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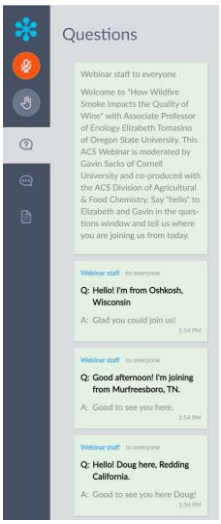

"Why am I muted?"
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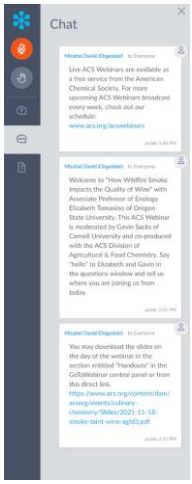
Chat

Announcements and hyperlinks from our team



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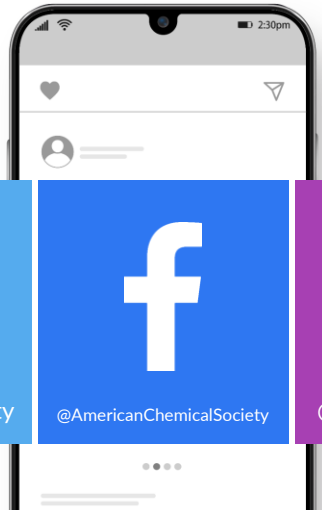

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https://chemidp.acs.org

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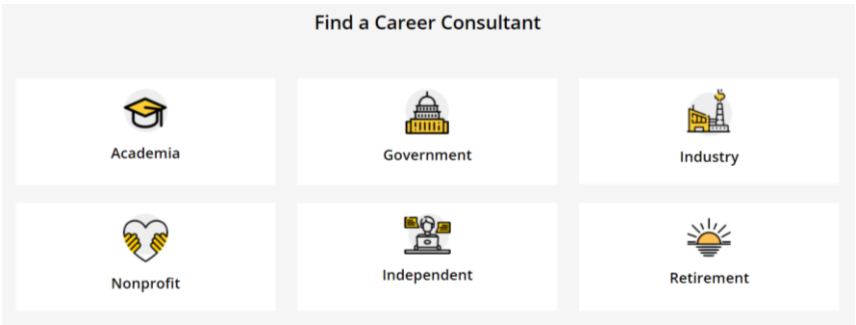
Career Consultant Directory



- ACS Member-exclusive program that allows you to arrange a one-on-one appointment with a certified ACS Career Consultant.
- Consultants provide personalized career advice to ACS Members.
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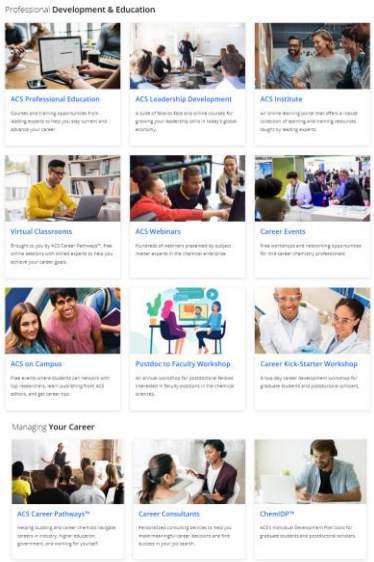
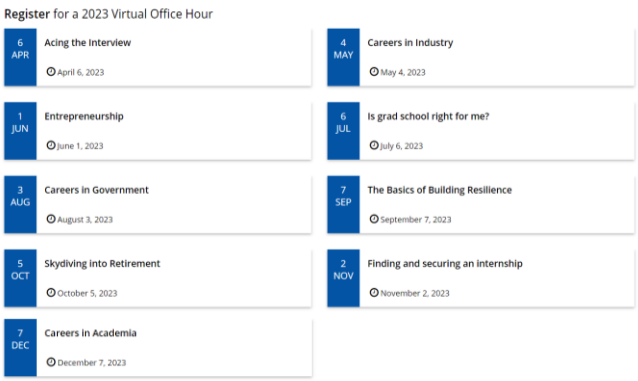
ACS Career Resources





https://www.acs.org/content/acs/en/careers/personal-career-consulting.html

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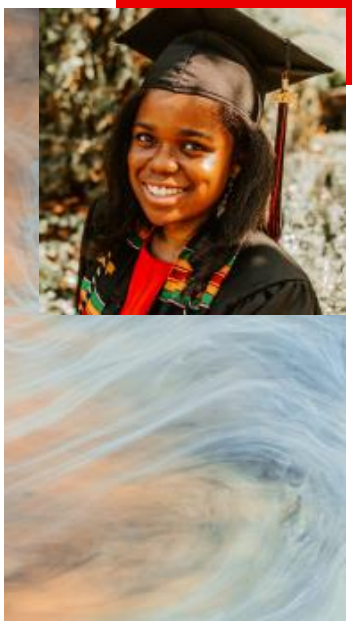

ACS Scholar Adunoluwa Obisesan

BS, Massachusetts Institute of Technology, June 2021
(Chemical-biological Engineering, Computer Science & Molecular Biology)

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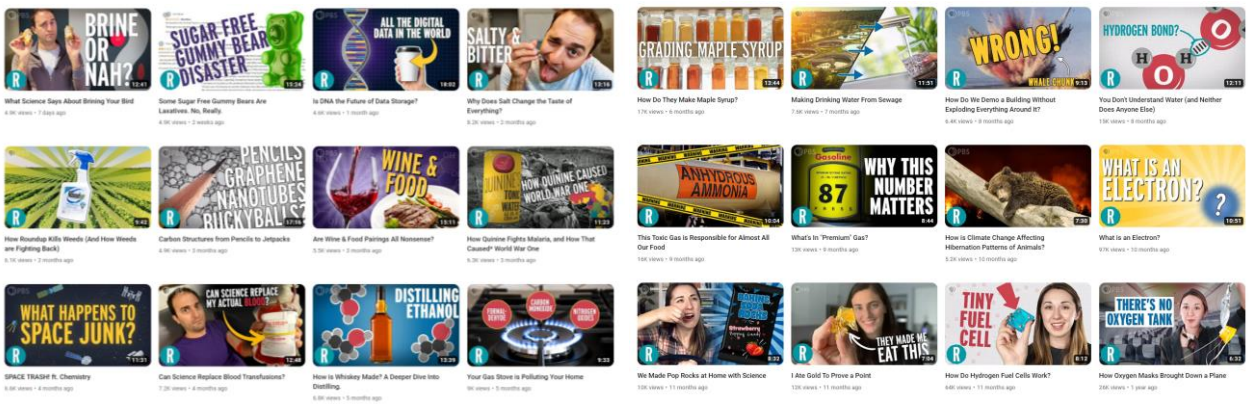

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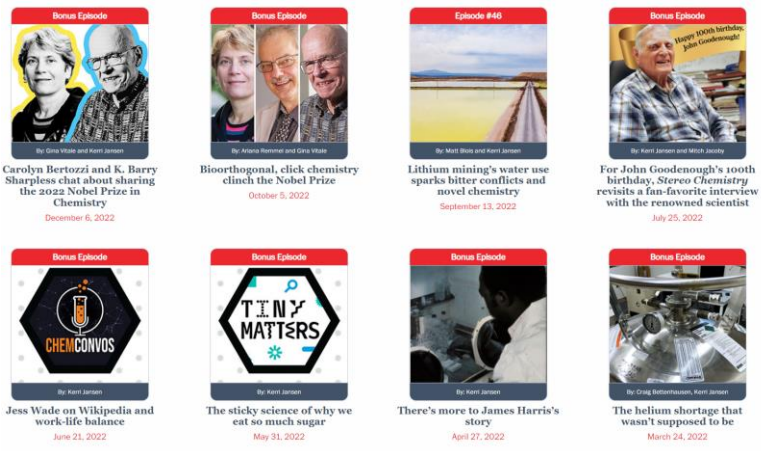
c&en's STEREO CHEMISTRY



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ACS ON CAMPUS

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ACS OFFICE OF DEIR

Advancing ACS' Core Value of Diversity, Equity, Inclusion and Respect

Resources

Inclusivity Style Guide
Designed to help staff and members use language and images that respect diversity in all its forms.

ACS Webinars on Diversity
Covering diversity and inclusion at the workplace

ACS Publications DEIR Hub
See what ACS Publications is doing for fostering inclusivity in scholarly publishing

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Quick Guide: Inclusion Moments
Learn more about what Inclusion Moments are and see ideas to host them during your meetings.

Quick Guide: How to host inclusive in-person events
Recommendations and best practices to ensure that your events can accommodate everyone.

Diversity, Equity, Inclusion, and Respect
**Adapted from definitions from the Ford Foundation Center for Social Justice:

Equity**
Seeks to ensure fair treatment, equality of opportunity, and fairness in access to information and resources for all. We believe this is only possible in an environment built on respect and dignity. Equity requires the identification and elimination of barriers that have prevented the full participation of some groups.

Diversity**
The representation of varied identities and differences (race, ethnicity, gender, disability, sexual orientation, gender identity, national origin, tribe, caste, socio-economic status, thinking and communication styles, etc.), collectively and as individuals. ACS seeks to proactively engage, understand, and draw on a variety of perspectives.

Inclusion**
Builds a culture of belonging by actively inviting the contribution and participation of all people. Every person's voice adds value, and ACS strives to create balance in the face of power differences. In addition, no one person can or should be called upon to represent an entire community.

Respect
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https://www.acs.org/diversity

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Friday, April 14, 2023 | 8:30-9:30am ET

An Indian Millennial Journey: Engineering to UPSC to MBA

Co-produced with the ACS International and ACS Publications

Monday, April 17, 2023 | 1-2pm ET

Algae Biorefinery: Extraction, Fractionation, and Purification

Co-produced *Chemists Celebrate Earth Week*, ACS GCI, and ACS Publications

Thursday, April 20, 2023 | 2-3pm ET

Cannabinoids: Stumbling Through Challenging Separations (Rebroadcast)

Co-produced with ACS Office of Career and Professional Education

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ACS Award in Chromatography
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Joanna Aizenberg
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Karen I. Winey
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Julia A. Kalow
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Arthur C. Cope Late Career Scholars Award
Vincent M. Rotello
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Arthur C. Cope Mid-Career Scholars Award
Javier Read de Alaniz
University of California, Santa Barbara

E. V. Murphree Award in Industrial and Engineering Chemistry
Qinghuang Lin
Lam Research Corp.

Kathryn C. Hach Award for Entrepreneurial Success
Philip J. Wyatt
Wyatt Technology Corp.

Priestley Medal
Cato T. Laurencin
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Laura L. Kiessling
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Engineering Polymers that Prevent Rejection of Gene Therapy and 3-D Printed Implants

KE ZHANG, PhD

Professor, Department of Chemistry and Chemical Biology, Northeastern University

MATTHEW L. BECKER, PhD

Hugo L. Blomquist Distinguished Professor, Department of Chemistry, Thomas Lord Department of Mechanical Engineering & Material Science Department of Biomedical Engineering and Department of Orthopaedic Surgery, Duke University

ADRIAN FIGG, PhD

Assistant Professor, Department of Chemistry, Virginia Tech

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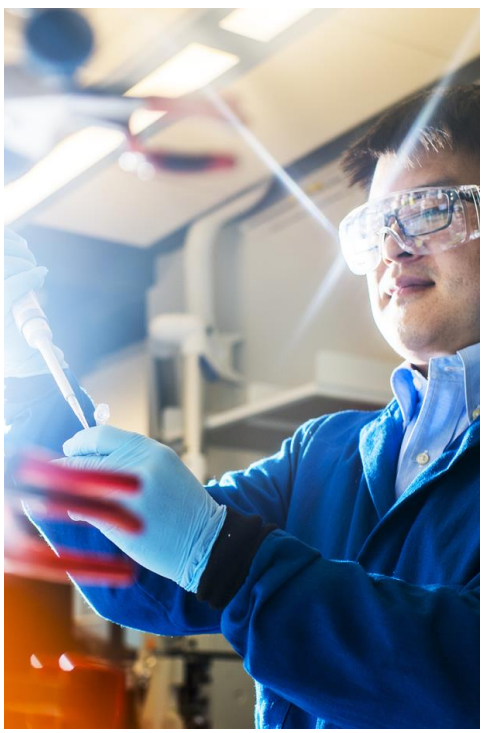

Making oligonucleotides better medicines

with bottlebrush polymers

Ke Zhang
Northeastern University

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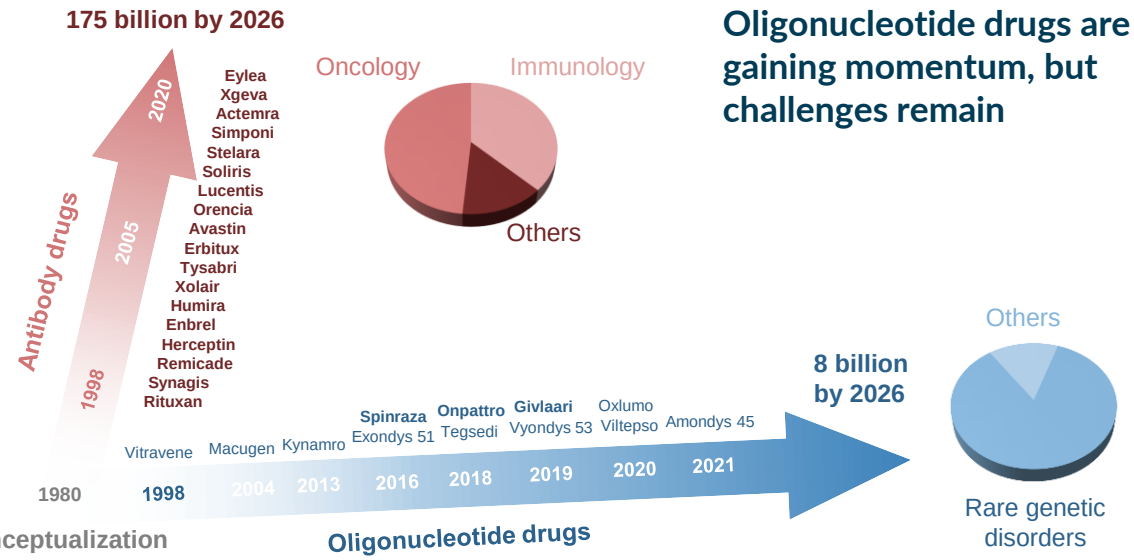
Disclosure

Ke Zhang declares financial interest (ownership) in pacDNA LLC

25

The history



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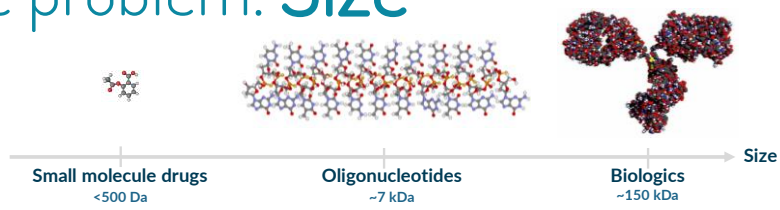
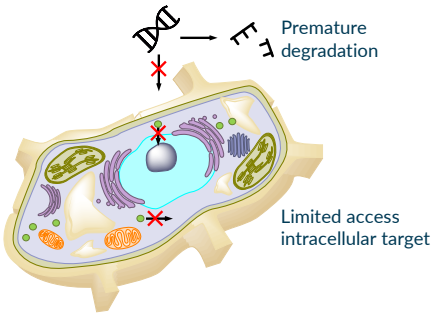
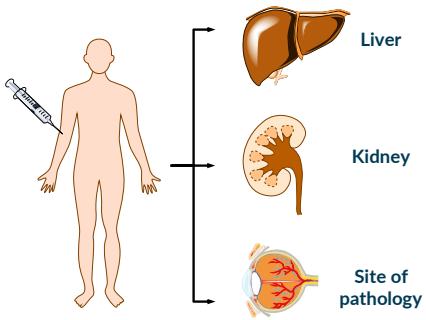
The problem: Size







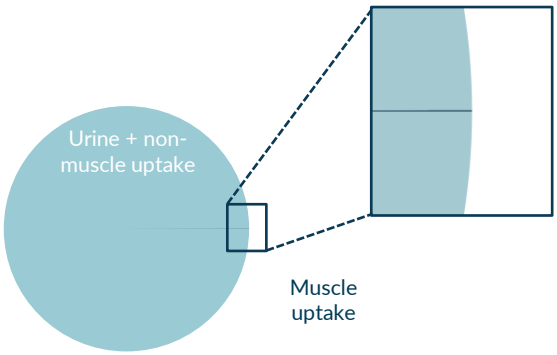
27 Multiple cellular barriers reduce intracellular target access

Limited organs to receive injected drug

27

The problem: Distribution

Duchenne Muscular Dystrophy
$6.4B by 2028*



- 70% renal clearance in 24 h**
- Est. 0.1% of the remainder 30% in target tissue (skeletal muscle)***

- Necessitates frequent, high-dose infusions (50 mg/kg/wk)
- Exceedingly expensive ($750k-$1.5M/yr)

28

*EvaluatePharma data; **Sarepta data in *Ann. Neurol.* **2013**, 74, 637; ***Estimated using general PMO biodistribution data from *Nucleic Acid Ther.* **2015**, 25, 275

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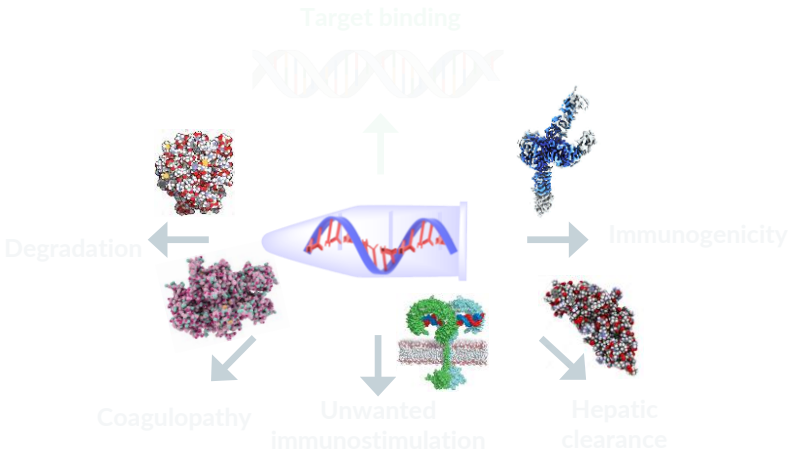
The problem: Selectivity



Need a selective form of nucleic acid...

29

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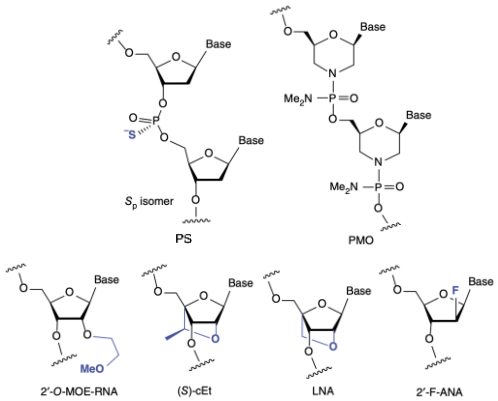
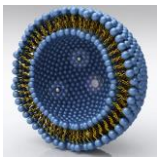
Current solutions

Chemical modifications

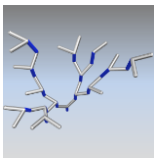


- Increased off-target binding, toxicity

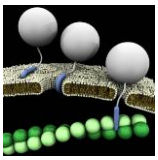
Carriers



Lipid NPs



Polyplexes



Peptides/proteins

- Carrier-associated toxicity
- Anti-carrier immunity

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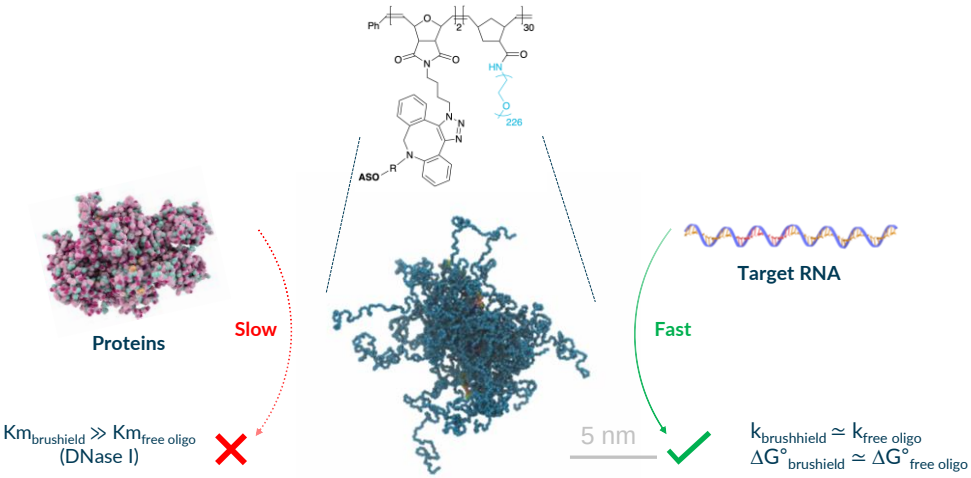
Our solution: Brushield



A selective form of oligonucleotide

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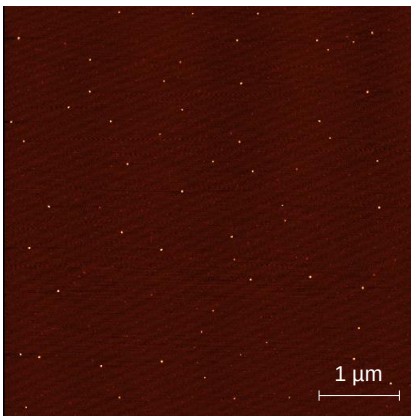
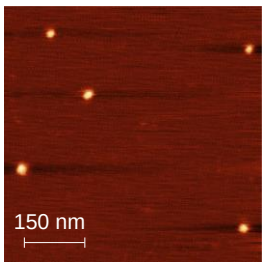
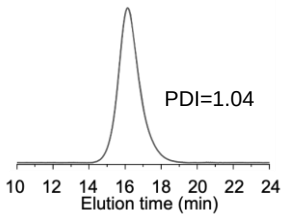
Characterization

AFM microscopy

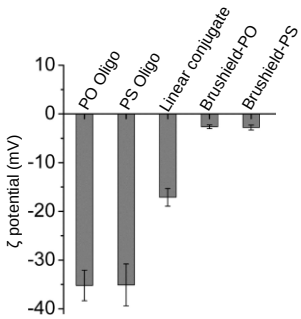




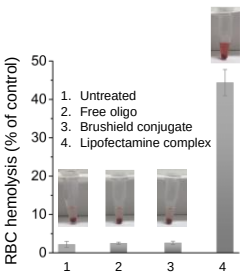
Size exclusion chromatography



ζ potential



Hemolysis



- Molecular nanoparticle (not assembly), ~20 nm
- Highly homogeneous
- Slightly negative ζ potential (near neutral)
- No hemolytic activity

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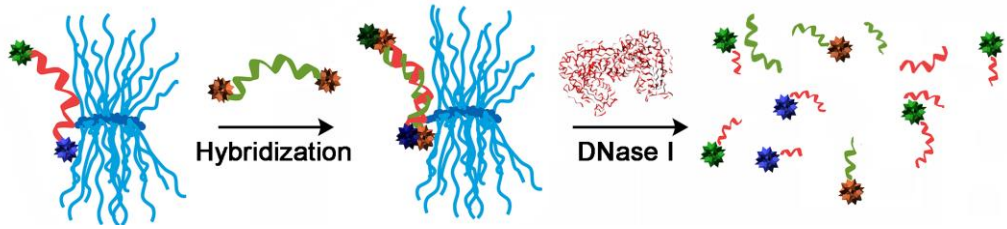
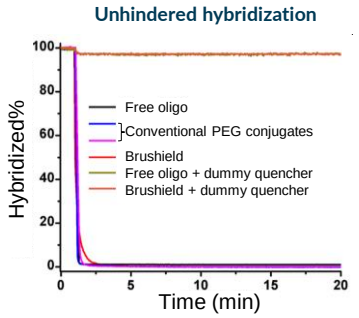
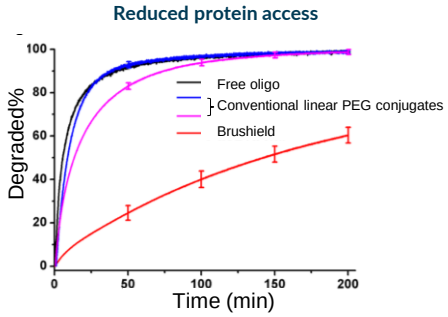
Validation: Selectivity







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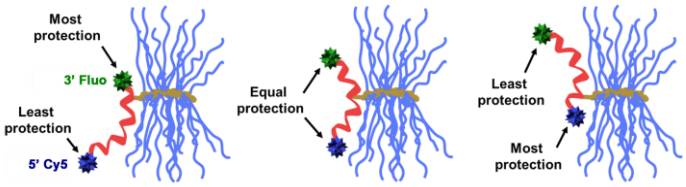
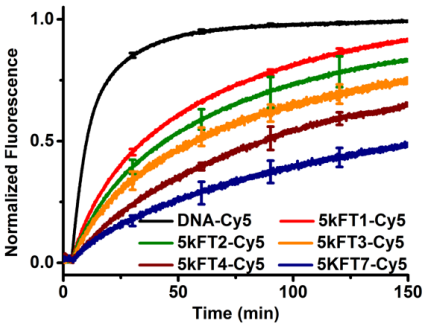
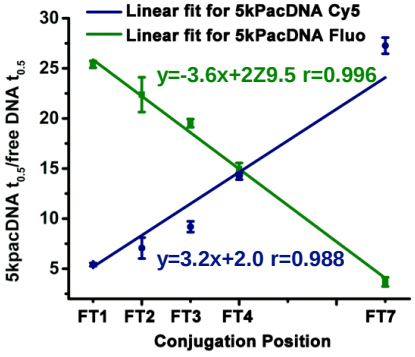
Sterics depth profile



- FT1: 5'-Cy5-GTG $(GTG)_5$ G*T*G-Fluo-3'
- FT2: 5'-Cy5-$(GTG)_5$ G*T*G GTG-Fluo-3'
- FT3: 5'-Cy5-$(GTG)_4$ G*T*G $(GTG)_2$-Fluo-3'
- FT4: 5'-Cy5-$(GTG)_3$ G*T*G $(GTG)_3$-Fluo-3'
- FT7: 5'-Cy5-G*T*G $(GTG)_5$ GTG-Fluo-3'
- DNA: 5'-Cy5-GTG $(GTG)_5$ GTG-Fluo-3'





Every nucleotide's length towards the core of the brush adds roughly a half-life of free DNA

34

JACS, **2017**, *139*, 10605

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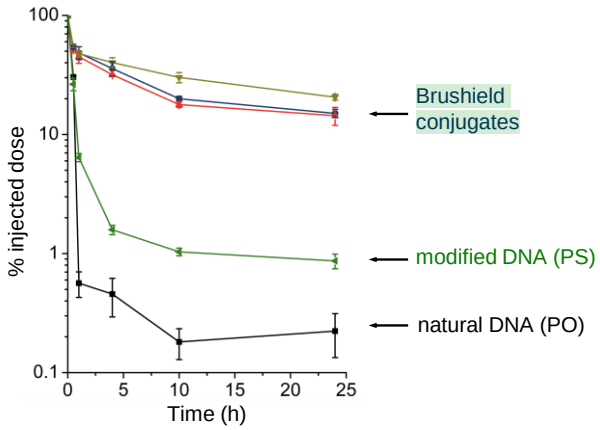
Validation: PK

Brushield improves oligonucleotide **plasma pharmacokinetics** and **blood availability***



Sample ID	$t_{1/2\alpha}$ (h)	$t_{1/2\beta}$ (h)	AUC_{∞} (nmol/mL·h)
PO oligo	0.26	0.5	2.7
Brushield	2.06	24.1	314.0

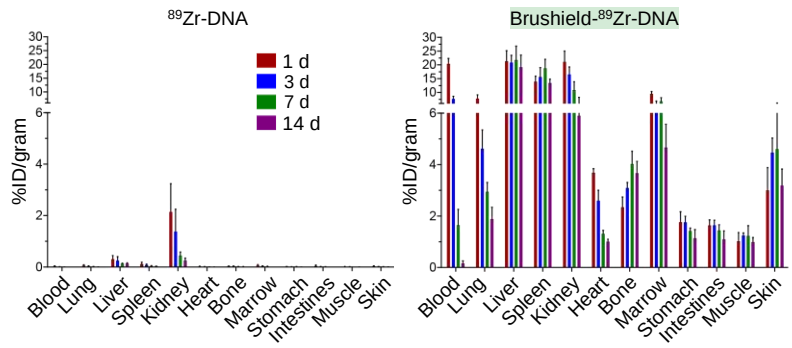
35

*Data obtained using immunocompetent C57BL/6 mice

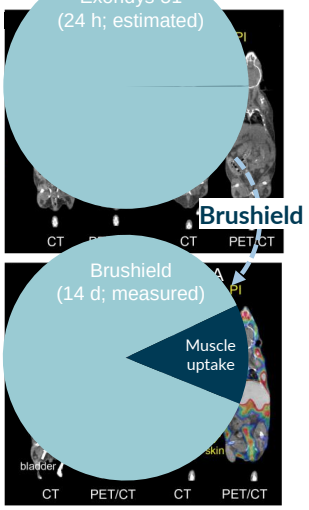
Validation: Distribution

Brushield enables **extrahepatic distribution** and prolongs **tissue retention**

Quantitative ex vivo biodistribution* following i.v. delivery



Representative PET/CT images of ^{89}Zr radiolabeled samples 1-day or 7-days post i.v. (decay corrected)



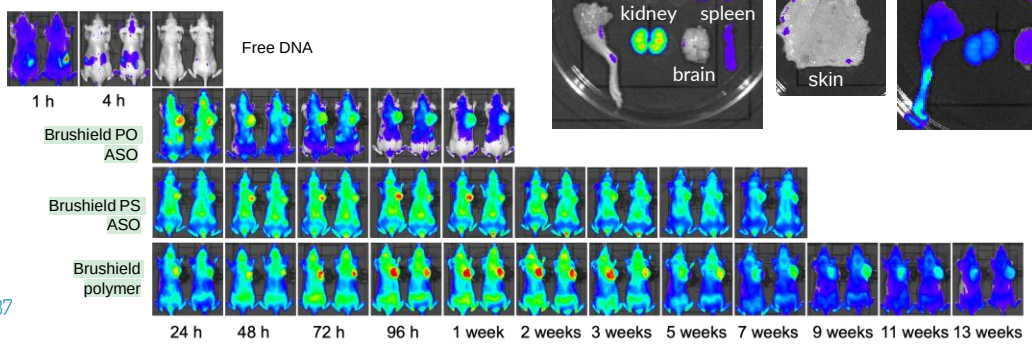
36

*Data obtained using immunocompetent CD-1 mice and ^{89}Zr radiolabeled samples; ^{89}Zr is chelated through a DFO chelator conjugated on the PO DNA

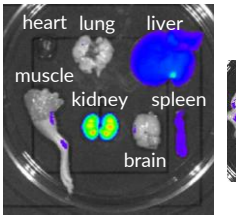
Validation: Distribution

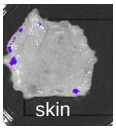
Brushield enables **extrahepatic distribution** and prolongs **tissue retention**

Live animal fluorescence imaging following a single i.v. dose of Cy5.5-lableled samples*

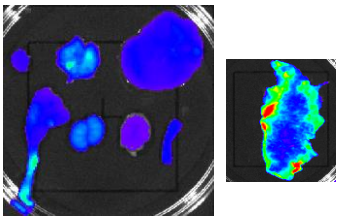


Unprotected oligonucleotide, 24 h**





Brushield, 3 days**



*Imaged with athymic nude mice with NCI-H358 tumor xenograft; **immunocompetent SKH1-Elite mice

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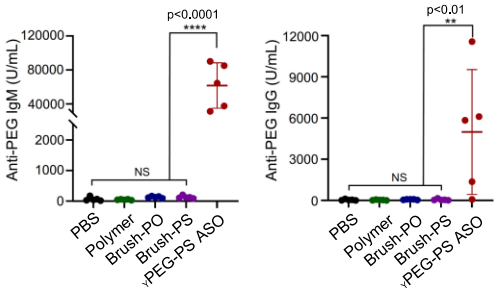
Validation: Safety

Brushield conjugates are **safe** and **non-immunogenic**

- **Predominantly GRAS chemical composition**
- **Non-cationic, non-surfactant-like**
- **No changes detected in:***
  - animal body weight/behavior
  - hepatic/renal function indices
  - blood parameters (hemolysis, coagulation, biochemistry, etc.)
  - histological features in major organs
  - cytokine profile or complement C3
  - adaptive immunity

Anti-PEG immunoglobin levels*



Brushield conjugates are uniquely non-immunogenic

*C57BL/6 mice; Brushield™-PO DNA conjugate; i.v. dosed at 0.5 µmol/kg (160 mg/kg) every 3rd day for 36 days

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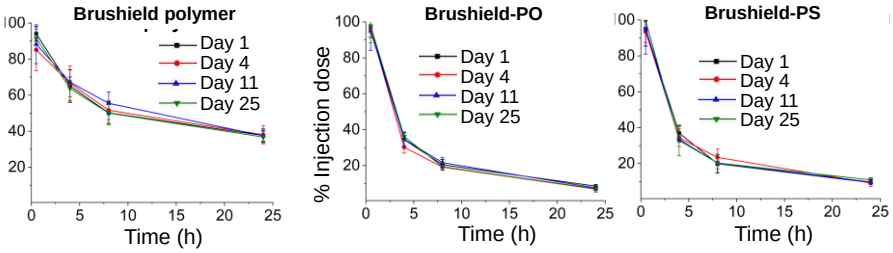
Validation: Immunogenicity

Brushield™ conjugates do not exhibit **accelerated blood clearance**

Healthy mice were given samples i.v. on the 1st, 4th, 11th, and the 25th day

No observed accelerated blood clearance (ABC) effect



39

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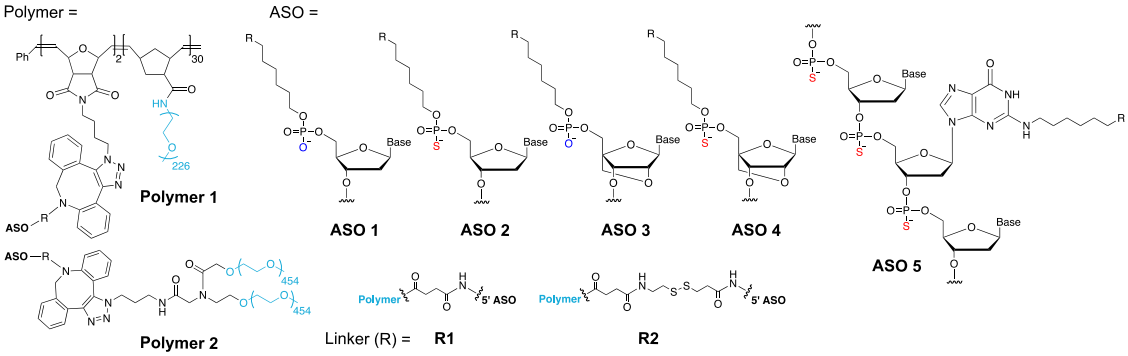
Efficacy: KRAS-driven cancer

Site: lung, multisystem
Modality: ASO

Brushield conjugates are **potent in vivo**

- The most mutated proto-oncogene
- Undruggable for 3 decades
- First inhibitors in 2021 for G12C
- Still an unmet clinical need



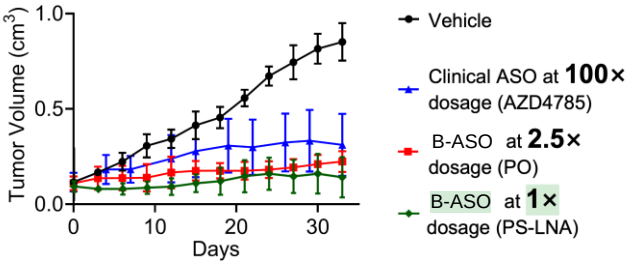
40

40

Efficacy: KRAS-driven cancer

Brushield conjugates are **potent in vivo**

***KRAS*^{G12C} mouse xenograft (NCI-H358)**



Sample ID	Dose (µmol/kg)	ROA	Frequency
AZD4785	10.0	s.c.	Daily
Brushield-PO	0.5	i.v.	Every 3rd day
Brushield-PS-LNA	0.1	i.v.	Weekly

2.5 mg/kg (ASO basis)

The Brushield

- massively improves oligo activity *in vivo*
- reduces dosage requirement compared to state-of-the-art
- relaxes the need for specific chemical modifications

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PNAS, **2022**, DOI: 10.1073/pnas.2113180119

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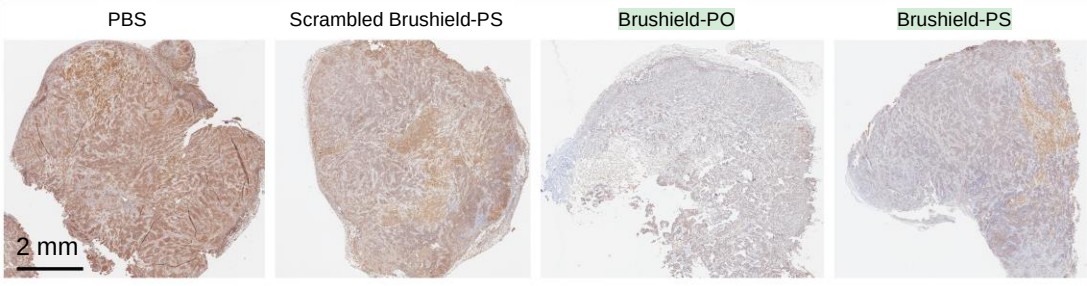
Efficacy: KRAS-driven cancer

Brushield conjugates are **potent in vivo**

Immunohistostaining of tumor cryosections for KRAS (brown deposits). Cell: NCI-H358



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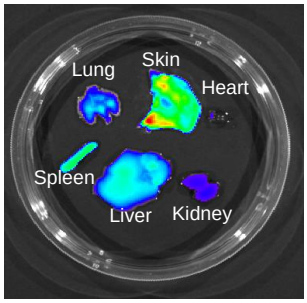
Efficacy: IL17RA (psoriasis)

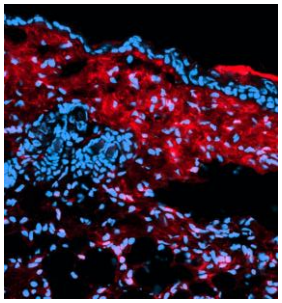
Site: skin
Modality: ASO

Brushield conjugates are **potent in vivo**

Brushield biodistribution 24 h after i.v. injection



Brushield distributes across all skin layers



Red: Brushield conjugate
Blue: nucleus

Significant uptake by

- keratinocytes
- macrophages
- skin-resident DCs
- fibroblasts
- adipocytes

Brushield conjugates accumulate across skin layers and are taken up by skin cells

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*Data obtained with C57BL/6 mice

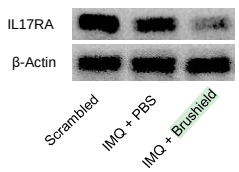
43

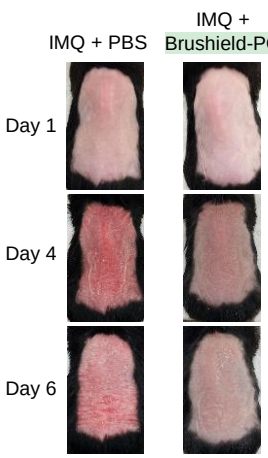
Efficacy: IL17RA (psoriasis)

Brushield conjugates are **potent in vivo**

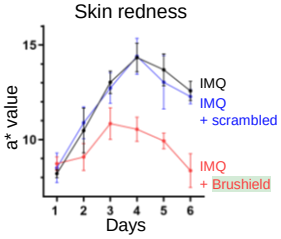
IMQ-induced psoriasis mouse model* **5 mg/kg ASO i.v.**

Target protein levels in mouse dorsal skin

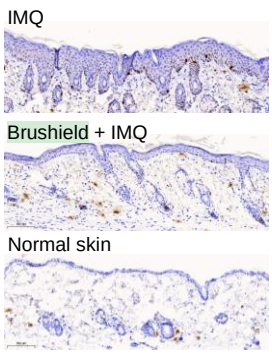




Skin redness



Ki67 IHC staining (Day 7)



Brushield conjugates suppress target expression and reduce the severity of IMQ-induced psoriasis translationally, phenotypically, and histologically

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*Data obtained with C57BL/6 mice

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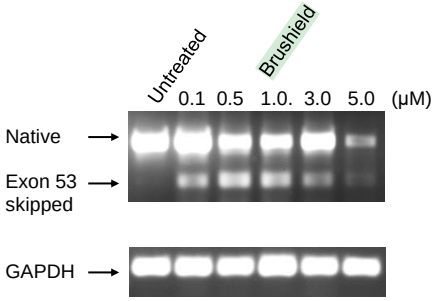
Efficacy: Dystrophin (DMD)

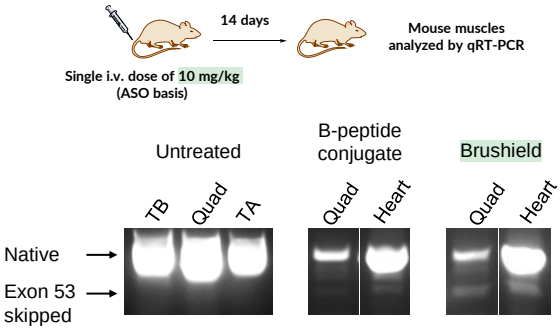
Site: muscle, heart
Modality: Exon-skipping

Brushield conjugates are **potent in vivo**

Exon 53 skipping *in vitro* using C2C12 myotubes



mdx4cv mouse model



The Brushield conjugate

- enters cell nucleus despite large size
- effectively engages target *in vivo* at low dosage

Preliminary; unpublished

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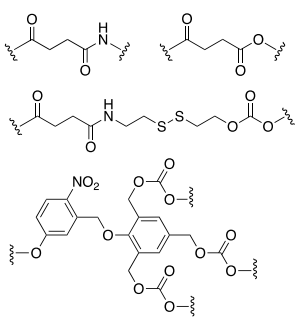
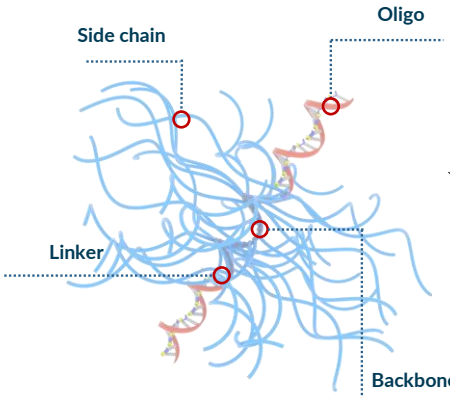
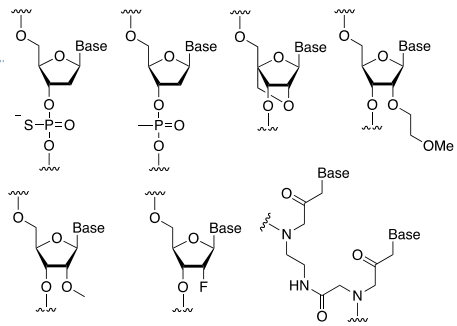
Customizability

Example linkers





Example oligo chemistries



The Brushield is not a single material; optimization is key

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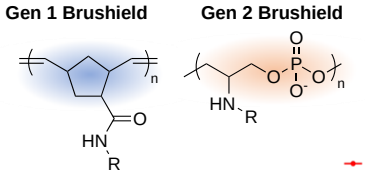
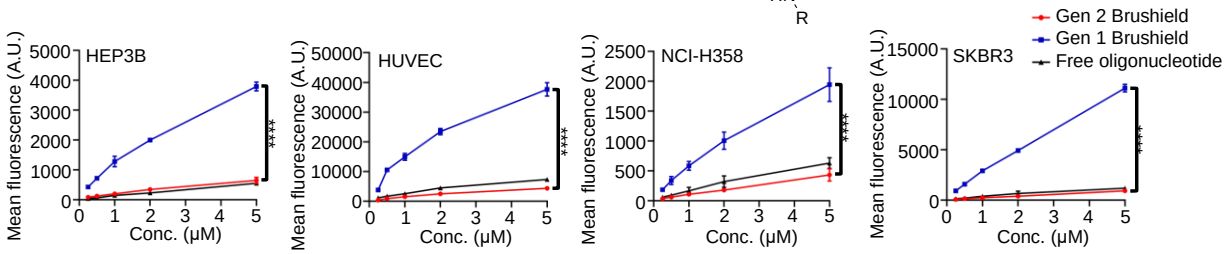
Backbone effect

Brushield™ backbone chemistry affects cellular uptake





Possible applications

- Gen 1: Cytosolic antisense (steric block), siRNA (with cleavable linker), mRNA editing
- Gen 2: Applications needing very long blood circulation times (e.g. aptamers), antisense/exon-skipping (with cleavable linker + if oligo is bioactive without carrier, e.g. PMO)

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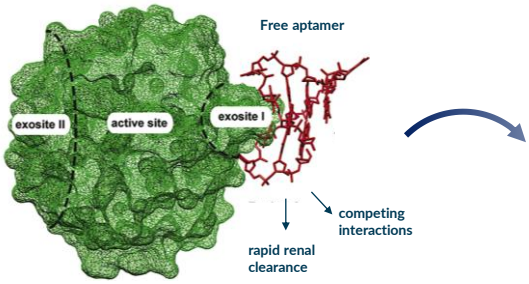
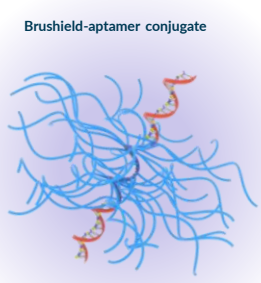
Works with aptamers

Brushield™ improves aptamer bioactivity

Thromboembolic risk *Site: blood* *Modality: aptamer*





- HD1 aptamer binds strongly and specifically to thrombin *in vitro*
- However, in clinical trial, aptamer activity is lost immediately when infusion is stopped

Can the Brushield restore aptamer activity in vivo?

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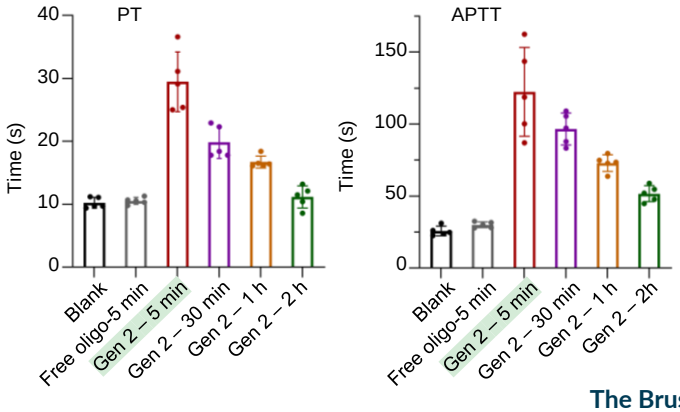
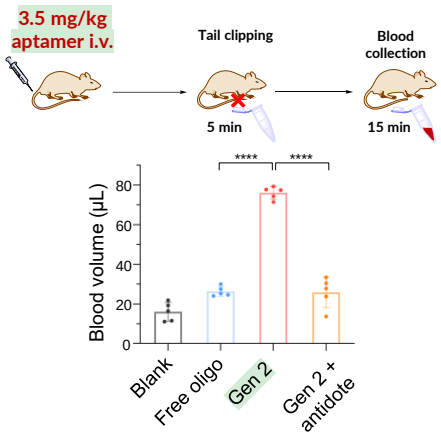
Works with aptamers

Brushield™ conjugates are **potent in vivo**

Anticoagulation mouse model



Mouse tail transection bleeding model



The Brushield conjugate

- rescues aptamer activity *in vivo*
- shows 50× higher potency than previous study

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Angew. Chem. Int. Ed., **2022**, DOI: 10.1002/anie.202204576

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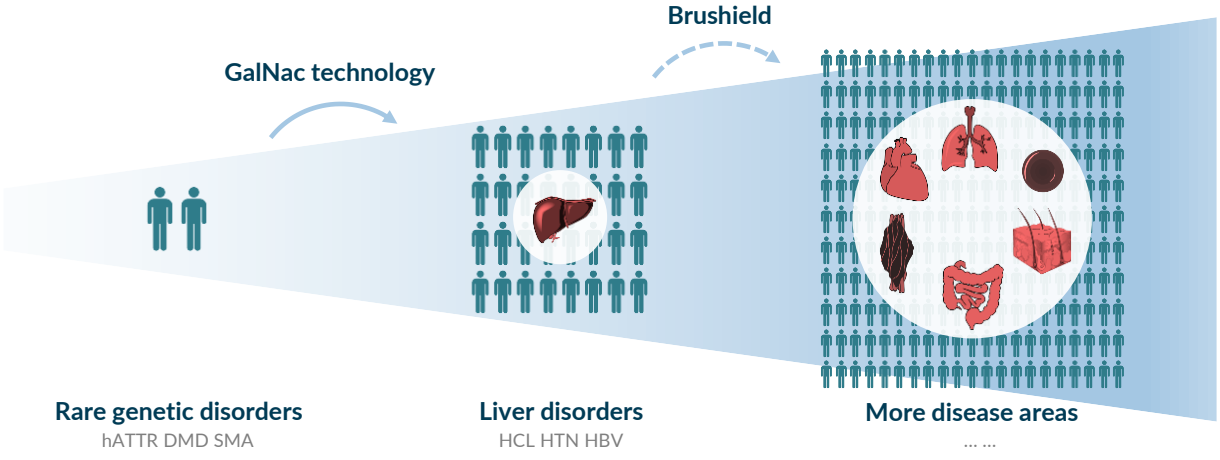
Summary



50

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Acknowledgement

Brushield Team

Xueguang (Alex) Lu (PhD)
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Tingyu Sun
Yao Li
Jiachen Lin
Jiansong Cai
Yun Wei
Peiru Chen
Mengqi Ren
Chenyang Xue
Christopher Oetheimer

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Thank you!

Selected relevant publications:

PNAS, 2022, in press. DOI: 10.1073/pnas.2113180119.
Sci. Adv. 2019, : 10.1126/sciadv.aav9322
J. Am. Chem. Soc. 2017, 139, 10605
Angew. Chem. Int. Ed. 2017, 56, 1239

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A Molecular Approach to Additive Manufacturing Medical Devices for use in the Clinic

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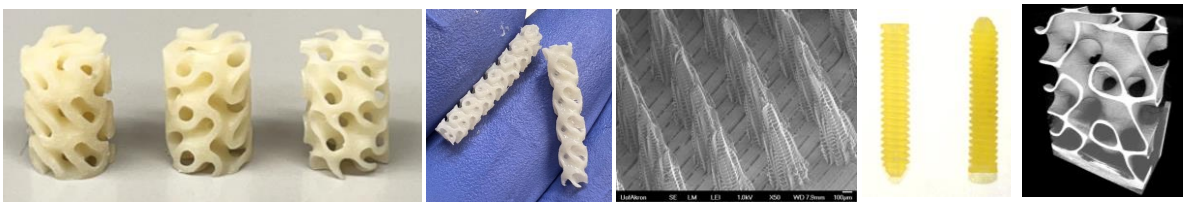
ORTHOPAEDIC SURGERY & BIOMEDICAL ENGINEERING



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Becker Laboratory for Functional Biomaterials

NIH NINDS 1R01NS124889-01A1, NIH NHLBI 1R44HL167315-01, NIH PSTP T32 GM133352-3
NIH NHLBI 1R44HL167315-01, NIH NIGMS 1R43GM140802, NIH NIDA 1R44GM140795-01A1
CDMRP W81XWH-15-1-0718, NSF – FDA Scholar in Residence, NSF (GFRP, aiM NRT)
Adaptilens, Avient, Carbon, Viamer Biosciences, Cook Biotech, Cook Medical, Deep Blue Medical

Adaptilens · National Institutes of Health · FDA · NSF · Department of Defense · Carbon

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Howard Levinson, MD
Thorsten Seyler, MD

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Examples of FDA-cleared additively manufactured long-term implants

Metal

Ti alloy
Craniofacial implant
Bioarchitects

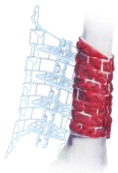
Ti Alloy
Fusion cage
restor3D

and many more…..

'Do no harm'
drives decision making

Polymers

PCL
Trephination hole plug
Osteopore



PCL
Graft cage
J&J

PEEK
Craniofacial implant
OPM

PEEK
Spinal implant
OPM

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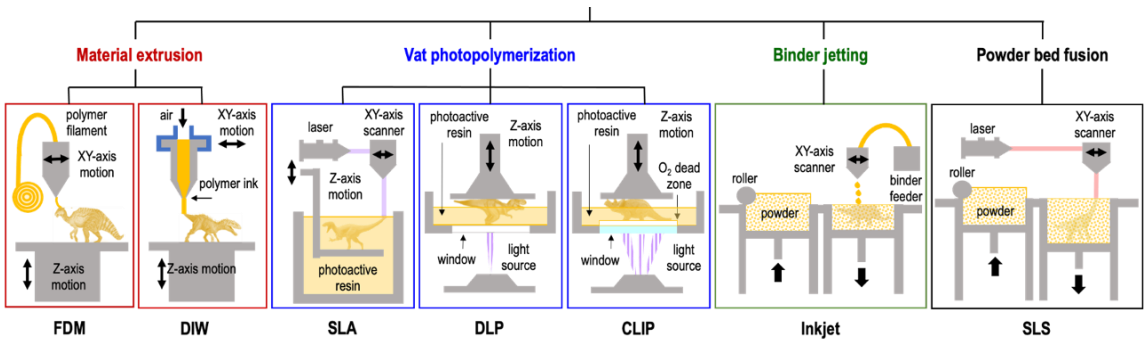
Polymer Additive Manufacturing Methods



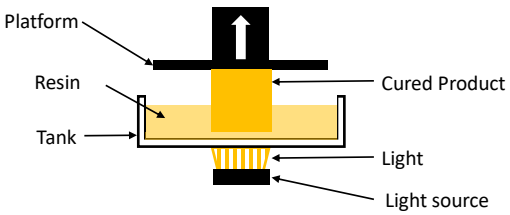
Advantages

High resolution: 10-50 µm

Good surface quality

Short build time

Design versatility



Disadvantages

High sol fraction

Toxic photoinitiators

Buoyancy Issues

Extractables

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A Kirillova, T Yeazel, D Asheghali, SR Petersen, S Dort†, K Gall, ML Becker* *Chemical Reviews*, **2021**, *121(18)*, 11238-11304.

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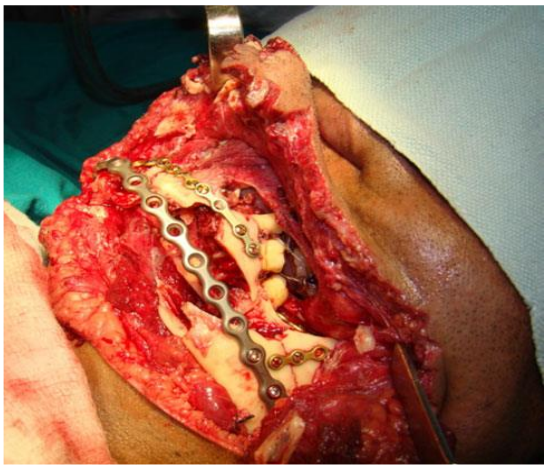
The Future: Patient Specific – Anatomically Correct



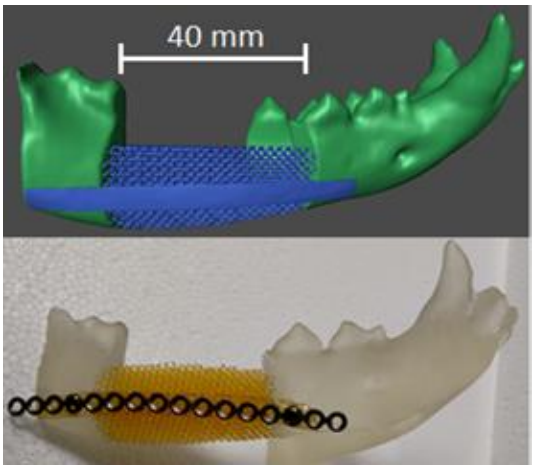


Image → Digital Design → Conversion to Print Code → Printing

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ONLY "WORKS" WHEN THE OPTIMAL MATERIALS ARE AVAILABLE

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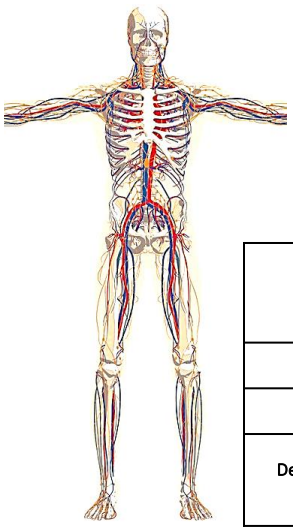
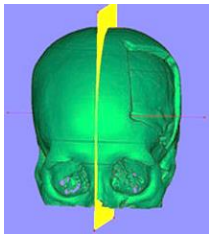
Very few resorbable resins available for Additive Manufacturing

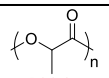
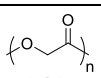
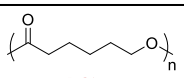
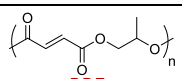




Patient specific
Anatomically correct

Pre-operative manufacturing saves $150-$300 per minute

Surgery 8-10 hours faster w/ 3D printing

	 PLLA	 PGA	 PCL	 PPF
T_g (°C)	60-65	35-40	-60-60	-40-30
T_m (°C)	173-178	225-230	58-63	-
Degradation time (months)	>24	6-12	>24	varies

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D Dean, K-J Min, A Bond Computer Aided Design of Pre-fabricated Cranial Plates. *J. Craniofacial Surgery*, **2003**, 14:819-832.

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Poly(propylene fumarate) as a Resorbable Resin

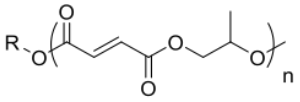
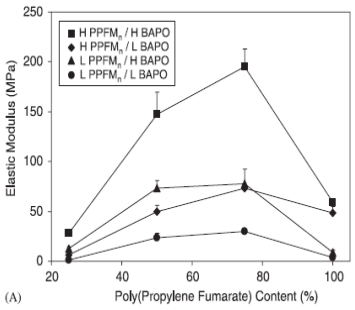
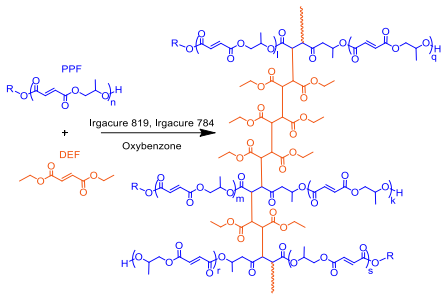


Photo-printable < 3500 Da

Poly(propylene fumarate) can degrade into non-toxic bioresorbable products
Fumaric acid and propylene glycol easily removed from the body



JP Fisher, D Dean, AG Mikos *Biomaterials*, **2002**, *23*, 4333-4343



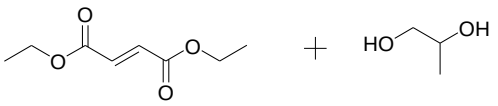
"On the Shoulders of Giants"
Mikos, Yaszemski, Fisher, Dean, Wang et al – & many others

More than 1500 papers – no human clinical trials – Why?

59

Two Synthetic Approaches for Poly(propylene fumarate)

a) Step-growth polymerization



Energy intensive (100-130 ^{0}C)
Side reactions
Uncontrolled polymer properties ($Đ_M$~2 or higher)

b) Chain-growth polymerization

Poly(propylene fumarate)

Mild conditions (45-100 ^{0}C)
Atom economical
Controlled polymer properties (M_n, $Đ_M$~1.2-1.8)
Reproducible

AM DiCiccio , GW Coates *J. Am. Chem. Soc.* **2011**,10724-10727.
Y Lu, CM Doulder, J Walker, R Mischra, D Dean, ML Becker* *Biomacromolecules* **2016**, *17(2)*, 690–697

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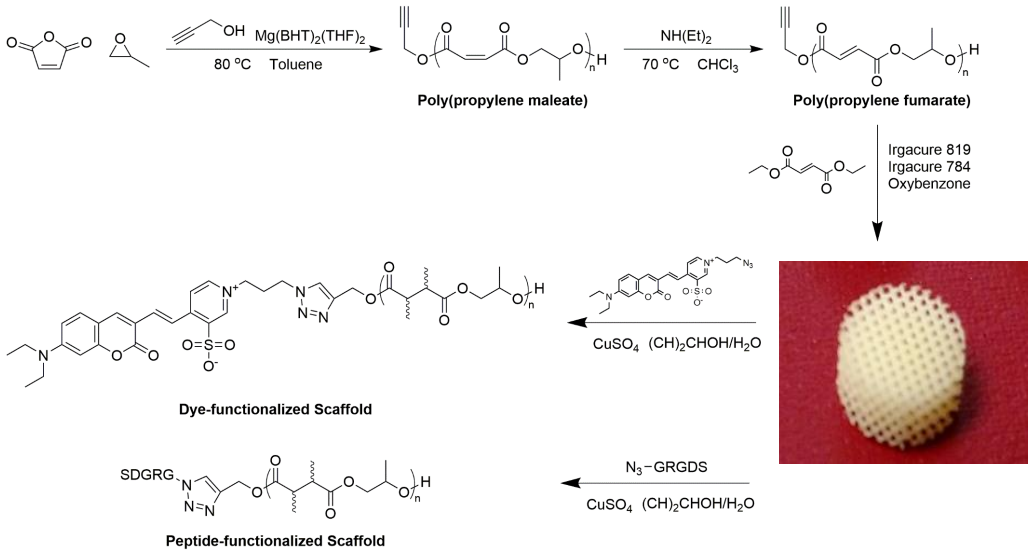
$Mg(BHT)_2(THF)_2$ Catalyzed ROCOP Polymerization of Anhydrides & Epoxides



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JA Wilson, AP Kleinfehn, D Luong, S Sallam, C Wesdemiotis, ML Becker* *J. Amer. Chem. Soc.* **2018**, *140(1)*, 277–284
Y Chen, JA Wilson, SR Petersen, S Sallam, J Mao, C Wesdemiotis, ML Becker* *Angew Chem* **2018**, 57(39), 12759-12764.

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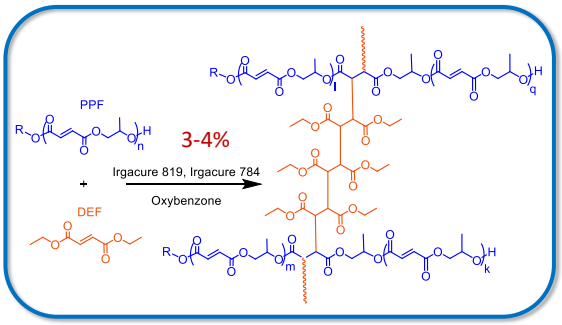
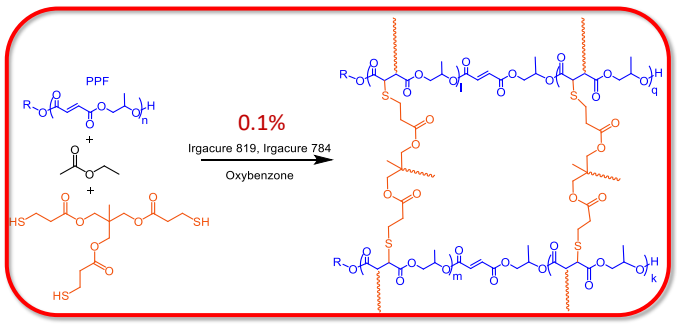
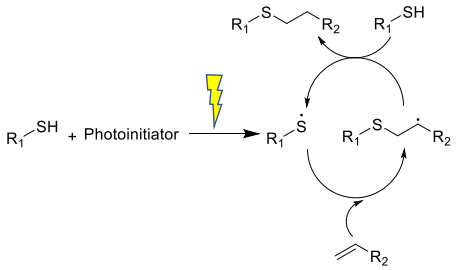
Photochemical Crosslinking: DEF vs Thiol-ene Addition Chemistry





Slow printing times
Stagnant Resin Formulations
C-C linkages

32 minutes



Highly efficient click chemistry
Fast printing times
Functional group tolerant

3 minutes

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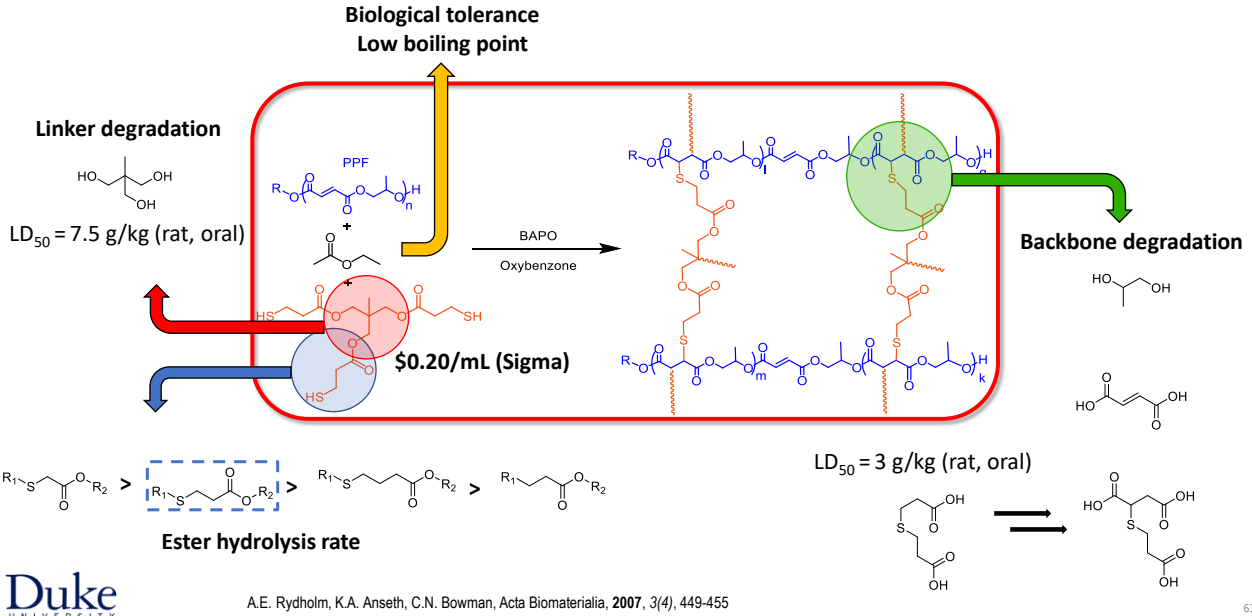
Designing a Degradable Thiol Cross-linker – Lots of Room for Innovation



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A.E. Rydholm, K.A. Anseth, C.N. Bowman, Acta Biomaterialia, **2007**, *3(4)*, 449-455

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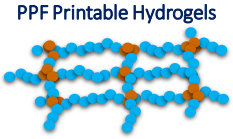
Fumarate-based Copolyester Resins & Inks

End-functionalized PPF

JACS, **2018**, *140(1)*, 277–284.
Adv Health Mater, **2019**, *8(17)*, 1900646.

PPF Printable Hydrogels



ACS Macro Letters, **2018**, *7*, 1254-1260
Macromolecules, **2021**, *54(7)*, 3458-3468
Advanced Materials, **2023**, *submitted*

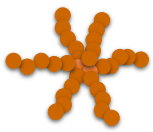
Functional Epoxide PPF

Angew Chem **2018**, *57(39)*, 12759-12764.

PPF ABA Elastomers

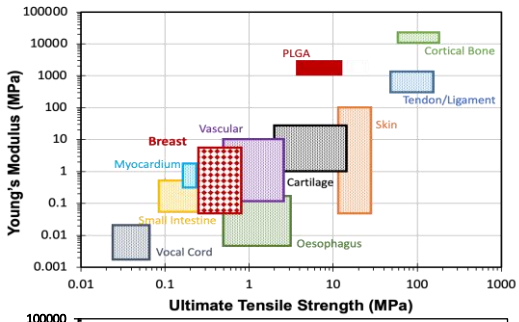
Biomacromolecules, **2022**, *23(5)*, 2106-2115.
Advanced Materials, **2023**, *submitted.*
Sci Trans Med, **2023**, *submitted.*

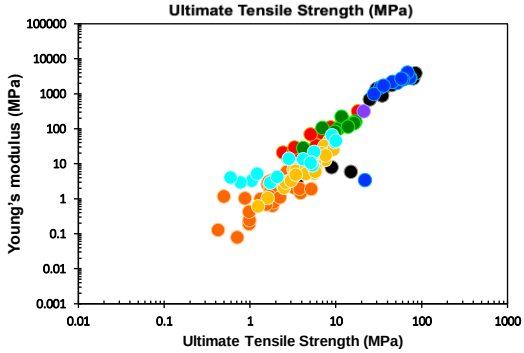
Star PPF



Polymer Chem **2019**, *10*, 4655 – 4664
ACS AMI, **2020**, 12(20), 22444–22452
ACS AMI, **2022**, *14(34)*, 38436-38447

- Carbon Resins
- Formlabs Resins
- ABA Triblocks
- Gradient Polyesters
- Linear PPF
- Hydrogel PPF
- Star PPF
- Star PPF Composites





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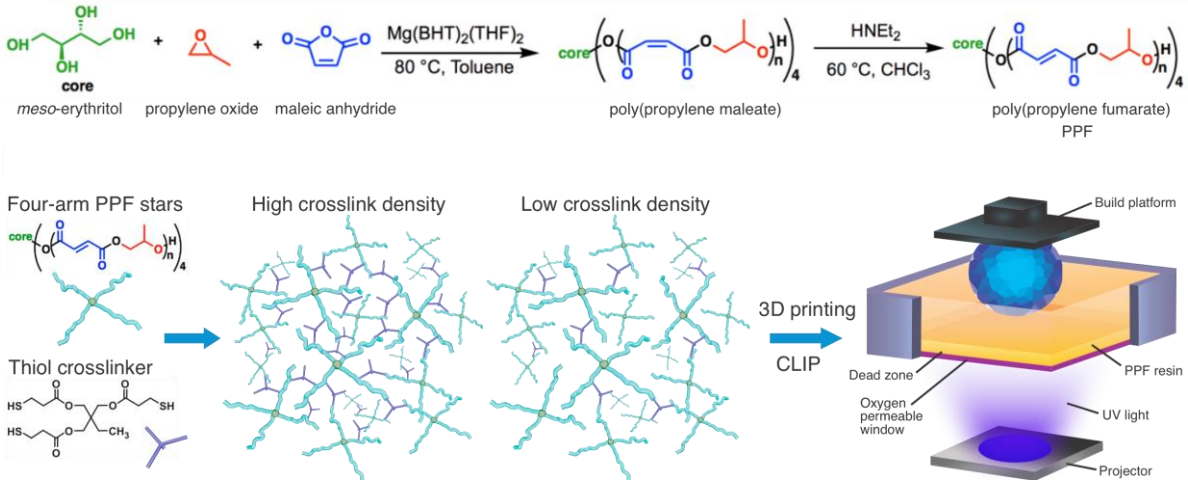
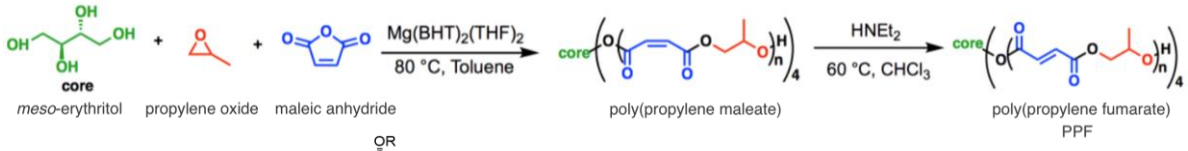
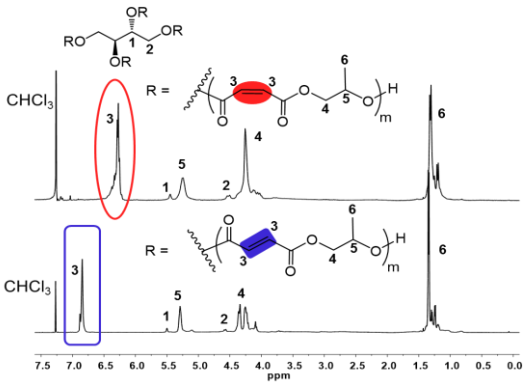
Synthesis & Thiol Printing of 4 arm PPF_{30} Stars Polymers

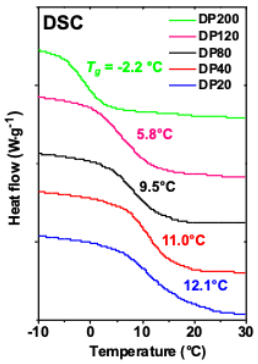


G Le Fer, Y Luo, ML Becker* *Polymer Chemistry* **2019**, *10,* 4655 – 4664
G Le Fer, ML Becker* *ACS Applied Materials & Interfaces*, **2020**, 12(20), 22444–22452
A Krillova, T Yeazel, K Gall*, ML Becker* *ACS Applied Materials & Interfaces*, **2022**, *14(34),* 38436-38447

Synthesis & Thiol Printing of 4 arm PPF_{30} Stars Polymers

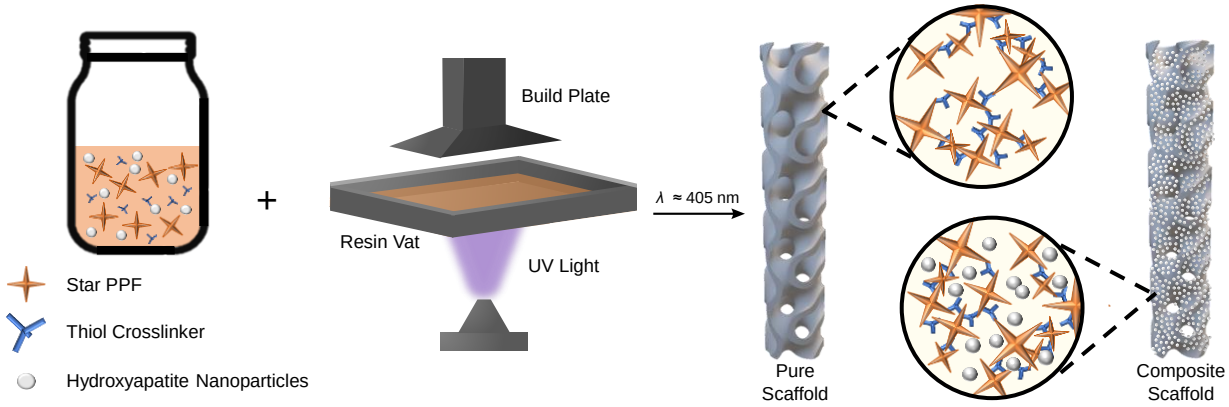






G Le Fer, Y Luo, ML Becker* *Polymer Chemistry* **2019**, *10,* 4655 – 4664
G Le Fer, ML Becker* *ACS Applied Materials & Interfaces*, **2020**, 12(20), 22444–22452
A Krillova, T Yeazel, K Gall*, ML Becker* *ACS Applied Materials & Interfaces*, **2022**, 14(34), 38436-38447

Composite 3D printing: 4 arm PPF_{30} Stars 10:1 w/ 5 wt% HA nanoparticles



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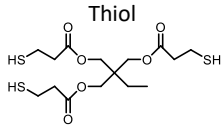
Fast 3D Printing w/ Thiol – & Less Additives are Needed (>30x less)

Polymer : EA = 7:3 (wt./wt.), 0.1% BAPO, 0.1% Oxybenzone

PPF : Thiol = 1:1, 2:1, 5:1 and 10:1 (mole/mole)

Tensile bar (ASTM D638 type V), DMA bar, solid disc, gyroid

Thiol



4 min print

Carbon® M2 printer

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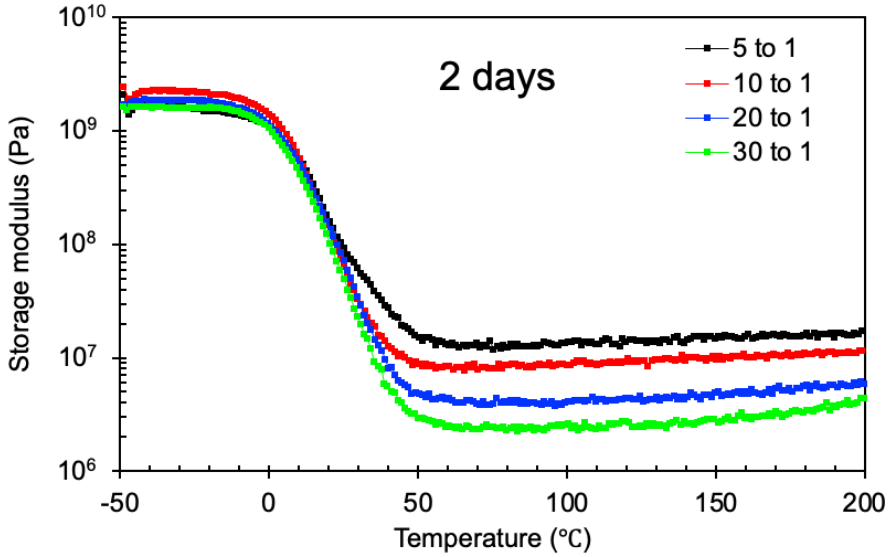
Evaluating Crosslinking w/ DMA



crosslinking density

Samples dried at 60 °C under vacuum post-printing

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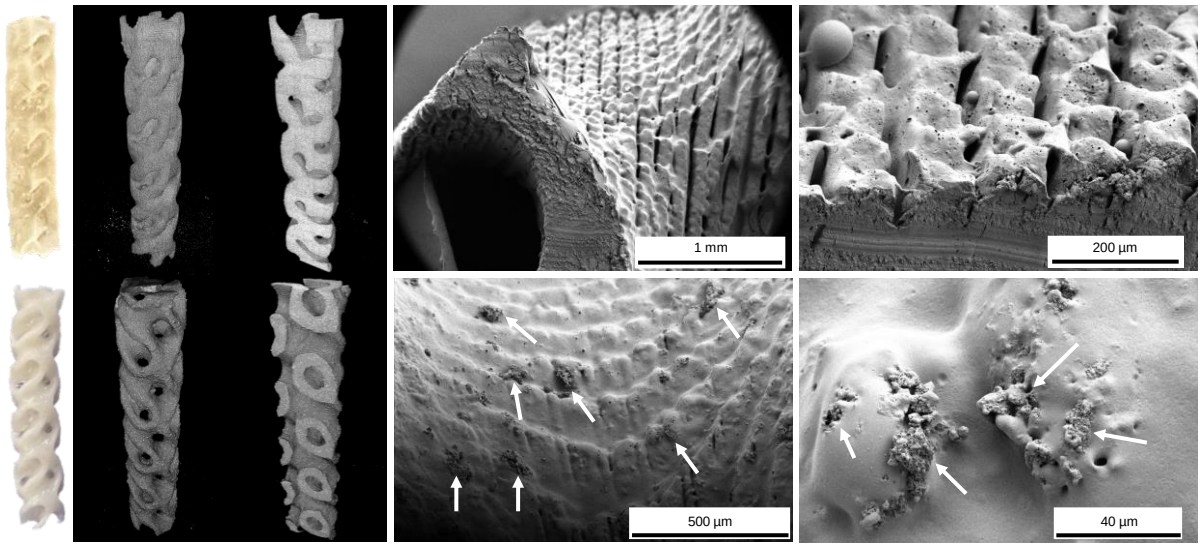
SEM of 3D Printed Scaffolds & Composites



70

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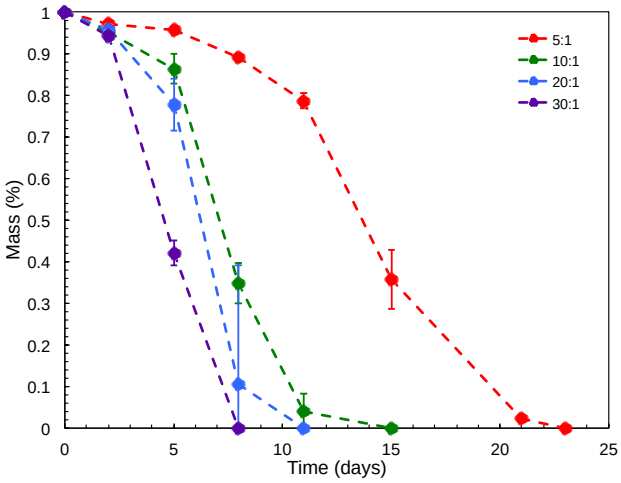
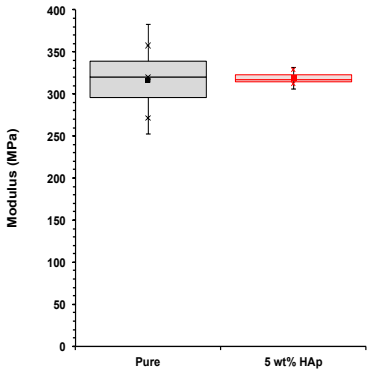
PPF Star Composite Scaffolds w/ Varying Crosslink Ratio: 80% Porous

Accelerated degradation (0.1 N NaOH)



Compression



All materials are fully degradable

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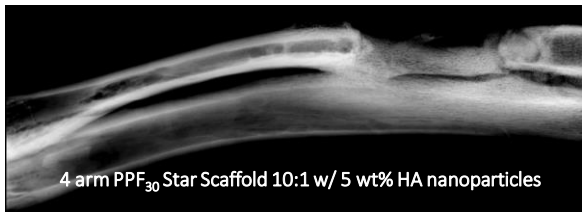
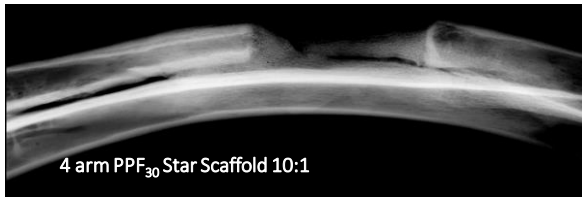
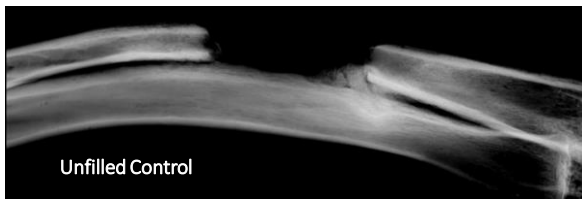
Rabbit Radial Segmental Defect Model – Partial Load Bearing – 4 Weeks







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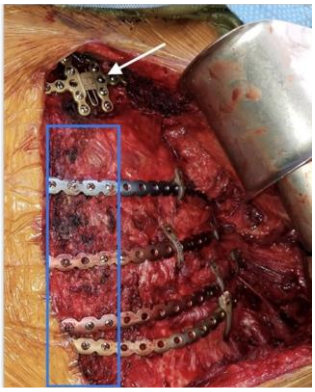
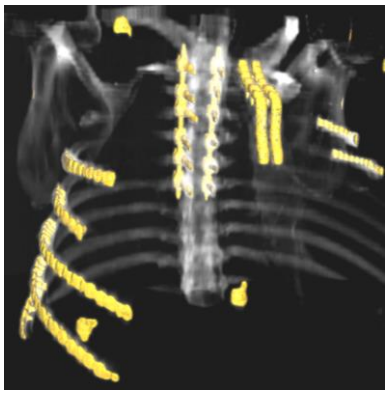
Post – Traumatic Intra & Extra Thoracic Rib Fracture Repair





Surgical Stabilization of Rib Fractures is Required for 'Flail Chest'

4 or more rib fractures

Don't Drink & Drive
Wear a seat belt
25 yr old male, Car accident

Rib fractures are one of the most common injuries following blunt trauma, occurring in approximately 10% of all trauma patients

64% of patients with isolated, multiple rib fractures still experience chest wall pain at two years & >50% will acquire a pneumonia

5X more common in military populations where body armor distributes forces to the chest wall

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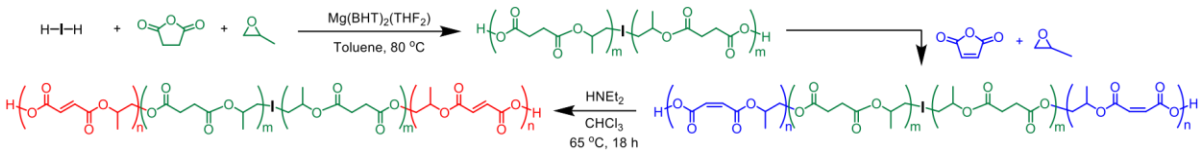
ABA Triblock Architecture Affords Wide Variation in Properties



Polymer	Ratio	Conversion (mol%)		Composition (mol%)		SEC		T_g (°C)	T_d (°C)
	MA:SA:I	MA	SA	FA	SA	M_n (kDa)	$Đ_M$		
PPF_{10}-*b*-$PPSu_{10}$-*b*-PPF_{10}	10:10:1	>99	>99	49	51	3.2	1.22	-12	333
PPF_{10}-*b*-$PPSu_{20}$-*b*-PPF_{10}	10:20:1	>99	>99	33	67	3.4	1.27	-12	343
PPF_{10}-*b*-$PPSu_{40}$-*b*-PPF_{10}	10:40:1	>99	>99	18	82	4.8	1.26	-11	339

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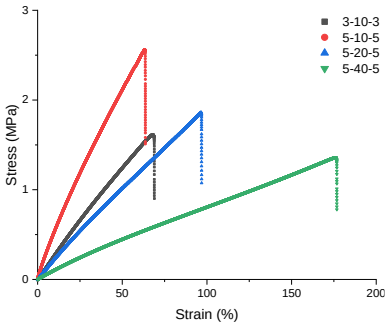
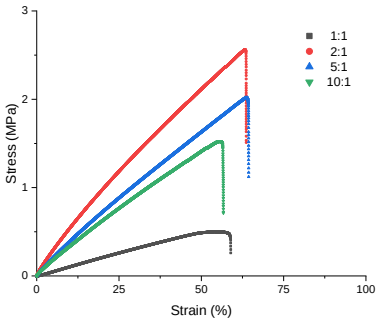
ABA Triblock Architecture Affords Wide Variation in Properties

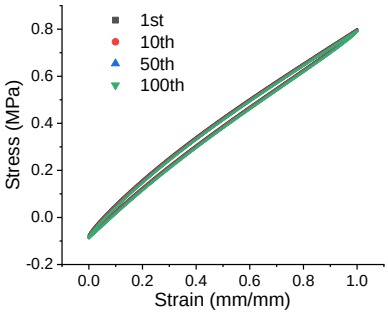
Variation in PPF:PPSu ratio



Variation of PPF:Thiol ratio



Negligible Hysteresis



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No yield point & negligible hysteresis will be important for most soft tissue applications

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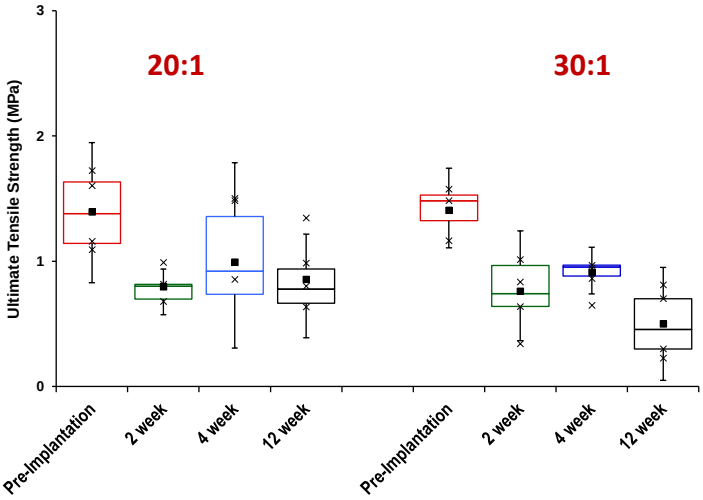
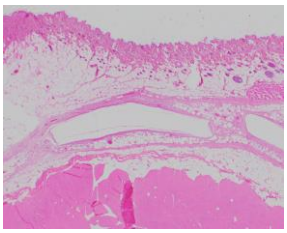
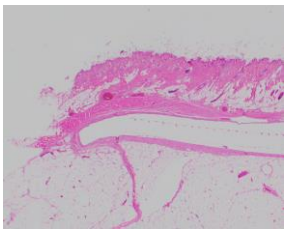
Resorbable PPF_5-PPS_{20}-PPF_5 ABA Triblock Properties in vivo



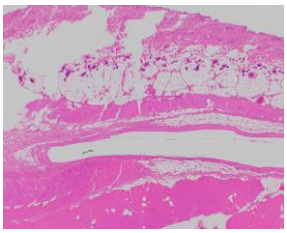
2 Weeks ~5%



4 Weeks ~12%



12 Weeks ~25%



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PPF_5-PPS_{20}-PPF_5 30:1 Crosslinked Elastomer

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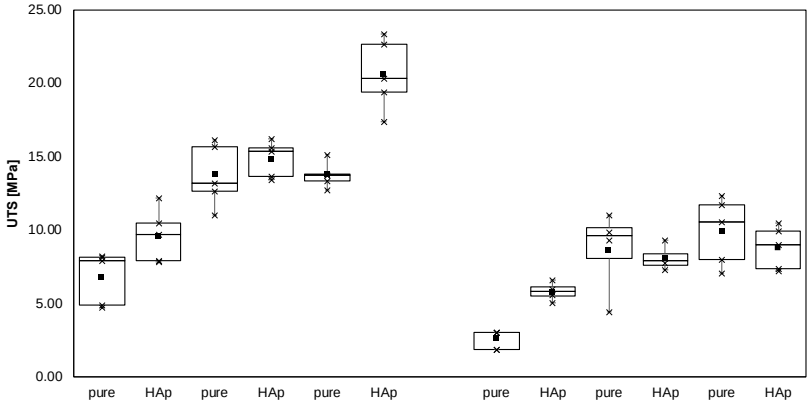
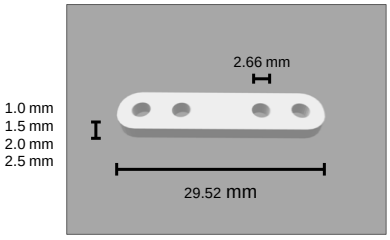
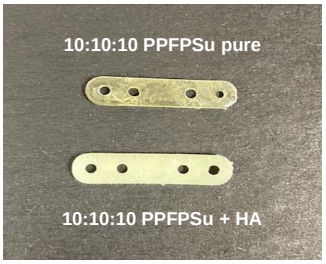
Resorbable Rib Plate Toughness can be tuned with Stoichiometry & Crosslinking







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Composite toughens (& stiffens) Resorbable Plates but Increases Water Penetration & Degradation

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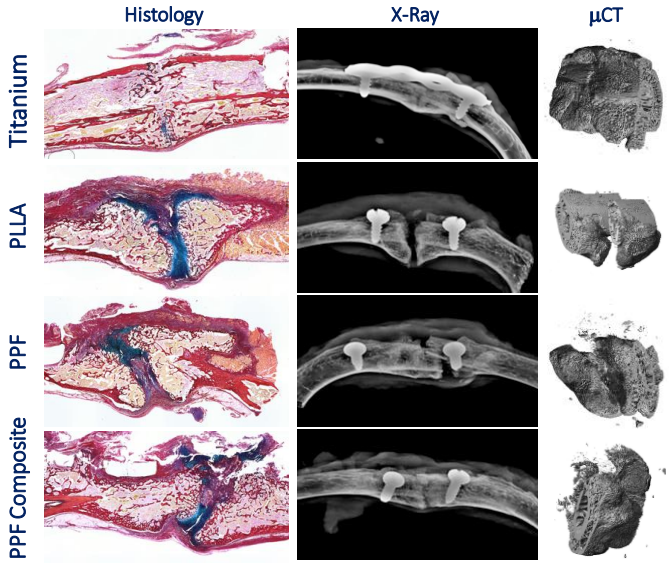
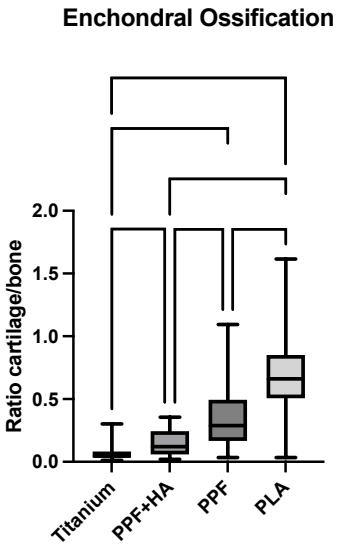
Rabbit Model – Patient Specific Rib Fracture Repair





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Conclusions

Early but exciting – **Do No Harm Applications**

Thiolene crosslinking >10 faster

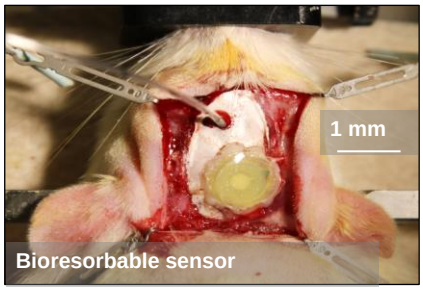
~ 30 fold less additives – no genotox problem

Fully degradable implants

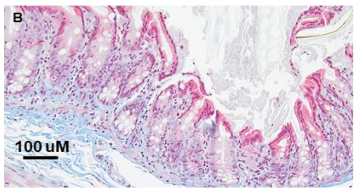
Sterilized by e-beam irradiation

Minimal inflammation w/ degradation

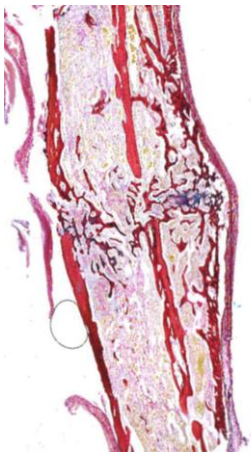
Covers a wide variation in tissues



Resorbable Electronics



Soft Tissue Repair



Rib fracture fixation

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Seeking Postdoctoral Fellows – matthew.l.becker@duke.edu

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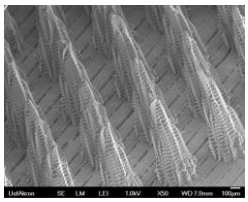
One Polymer Family Leads to Multiple Products

Ortho Plates

Bone Defects

Interference Screws

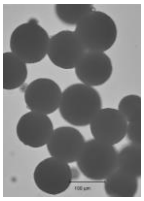
Microneedles



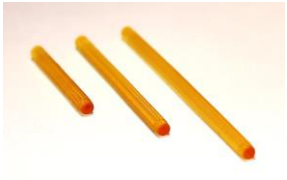
Vascular Sheaths

Bone Screws

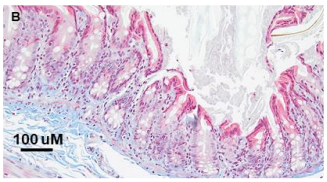
Microparticles



Bone Pins



Intestinal Stents



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Hernia Clips, Drug reservoirs, urethral Supports, Tissue Expanders

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NIH NINDS 1R01NS124889-01A1, NIH NHLBI 1R44HL167315-01, NIH PSTP T32 GM133352-3
NIH NHLBI 1R44HL167315-01, NIH NIGMS 1R43GM140802, NIH NIDA 1R44GM140795-01A1
CDMRP W81XWH-15-1-0718, NSF – FDA Scholar in Residence, NSF (GFRP, aiM NRT)
Adaptilens, Avient, Carbon, Viamer Biosciences, Cook Biotech, Cook Medical, Deep Blue Medical

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Samuel Adams, MD
Howard Levinson, MD
Thorsten Seyler, MD

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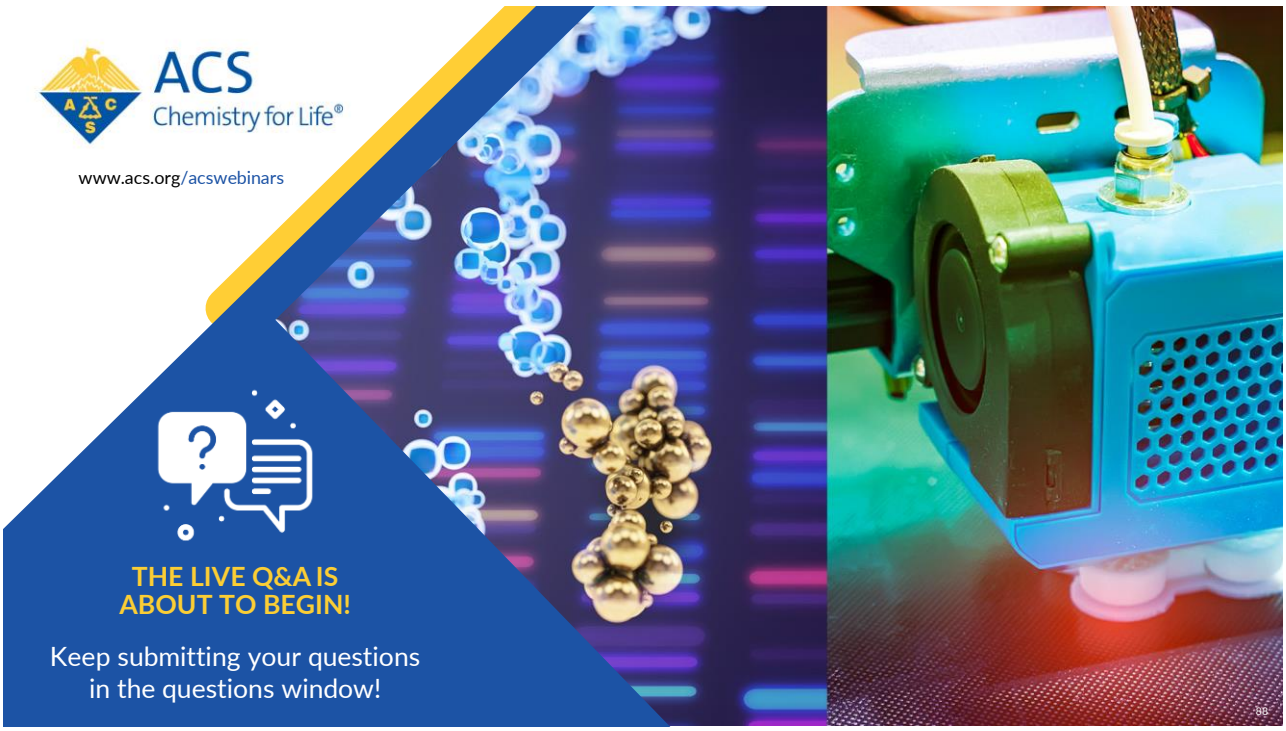

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