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The 2017 Young Innovators of Cellular and Molecular Bioengineering

We are proud to present to you the eleven Young Innovators of Cellular and Molecular Bioengineering, whose work is featured in this October issue. This is the fourth year of the Young Innovators competition, and the number of self-nominations under consideration continues to rise. All potential authors who hold the rank of Assistant Professor (or equivalent) at the time of nomination are eligible for selection, and while most authors are active members of the Biomedical Engineering Society (BMES), membership in BMES is no longer a requirement for inclusion. The research described in this issue will be presented by the awardees in a special, two-part invited platform session on Friday, October 13 at the 2017 Annual Meeting of BMES in Phoenix, Arizona. These articles represent some of the most important and impactful bioengineering studies directed by junior faculty in our field, and includes > 50% female faculty for the first time. We note that this October 2017 issue of CMBE is the first issue to exclusively feature abstracts in the new structured abstract format, which was adopted earlier this year to better serve our biomedically oriented readership.[1]

Two of this year's Young Innovator articles are focused on signal transduction from the matrix or cell scaffold to the cells to influence cellular activity. With the ultimate goal of engineering vascularize cardiac tissue with parallel microvasculature, work by Ngan Wang and colleagues shows that differentiation of iPSCs into endothelial cells is more pronounced on three-dimensional poly(caprolactone) fibrous scaffolds as compared to two-dimensional scaffolds. They further demonstrated that parallel fiber alignment supports longer endothelial tubules with fewer branch points. Work by Kristopher Killian and colleagues shows that matrix mechanics influences the phosphorylation state and cellular localization of histone deacetylase HDAC4. This mechanotransduction also regulates gene expression associated with fibroblast–myofibroblast transitions. The work establishes a link between outside-in signaling and epigenetic regulation. Together, these papers emphasize the important role of physicochemical features of the extracellular matrix in regenerative medicine.

Four of this year's Young Innovators work in the area of nanotechnology and drug delivery. All focus on intracellular delivery of biomolecules or small molecule drugs. The work by Jeanne Stachowiak and colleagues is focused on membrane fusing liposomes. With the goal of enhancing membrane fusion to increase transfer of liposome contents to the cell cytoplasm, they concentrated fusion-promoting lipids in patches on the surface of liposomes using phase separation. They further demonstrate an increase of macromolecular delivery to the cell cytoplasm setting the stage for improved biomolecule delivery. Also with a focus on intracellular biomolecule delivery, Evan Alexander Scott and colleagues have developed an immunotheranostic polymersome delivery system to simultaneously deliver antigen and adjuvants to the cytoplasm, while also fluorescently tagging the cells for later identification. To achieve fluorescent tagging that is also an indicator of cytoplasmic delivery, they flanked perylene bisimide (PBI) with two oxidation-sensitive hydrophobic poly(propylene sulfide) PPS blocks to enhance π stacking and introduced a mechanism for disrupting π–π interactions to shift PBI fluorescence in response to oxidative conditions, thus engineering in a fluorescent shift upon exposure to the cytoplasm. Again focused on intracellular delivery, but of small molecule agents aimed at triple negative breast cancer, Dipanjan Pan and colleagues focused efforts on the development of multicomponent-carbon nanoparticles for combinatorial therapeutic delivery. Using approved therapeutics, they demonstrate enhanced efficacy of a cocktail of agents delivered intracellularly from multicompartment carbon nanoparticles as compared to intracellular nanoparticle delivery of individual agents. This combinatorial approach can help to rapidly identify appropriate dosing regimens for various cancers and diseases. Work by James Moon and colleagues is focused on using spiky gold nanoparticles (SGNPs) for efficient delivery to immune cells. Their goal was to develop a nanoparticle (NP) platform that can induce activation of innate immune cells. Taking advantage of the large surface to volume ratio of the SGNPs, they decorated their surfaces with Toll-Like Receptor (TLR) agonists and endowed them with immunostimulatory properties. Particle coating was done using electrostatic layer-by-layer deposition, while efficacy was demonstrated in bone marrow derived dendritic cells. Together, these Young Innovators have shown the great potential of nanoparticles for intracellular delivery.

Five of the Young Innovator papers are focused on biological studies at the cellular level, and reveal new insights into physiological processes or responses to treatment. Ben Cosgrove and colleagues utilize a data-

driven modeling approach to tease out several new aspects of the complex signaling interactions involved in the proliferation and differentiation of myoblasts in response to different external stimuli. They found an unexpected negative feedback circuit in which the phosphatase DUSP6/MKP3 auto-regulates MEK-ERK signaling. Kara Spiller and colleagues explored the mechanism of action of macrophage responses to biomaterial therapy in wound healing. In their study, human cryopreserved viable amniotic membrane (hCVAM) induced different pro-inflammatory marker expression when presented to primary human M1 macrophages in either soluble or intact substrate form. Insights gained from the changes in inflamatory molecule expression in response to contact with hCVAM should lay the groundwork for developing immunomodulatory surfaces to aid in wound repair. Jennifer Munson and colleagues examine the unique tumor microenvironment at the outer periphery of tumors, and use a combination of 3-D *in vitro* systems and computational modeling to determine how cells at the tumor border might respond differently to the doxorubicin chemotherapeutic. Their results suggest that stromal fibroblasts more commonly found in the region surrounding the tumor may confer additional drug resistance in breast cancer. Shilpa Sant and colleagues have explored how reactive oxygen species (ROS)-modulating shape-specific cerium oxide nanoparticles inhibit oxidative stress-induced valvular calcification. In primary human valvular interstitial cells isolated from either healthy donors or patients with calcified aortic valves, they found that rod- and sphere-shaped nanoparticles scavenged ROS in a dose- and shape-dependent manner. Finally, Penney Gilbert and colleagues examined the molecular mechanisms of how substrate stiffness controls Notch signaling to control myogenic progenitor cell differentiation, in a combined in vivo and in vitro study. They show that tethered Jagged-1 is a key molecular player that tunes Notch activity in this context.

We hope that you will enjoy this collection of original research articles, and that you will encourage your colleagues to nominate themselves for next year's CMBE Young Innovator competition. Self-nominations are due by November 10, 2017. Interested researchers who hold a position at the rank of Assistant Professor (or equivalent) are invited to submit a 250-word structured abstract and a two-page NIH-style biosketch to Editor-in-Chief Michael King at mike.king@vanderbilt.edu. A great way to engage with the Cellular and Molecular Bioengineering journal and learn about our latest published articles and other activity is to follow us on Twitter (www.twitter.com/CMBEjournal) and Facebook (www.facebook.com/CMBEjournal). One exciting recent development is that CMBE has achieved its highest ISI Impact Factor yet in 2016, 2.535, representing a 60% increase over the previous year. While journal impact factor is only one metric that authors use when selecting where to submit their work for publication, we are neverthe less pleased with this evidence of the rapidly expanding impact of the journal in the field of bioengineering. See you in Phoenix at the 2017 BMES Annual Meeting, in Key Largo at the 2018 CMBE Conference, and online!

REFERENCE

[1]King, M. R. CMBE moves to the structured abstract format: a note from the editor. *Cell. Mol. Bioeng.* 10(2):143, 2017.

MICHAEL R. KING
Department of Biomedical Engineering,
Vanderbilt University,
5824 Stevenson Center,
Nashville, TN 37235 USA
Electronic mail: mike.king@vanderbilt.edu

ALYSSA PANITCH
Department of Biomedical Engineering,
University of California at Davis,
451 E. Health Sciences Dr., GBSF, Room 2303,
Davis, CA 95616 USA

RICHARD E. WAUGH
Department of Biomedical Engineering,
University of Rochester,
218 Robert B. Goergen Hall,
Rochester, NY 14627 USA