Cell ‘secret handshake’ photo takes top prize

Sebastian F. Barreto, a doctoral student of chemical and biomolecular engineering in the laboratory of Sharon Gerecht, won the grand prize for his image “Cells Performing Secret Handshake” from the Regenerative Medicine Foundation (RMF). Another image that Barreto submitted received 3rd place, and a third image (not shown) received honorable mention.

Late last year, RMF issued an international call for macro-photography of regenerative medicine images taken through a microscope. This inaugural contest resulted in nearly 100 images representing scientists from the United States, Australia, Canada, Germany, the Netherlands and the United Kingdom.

Barreto’s image was included in the “Art of Science: Under the Surface” exhibition that featured an opening lecture and public reception with global expert in regenerative medicine Anthony Atala, M.D. and award winning photographer, painter and sculpture, Kelly Milukas, whose talk focused on the impact of art on healing. The winning images were featured in a special public patron gallery exhibition component during the Regenerative Medicine Foundation annual meeting held in San Francisco, May 5-7, 2014.

Barreto is affiliated with both the Johns Hopkins Institute for NanoBioTechnology and with the Physical Sciences-Oncology Center.
Center Project Updates: Recent Publications

Here’s a roundup of recent publications from researchers associated with the three main projects of Johns Hopkins Physical Sciences-Oncology Center.

PROJECT: Functional interactions between HIF-1 and extracellular matrix in cancer

Cyclin-dependent kinases regulate lysosomal degradation of hypoxia-inducible factor 1α to promote cell-cycle progression.

Hypoxia-inducible factor 1 (HIF-1) is a transcription factor that mediates adaptive responses to oxygen deprivation. Here we report that HIF-1α physically and functionally interacts with cyclin-dependent kinase 1 (Cdk1) and Cdk2.


Hypoxia and the extracellular matrix: drivers of tumour metastasis.

Emerging data indicate that hypoxia and the extracellular matrix (ECM) might have crucial roles in metastasis. Originally thought of as independent contributors to metastatic spread, recent studies have established a direct link between hypoxia and the composition and the organization of the ECM, which suggests a new model in which multiple microenvironmental signals might converge to synergistically influence metastatic outcome.


Hydrogels to model 3D in vitro microenvironment of tumor vascularization.

In this review, we explore current use of hydrogels and their design parameters to engineer vasculogenesis and angiogenesis and to evaluate the angiogenic capability of cancerous cells and tissues. By coupling these hydrogels with other technologies such as lithography and three-dimensional printing, one can create an advanced microvessel model as microfluidic channels to more accurately capture the native angiogenesis process.


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Hyaluronic acid hydrogel stiffness and oxygen tension affect cancer cell fate and endothelial sprouting.

Three-dimensional (3D) tissue culture models may recapitulate aspects of the tumorigenic microenvironment in vivo, enabling the study of cancer progression in vitro. Both hypoxia and matrix stiffness are known to regulate tumor growth. We observed that increased matrix stiffness reduced endothelial sprouting and invasion in atmospheric conditions; however, we observed increased endothelial sprouting and invasion under hypoxia at all levels of matrix stiffness with the upregulation of vascular endothelial growth factor (VEGF) and angiopoietin-1 (ANG-1).

Summer research intern investigates cell motility

Sierra Atwater just completed her freshman year as a biology major at the University of North Carolina Chapel Hill. She worked in the chemical and biomolecular engineering laboratory of Denis Wirtz, professor and director of the Johns Hopkins Physical Sciences-Oncology Center. She was part of the Institute for NanoBioTechnology REU program. REU stands for Research Experience for Undergraduates and is a National Science Foundation funded program administered by INBT. Atwater explained that the Wirtz group is “looking at cell motility and proliferation to see how different cancer cells move and what affects that movement.” “I’ve been looking at cell division and cell density over a 16-hour period,” she added. “I have learned how to do a lot in this lab such as how to make 3D collagen gel matrices and how to make 2D gels, how to use T2000 microscopes and the confocal microscopes and how to do ELISAs,” which are enzyme-linked immunosorbent assays or tests used antibodies to detect substances. Hasini Jayatilaka, a doctoral student in ChemBE, was Atwater’s mentor. In addition, Atwater said she felt that she could call upon the expertise of other students working in the Wirtz lab. This was her first research experience, and she said the hardest thing so far has been just remembering how to do so many different techniques.
Osmotic Engine Model describes cell migration in tight spaces

Researchers in the laboratories of Konstantinos Konstantopoulos, professor and chair in chemical and biomolecular engineering, and Sean Sun, professor in mechanical engineering, have developed a mathematical model that accurately predicted experimentally how cancer cells use water to move through tight microchannels within tumors.

“A critical step during cancer progression is called metastasis or the migration of cancerous cells from the primary tumor to other organs in the body,” Konstantopoulos said. “In vivo, tumor cells migrate within three-dimensional extracellular matrices and through pre-existing three-dimensional longitudinal tracks, where the cells are confined within small micron-sized spaces.”

To mimic the environment of these confined spaces and how they affected cell behavior, the team built a lab-on-a-chip device with microchannels. The team discovered that the cells use a new mechanism, which they describe mathematically as the Osmotic Engine Model, to propel themselves through these microchannels. Sun explained the mechanism like this: “Imagine that two compartments with different concentrations of proteins and ions are separated by a membrane. Water will flow from the low solute region to the high solute region, driven by entropy. This will lead to swelling of the high solute concentration region, and a movement of the membrane forward. Cells, including cancer cells, have specialized water channels called aquaporins that allow the movement of water into and out of the cell. The mechanism works like a small jet.”

Sun and Konstantopoulos were able to prove, both mathematically and experimentally, that their model was correct.

“From the theoretical work, it became very clear that external solute concentration in the medium surrounding the cell is an important variable for determining the cell migration speed,” Sun said. “In fact, by changing the external concentration, it is possible to reverse the direction of water flow and reverse the direction of cell migration.”

Kim Stroka, a former postdoctoral fellow who worked on the project, said the mathematical model was powerful because it could also predict a number of other observations. “For instance, genetically ‘knocking down’ water channels in the cell will slow the cell down because water cannot flow as fast across the cell membrane. Knocking down ion pumps that are responsible for establishing local ionic concentrations will also change the migration speed. The work showcases the power of mathematical modeling in understanding biological systems.”