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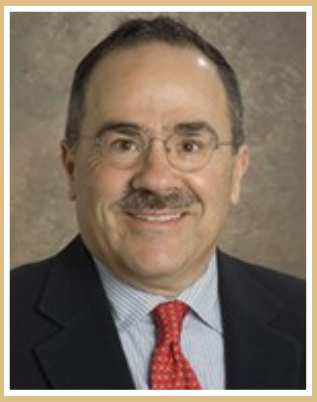

SEPTEMBER 14, 2015

Eleftherios Terry Papoutsakis , Ph.D.

EUGENE DUPONT CHAIRED PROFESSOR

CHEMICAL & BIOMOLECULAR ENGR, BIOLOGICAL SCIENCES

UNIVERSITY OF DELAWARE

"Microparticles as cellular communicators to empower therapies: the case of megakaryocytic microparticles"

A long-standing goal in cell-culture technologies is the ability to produce human blood cells for transfusion medicine. Another important goal is to develop robust differentiation technologies of stem cells, technologies that could be transferred to the clinic but also used in in vitro investigational experimentation. Among blood cells, platelets, needed for blood coagulation and vascular repair, are an expensive "product" in limited supply. Production of platelets in a "blood factory" is recognized as a grand challenge that remains elusive. Platelets derive from polyploid megakaryocytes (Mks) in the bone marrow and lung vasculature, under the action of biomechanical forces. We will show how important these forces are for producing functional platelets and their precursors, as well as small, anuclear particles, Mk microparticles (MkMPs)*. MkMP generation was dramatically enhanced (up to 47 fold) by shear flow. Significantly, co-culture of MkMPs with hematopoietic stem and progenitor cells (HSPCs) promoted HSPC differentiation to Mks without exogenous thrombopoietin, thus identifying, for the first time, a novel and previously unexplored potential physiological role for MkMPs. This demonstrates the extraordinary ability of these MkMPs in programming HSPCs. I will discuss our efforts to understand the mechanisms by which MkMPs target and act upon cells. How general is the production and biological activity of MPs? Most cells release into the extracellular environment these very small MPs (typically less than 1 micron) under some stress or activation process. MPs result from direct budding off the the plasma membrane, and are increasingly recognized as important players in intercellular communication by transferring proteins, lipids, RNA, and perhaps DNA, between cells. They do so with good target specificity and thus, one can argue for producing and using them for regenerative-medicine applications, as well as in experimental investigations to deliver "cargo" to specific cell types.

* Jiang, J; Woulfe, DS; Papoutsakis, ET. Shear enhances thrombopoiesis and formation of microparticles that induce megakaryocytic differentiation of stem cells BLOOD 124: 2094-2103 (SEP 25 2014).

10:30am in 322 ISE Lab. *Refreshments served at 10:15am.*

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