

The Center for Integrative Nanotechnology Sciences


EXHIBIT D



Promoting
excellence in
research,
education, and
development.

Alex Biris, PhD

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A scanning electron micrograph (SEM) showing a dense field of cells. Several large, rounded cells are prominent in the foreground, while many smaller cells are visible in the background. The image is in grayscale, typical of SEM, and has a slightly textured appearance.

Our Mission: *To advance the knowledge of nanoscience and nanotechnology through research and outreach, and accelerate technological innovations into practical applications for society.*

About CINS: Beginnings

- CINS was founded in 2006 with a \$5.9 million investment from the State and strong support from UALR
- Construction on the new facility was completed in 2012



Research Funding

CINS has received over \$25.7M in research funding from state and federal agencies, including...

- U.S. Department of Energy
- U.S. Small Business Administration
- Arkansas Research Alliance
- Arkansas Economic Development Commission
- National Aeronautics and Space Administration
- **U.S. Department of Defense**
- National Science Foundation
- U.S. Food & Drug Administration



Research for Economic Development and Education



Since 2006, the state of Arkansas has invested over \$12 million to help develop the Center for Integrative Nanotechnology Sciences into a productive research center.



Bolstered by the support of the state, we have earned over \$20 million in federal and local agency funding. These awards have funded research in cancer treatments, green energy, tissue regeneration, and more, as well as the education of dozens of students. The results of some of these projects are summarized on the following page.



Department of Defense Funding

- TATRC \$1,751,000
- TATRC \$2,097,000
- MRMC \$5,059,000
- JWMRP \$5,813,787
- PRORP \$750,000

Impacting Arkansas and Beyond

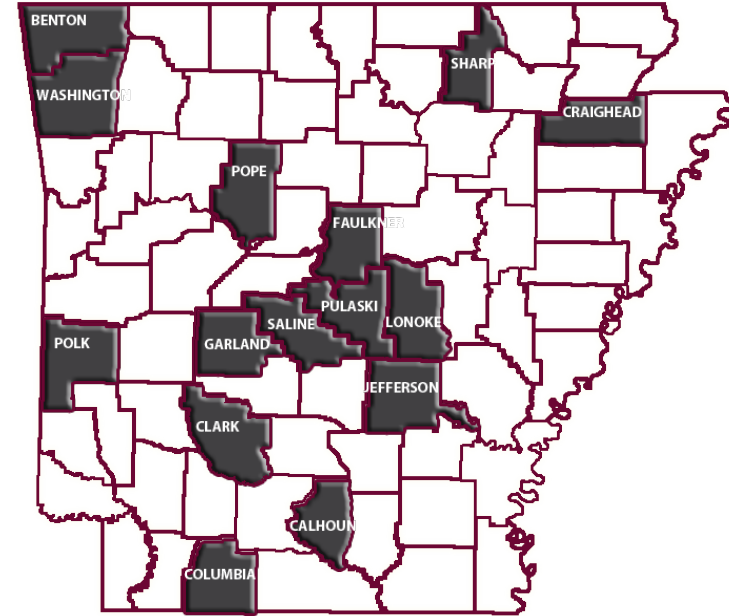
The impact of CINS research reaches far beyond the UALR campus.

7+ Arkansas colleges & universities

15+ Arkansas counties

11+ states

12+ additional countries around the globe



Start-Up Companies

- **NuShores Biosciences LLC:** licenses bone and tissue engineering technologies. They competitively bring federal funding into the state of Arkansas.
- **Poly Adaptive, LLC** (2010-Current) Licenses technologies for the prevention or removal of particulate matter or dust on various surfaces.
 - Awarded \$100,000 NASA SBIR in 2011
 - Awarded \$150,000 DOT SBIR in 2012
 - Will continue to compete for SBIR/STTR dollars as part of a strategy to refine the technology for specific applications and make it more market-ready for customers

Patents

22 patents issued to CINS

15 patents submitted and/or pending



Our Tools

Valued at over \$6M, many of our instruments are not available elsewhere in the region. External organizations frequently partner with us to utilize them, including ~20 commercial entities.



Research: Innovations

CINS research has led to innovations in the following applications:

- Organic solar panels
- Anticounterfeit sensors
- Nano-antennas
- Anti-icing applications
- Nanoelectronics
- Tissue scaffolds for bone generation
- Targeting and destruction of cancer cells by nanoparticles



Tissue Regeneration

The Problem:

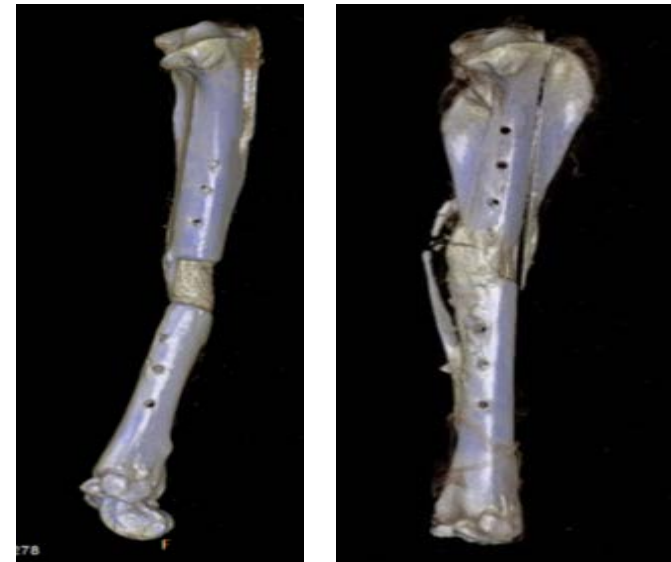
- Loss of bone tissue is common in soldiers as a result of combat, especially explosives
- Civilians face this risk from accidents and disease.
- The current regeneration techniques are limited and inadequate.



(image source: <http://www.premierexhibitions.com/exhibitions/4/4/bodies-exhibition/blog/what-happens-when-you-break-bone>)

The Nano Solution:

Nanomaterial-based implant that helps regenerate bone and delivers drugs to prevent infections



Lab tests (above) show that scaffold aids bone growth in goats.

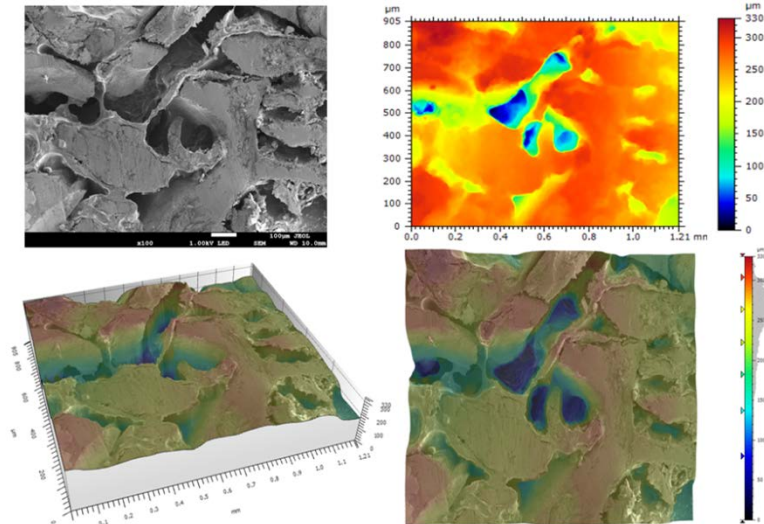
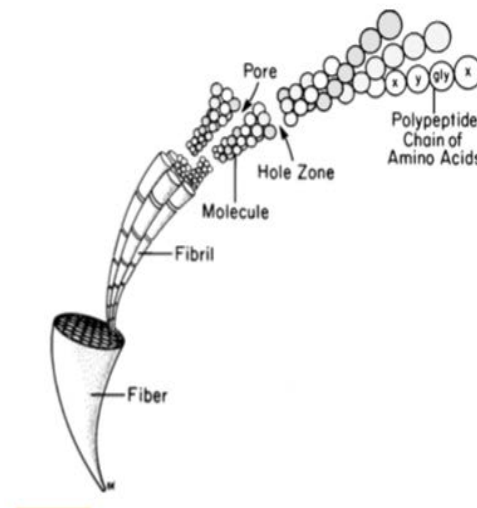
(image source: Dr. David Anderson, UTK)

The NuCress™ Bone Regeneration Scaffold

We have developed and patented an implantable device that helps regenerate strong bone tissue faster and better than currently marketed options.

Scaffold features:

- Can deliver antibiotics directly to the wound to fight infection
- Can “lock” itself into the defect without additional tools to hold it in place
- A surgeon can trim the size/shape of the implant to match the actual bone defect



Scaffold is built at the nano and molecular level to allow mineralization

Bone cells generate bone once they attach and proliferate over the scaffold

The NuCress™ Bone Void Filler

We have developed a tunable, biodegradable device that helps bone tissue regenerate faster and better than any other current option.

Scaffold features:

- A viable solution for many amputation cases
- Can “lock” itself into the defect without additional tools to hold it in place
- A surgeon can trim the size/shape of the implant to match the bone defect
- The scaffold has been successful in 6 species of large and small animals
- The scaffold’s development is at TRL 7
- Can deliver antibiotics directly to wounds to fight infection, a major problem in battlefield wounds



Before surgery



6 weeks after surgery



(image sources: University of Tennessee, Knoxville; Pat Finn)

Long Bone Results

2.5-cm defect after 3 months

Control—no
scaffold



Scaffold alone



Scaffold +
BMP2



All goat data collected by
Dr. David Anderson and
team at the University of
Tennessee, Knoxville.

Long Bone Results

2.5-cm defect



Day 0



Month 3



Month 8

All goat data collected by Dr. David Anderson and team at the University of Tennessee, Knoxville.

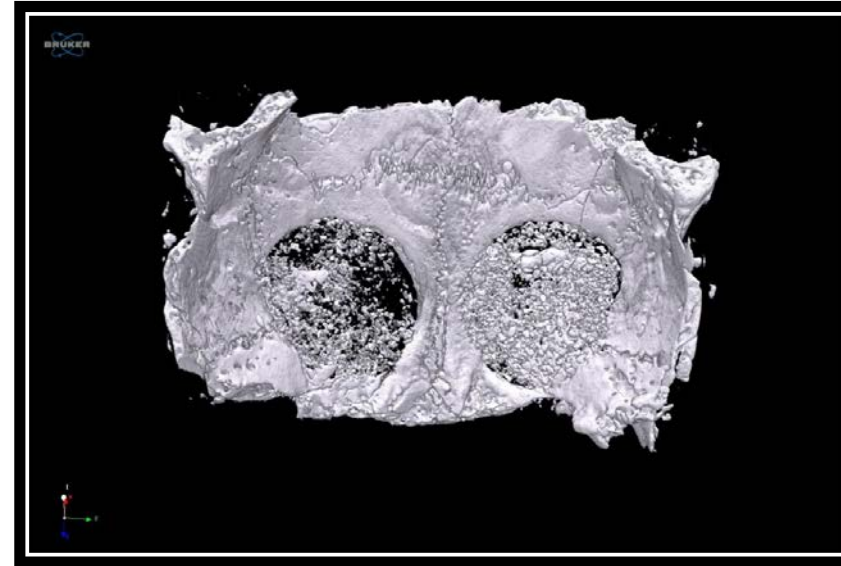
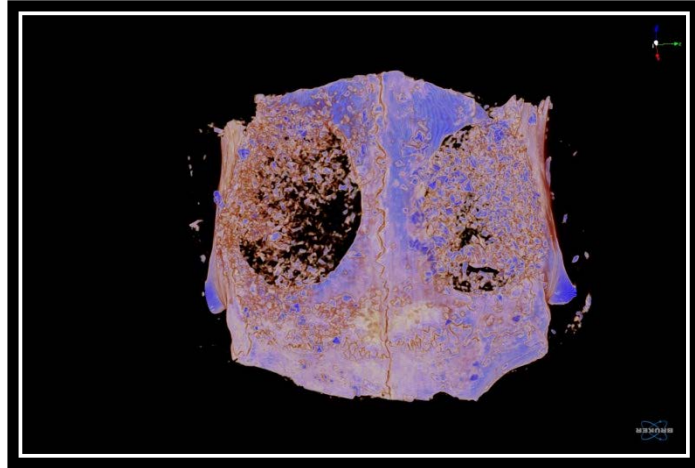
Long Bone Results

10-cm defect



All goat data collected by Dr. David Anderson and team at the University of Tennessee, Knoxville.

Spine/Craniomaxillofacial Bone Results

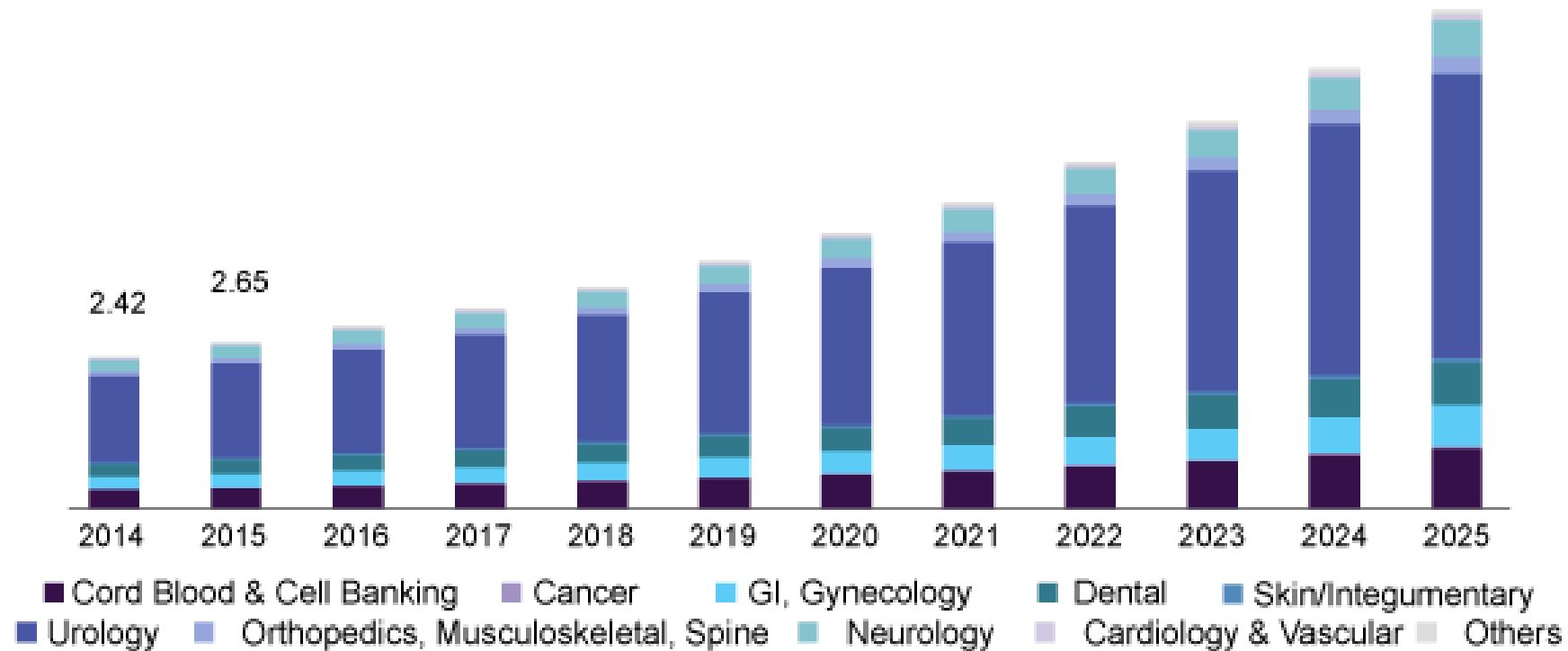


Credit:

- NuShores Biosciences
- Stony Brook University
- National Institutes of Health

Global Tissue Engineering Market

U.S. tissue engineering market size, by application, 2014-2025 (USD Billion)



Source: Grand View Research, 2018. <https://www.grandviewresearch.com/industry-analysis/tissue-engineering-and-regeneration-industry>

NuShores Biosciences LLC

NuShores Biosciences LLC is the exclusive, global licensee of CINS bone and tissue engineering technologies; the company is currently working with UA Little Rock to pursue FDA clearance for human use of the NuCress™ scaffold.

- Operates at leased facility in West Little Rock that includes a clean room
- Received **\$8.9M in competitive federal awards** between 2018-2021 to support development of technology
- Received **\$50,000 in SBIR Matching Grant funds** from the Arkansas Economic Development Commission



Dr. Biris with Sharon Ballard, CEO of NuShores



Nikki Mullen

Mechanical and Materials
Ph.D. Research Student

What Does and Mechanical and Material Engineer Do?

- Tensile and Compression Testing
- Swell Force Testing
- Material Characterization
 - Surface Area
 - Material Porosity
 - Thermal Composition
 - Establish methods for measuring various characteristics

Photo credit to Nikki Mullen



Specific Projects

Bone Decellularization Project

Synthetic Bone Project

Bone Scaffold Project

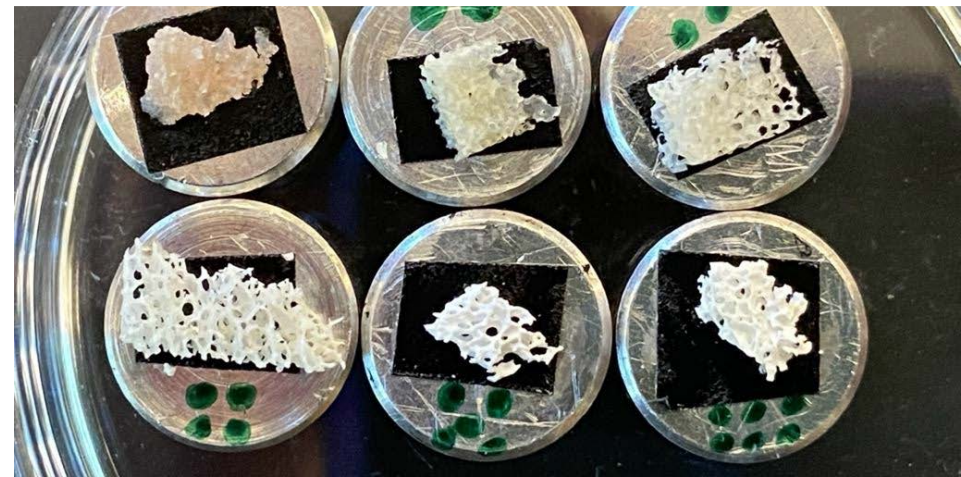
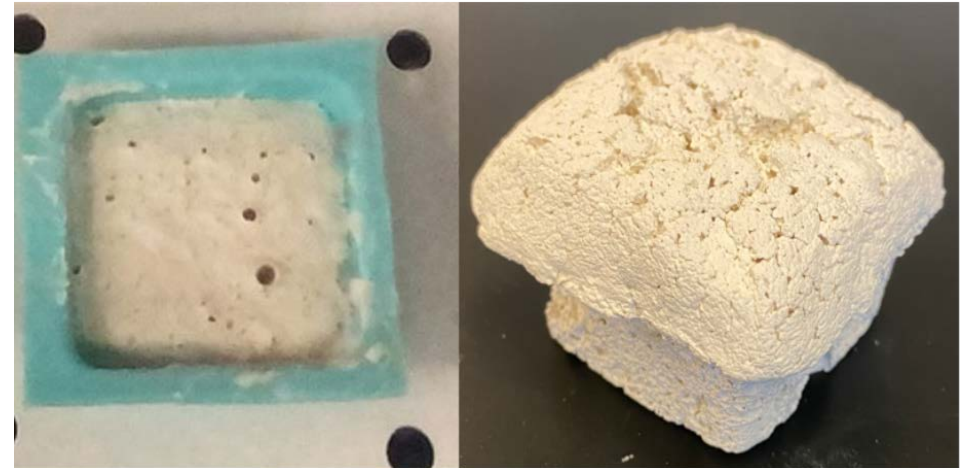
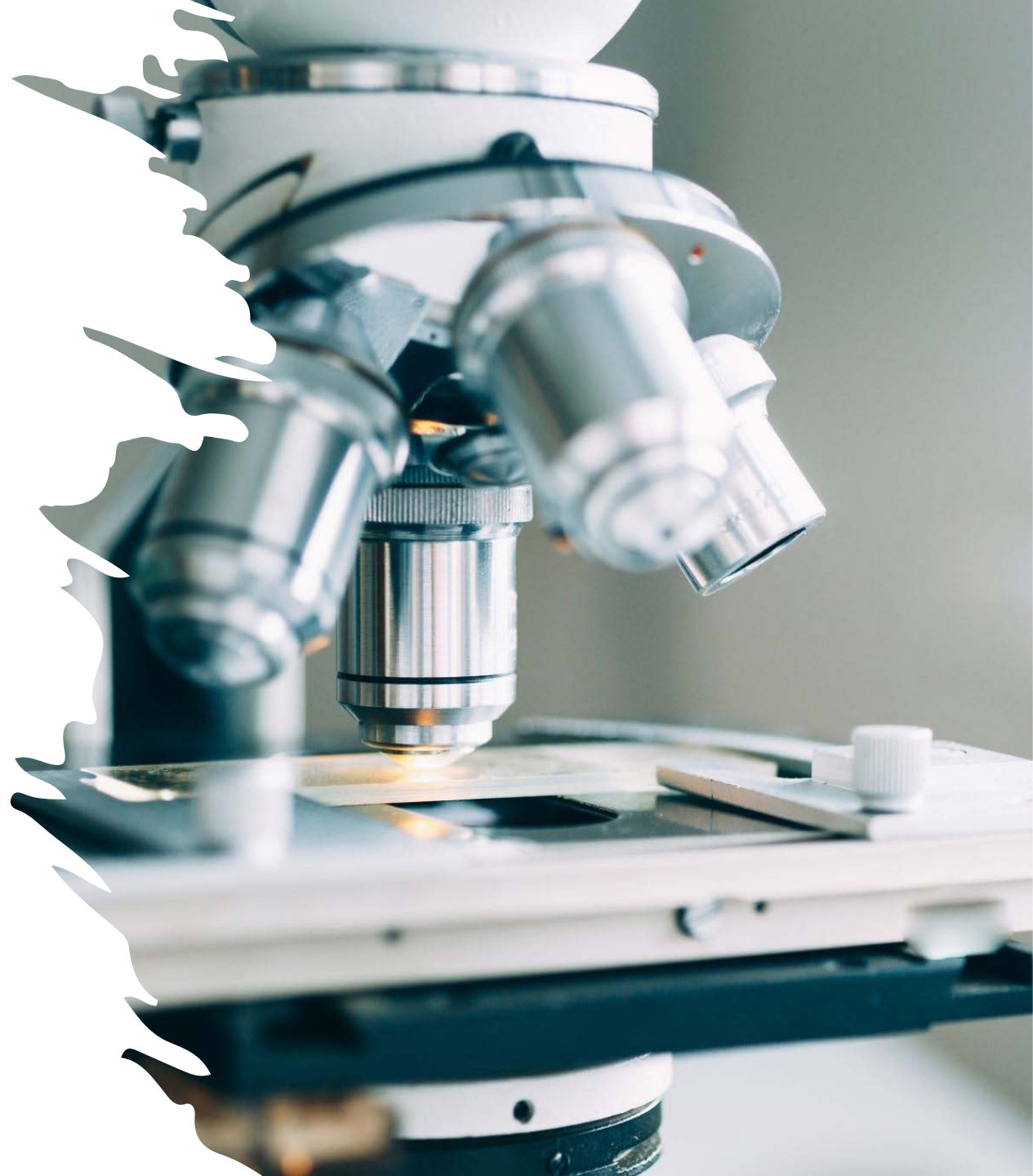


Photo credit to Nikki Mullen



Significance

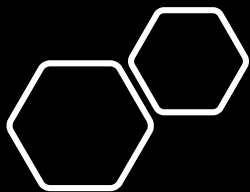
- This research is only available at UALR
- Place for students to do real research
- Unique environment





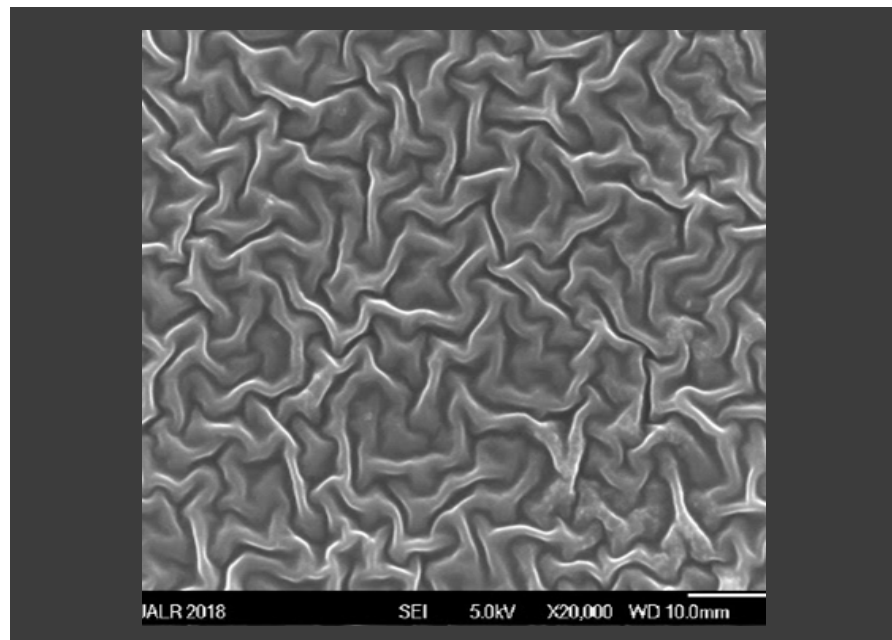
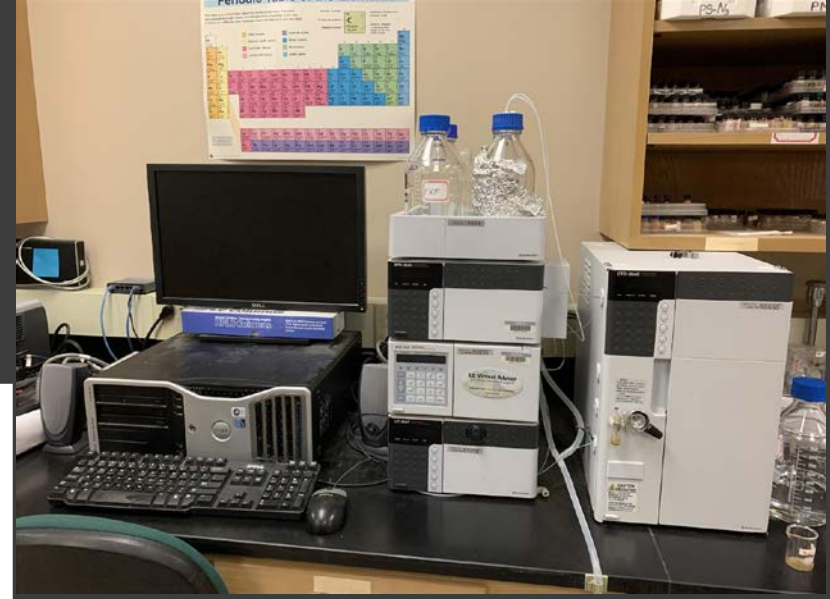
Christopher Griffin

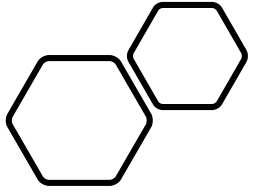
Research Student
Ph.D. Chemistry



Introduction

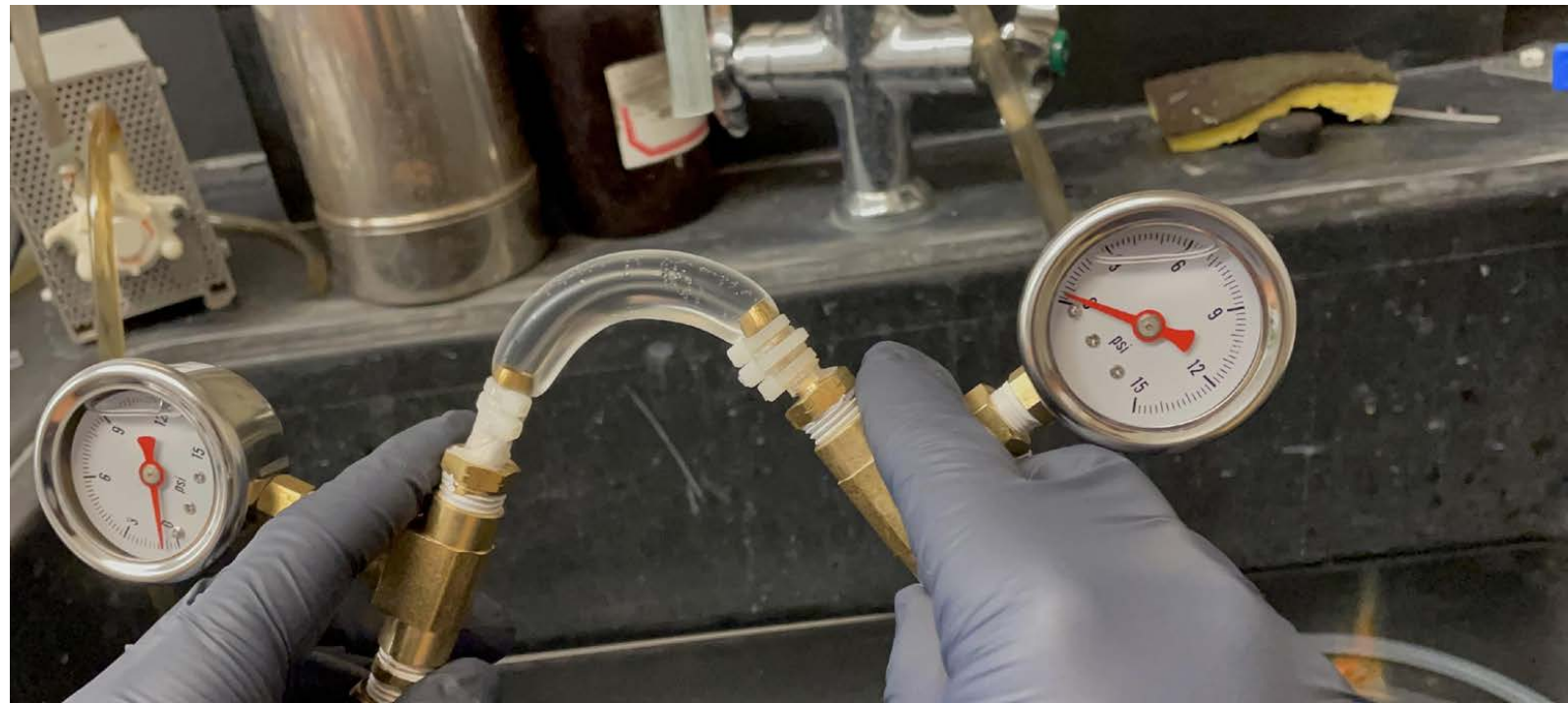
- Born in Little Rock, Arkansas
- Graduate Catholic High 2013
- Graduate Hendrix College 2017
- PhD candidate Chemistry (May 2022)





Research

- In addition to my thesis work:
- Vascular grafts
- Trauma sponges
- Graphene composites
- Bone scaffolds
- Printed nerve conduits
- Artificial skin grafts
- Intestinal surgical stents.



Publications

- Safina, I.; Alghazali, K. M.; Childress, L.; **Griffin**, C.; Hashoosh, A.; Kannarpady, G.; Watanabe, F.; Bourdo, S. E.; Dings, R. P. M.; Biris, A. S.; Vang, K. B. Dendritic Cell Biocompatibility of Ether-Based Urethane Films. *J. Appl. Toxicol.* **2021**, No. December 2020, 1–11. <https://doi.org/10.1002/jat.4136>.
- Pedersen, A. P.; Alghazali, K. M.; Hamzah, R. N.; Mulon, P.; McCracken, M.; Rifkin, R. E.; Mhannawee, A.; Nima, Z. A.; **Griffin**, C.; Donnell, R. L.; Biris, A. S.; Anderson, D. E. Development and in Vivo Assessment of a Rapidly Collapsible Anastomotic Guide for Use in Anastomosis of the Small Intestine: A Pilot Study Using a Swine Model. *Front. Surg.* **2020**, 7 (November), 1–9. <https://doi.org/10.3389/fsurg.2020.587951>.
- Newby, S. D.; Masi, T.; **Griffin**, C. D.; King, W. J.; Chipman, A.; Stephenson, S.; Anderson, D. E.; Biris, A. S.; Bourdo, S. E.; Dhar, M. Functionalized Graphene Nanoparticles Induce Human Mesenchymal Stem Cells to Express Distinct Extracellular Matrix Proteins Mediating Osteogenesis. *Int. J. Nanomedicine* **2020**, Volume 15, 2501–2513. <https://doi.org/10.2147/IJN.S245801>.
- Bow, A.; Newby, S.; Rifkin, R.; Jackson, B. K.; Matavosian, A.; **Griffin**, C.; King, W.; Alghazali, K.; Mhannawee, A.; Berryhill, S. B.; Morello, R.; Hecht, S.; Biris, A. S.; Anderson, D. E.; Bourdo, S. E.; Dhar, M. Evaluation of a Polyurethane Platform for Delivery of Nanohydroxyapatite and Decellularized Bone Particles in a Porous Three-Dimensional Scaffold. *ACS Appl. Bio Mater.* **2019**, 2 (5), 1815–1829. <https://doi.org/10.1021/acsabm.8b00670>.
- Beenken, K. E.; Campbell, M. J.; Ramirez, A. M.; Alghazali, K.; Walker, C. M.; Jackson, B.; **Griffin**, C.; King, W.; Bourdo, S. E.; Rifkin, R.; Hecht, S.; Meeker, D. G.; Anderson, D. E.; Biris, A. S.; Smeltzer, M. S. Evaluation of a Bone Filler Scaffold for Local Antibiotic Delivery to Prevent Staphylococcus Aureus Infection in a Contaminated Bone Defect.

Thank You



Questions?

