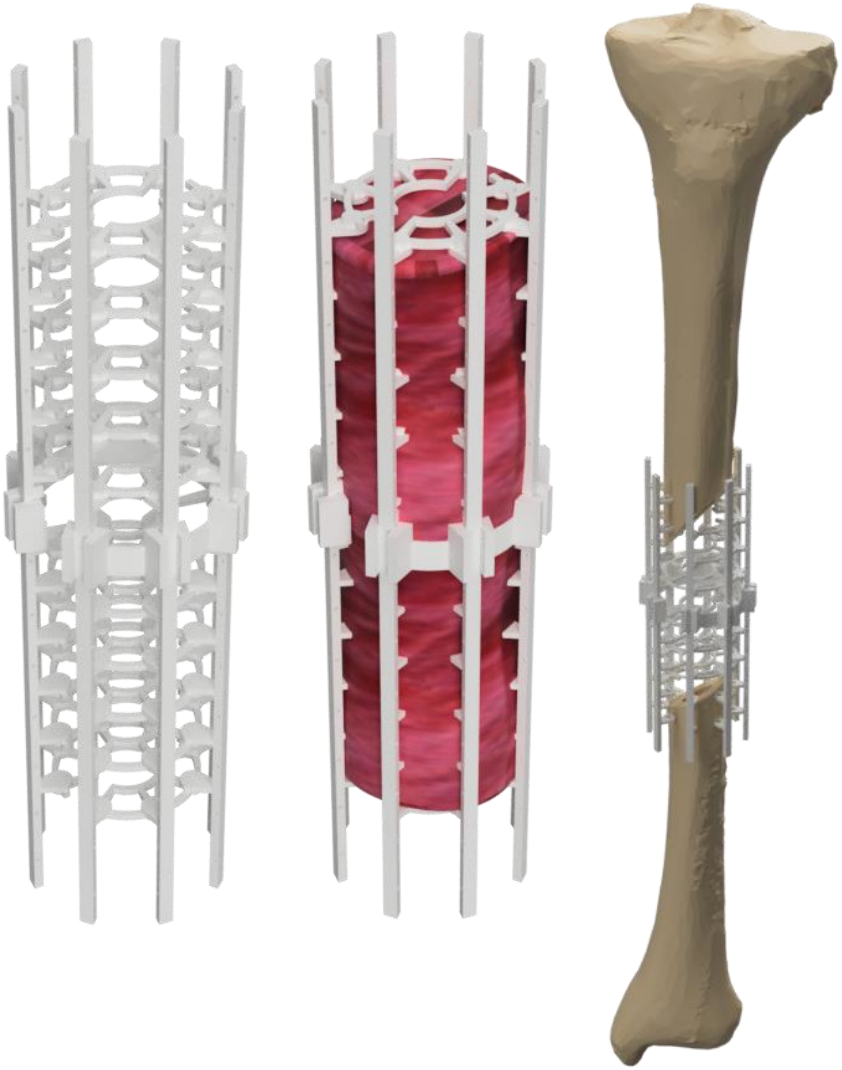
Breakthrough Device Designation



$2.2M through CDMRP (~$300k InPrint Bio; ~$400k UConn
$600k through CDMRP to UConn

SBIR phase I, ~$300k
Submitted: STTR phase I

Bone graft containment system



INCREASE the chance of using bone grafts for segmental large bone defects

REDUCE the chance of amputation

REDUCE complexity and numbers of the surgeries

SHORTEN the recovery time

IMMEDIATELY being ready-to-use intraoperatively

ELIMINATES the risk of dysfunction due to damage, distort or mismatch

ENABLES patient-specific solution without any delay

Accomplishments from Spark Grant

Submitted: SBIR phase I

510K Pathway

- **Aim 1:** Optimization and characterization of OrthoCage for enhanced mechanical stability, bone graft retention capacity, and facile implantation (Months 1-6).
- **Aim 2:** Development of BMP2-eluting OrthoCage+ and characterization of biological properties of OrthoCage(+) in vitro and in vivo (Months 6-11).
- **Aim 3:** Ex vivo assessment of the implantability of OrthoCage to contain bone graft in a segmental large bone defect model (Months 8-12).

Thank you!

Ali Tamayol

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