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Mentor-Graduate Student Spotlights Series 2020

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With over 25 years of research experience, Dr. Mark Grinstaff received his PhD from the University of Illinois at Urbana-Champaign in 1992, under the guidance of Dr. Kenneth S. Suslick. After completing his PhD, Dr. Grinstaff moved to the California Institute of Technology, on a NIH Postdoctoral Fellowship, to work under the tutelage of Dr. Harry B. Gray. His research focused on elucidating the mechanism of catalytic oxygenation of alkanes by halogenated iron porphyrins. Dr. Grinstaff is now the Director of the NIH T32 Program in Biomaterials and the Nanotechnology Innovation Center at Boston University, and a tenured professor with joint appointments in the Departments of Biomedical Engineering and Chemistry at Boston University. He is a co-founder of several companies that are commercializing his ideas, and he has several products being sold and used in the clinic.

Dr. Grinstaff's research interests are diverse and include the synthesis of new macromolecules and biomaterials, self-assembly chemistry, imaging contrast agents, drug delivery, and wound repair, and can be categorized into six major research areas:

1. Therapeutics: The lab develops novel superhydrophobic drug-loaded buttresses for prolonged high dose delivery after implantation during a surgical resection; responsive nanoparticles for image guided resection as well as for targeted tumor drug delivery; responsive materials for lysosomal pH modulation; and new antibodies and antibody drug conjugate therapies for various biomedical applications.
2. Musculoskeletal Disorders: The Grinstaff lab develops novel quantitative contrast enhanced computed tomography and magnetic resonance imaging techniques for diagnosing and staging osteoarthritis (OA) in animal models and human patients, as well as advancing an innovative therapy for OA. In addition, they are evaluating relaxin-2 as a new therapeutic to treat shoulder arthrofibrosis.
3. Wound Management: The closure and repair of wounds after traumatic or surgical injury is of significant clinical importance and a daily occurrence. While sutures remain the common wound closure technique, they possess many disadvantages. Consequently, the lab identifies hydrogels with targeted biodegradation, mechanical, adhesive, and swelling properties for repair of ocular wounds and cartilage defects.
4. Biosensors: The Grinstaff lab has developed novel electrochemical DNA sensors based on nucleic acid conformational changes (e.g., hairpin and wrap assay formats), and is constructing and evaluating novel optical and electrochemical biosensors for analytes of interest such as hormones (e.g., progesterone) and addictive agents (e.g., nicotine).

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5. Nature-inspired Carbohydrates: To overcome the challenges with using heterogeneous polysaccharides in biological applications, the lab synthesizes enantiopure poly-amido-saccharides (PASs) with defined molecular weights and narrow dispersities using an anionic ring-opening polymerization of a β-lactam sugar monomer. PASs offer the advantages associated with synthetic polymers, such as greater control over structure and derivitization.
6. Sustainability and Biopolymers: Recognizing glycerol as a nontoxic, renewable raw material amenable to polymerization methodologies, the Grinstaff lab prepares and studies the: 1) linear poly(1,3-glycerol carbonate)s; 2) atactic and isotactic linear poly(1,2-glycerol carbonate)s; and, 3) dendritic glycerol-lactic acid/succinic polymers. These polymers are of utility for biomedical and green consumer product applications as they degrade to non-toxic products.

With over 345 publications, the notable recent publications from the Grinstaff Lab are:

1. J. Zeng, O.S. Shirihai, and M.W. Grinstaff. (2019). Degradable Nanoparticles Restore Lysosomal pH and Autophagic Flux in Lipotoxic Pancreatic Beta Cells. *Advanced Healthcare Materials*. *8 (12),* 1801511
2. W. A. Blessing, S.M. Okajima, M.B. Cubria, J.C. Villa-Camacho, Miguel Perez-Viloria, Patrick Williamson, A.N. Sabogal, S. Suarez, L. Ang, S. White, E. Flynn, E.K. Rodriguez, M.W. Grinstaff, and A. Nazarian. Intra-Articular Injection of Relaxin-2 Alleviates Shoulder Arthrofibrosis. *Proceedings of the National Academy of Science USA*, 2019, *116*, 12183-12192.
3. I. Ekladious, Y.L. Colson, M.W. Grinstaff. Polymer–drug conjugate therapeutics: advances, insights and prospects. *Nat Rev Drug Discov* 2019, *18*, 273–294.
4. R. Xiao, J. Zeng, and M.W. Grinstaff (2018). Biologically Active Branched Polysaccharide Mimetics: Synthesis via Ring-opening Polymerization of a Maltose-based β-Lactam. *ACS Macro Letters*. *7 (7),* pp 772-777.
5. R. Liu, A.H. Colby, D. Gilmore, M. Schulz, J. Zeng, R.F. Padera, O.S. Shirihai, M.W. Grinstaff, Y.L. Colson (2016). Nanoparticle tumor localization, disruption of autophagosomal trafficking, and prolonged drug delivery improve survival in peritoneal mesothelioma. *Biomaterials*. 102:175-186
6. M. D. Konieczynska, J. C. Villa-Camacho, C. Ghobril, M. Perez-Viloria, K. M. Tevis, W. A. Blessing, A. Nazarian, E. K. Rodriguez, M. W. Grinstaff (2016). *Angew. Chem. Int. Ed.*, *55*, 9984

Dr. Grinstaff's key advice to current and future postdocs "*Always learn something new, read, ask lots of questions, and do the right experiment with controls."*

Check out the lab's webpage: https://www.grinstaff.org/

Dr. Jialiu Zeng obtained her PhD from Boston University in 2020 under the mentorship of Dr. Mark Grinstaff, and co-supervised by Dr. Orian Shirihai at the University of California, Los Angeles. Her doctoral thesis focused on the topic of "*Nanoparticles modulate lysosomal acidity to rescue autophagy dysfunction in cell and mouse models".* After her Ph.D., Dr. Zeng joined Dr. Sreeganga Chandra's lab at the Department of Neurology, School of Medicine at Yale University.
With 10 years' worth of research experience, Dr. Zeng has 10 publications in renowned journals.
Please read the Zeng et. al. manuscript titled "*Modulating lysosomal pH: a molecular and nanoscale materials design perspective*" published in the December issue of *JoLS, Journal of Life Sciences*.