A NIH and NSF Jointly Supported Workshop for Integrative Additive Biomanufacturing and Tumor Engineering

PROJECT DESCRIPTION

Vision and Objectives

Cancer is still one of the leading causes of death, albeit enormous efforts to find cures for the disease. One of the significant challenges in cancer therapy is the heterogeneous nature of tumors due to their genomic variations such as copy number variation and point mutations. Such heterogeneity leads to different cellular morphology, metabolism, motility, proliferation, and gene expression. Oncology research and drug screening for cancer therapy have long focused on using animal models. In lieu of the fact that many effective anti-cancer drugs have been successfully discovered using animal models, complementary and alternative tumor model systems need to be developed and for use in oncology research and drug screening. Animal models are effective for validating drugs when the leading drug candidates have been identified. They are, however, less powerful for initial screening due to the cost and limitation of number of mice. Other challenges include the considerable differences in immune system and physiology between mice and humans, leading to the development of less efficient treatments when mice are used as a model system for drug screening and oncology study.

The integration of additive biomanufacturing with tumor engineering offers new opportunities for building vascularized and functional human tumor models for oncology research and drug screening. Construction of 3D tumor models has been proposed and extensively explored in the last decades. The field has been significantly advanced. Nevertheless, challenges have still remained. There has been and will continuously be significant challenge for building biologically functional tumor models suitable for oncology study and drug screening. The recent advances in additive biomanufacturing, oncology, stem cell biology, tissue engineering, microfabrication, and materials science offers new opportunities for creating sophisticated 3D tumor models in a lab setting by printing or depositing materials and cancer and its surrounding cell-laden materials layer-by-layer precisely with the help of a high-precision robot. The procedure involves the deposition of a layer of synthetic/natural polymer in an aqueous state and crosslink it into a hydrogel layer that supports the deposition of another layer of cell-laden hydrogel polymer. The controlled deposition and crosslinking of cell-laden hydrogel polymer allows for assembling multiple types cells in an organized way representing a planar layout of tumors in vivo. The continuous deposition or printing hydrogel and cancer cell-laden hydrogel will eventually build architecture of desired tumors. The key architectural and compositional components of tumors...
can be acquired through bioimaging and cell molecular analysis. The realization of these technologies will open up a new field for oncology study and drug screening.

Clearly, the advancing of this field requires multi- and/or inter-disciplinary efforts and the coordination of multiple agencies. Here we propose a NSF-NIH jointly supported Workshop in integrative advanced biomanufacturing and tumor engineering. **The overarching objective of this workshop is to bring together scientific leaders to review the progress made in the last decade, to identify grand challenges in integrating additive manufacturing with tumor engineering, and finally to articulate a vision to advance physical sciences and engineering in life sciences and oncology.** The emerging of additive biomanufacturing, human genome editing, stem cell engineering, material genome techniques, computational and synthetic biology, and personalized medicine offers new opportunities to spur research, education, industry growth and innovation in tumor engineering. **The following objectives are expected to achieve through the workshop:**

- Identify challenges in additive biomanufacturing of tumor models
- Develop a community to share ideas, resources, and technologies to address challenges identified through the workshop
- Establish a forum for engineers to collaborate with oncologists or vice versa in tumor engineering research
- Increase public awareness of tumor engineering research
- Promote tumor engineering research and education programs
- Train and educate students in tumor engineering research

**Conference Program**

**Workshop Location, Date, and Expected Outcomes**

**The workshop will be held at NIH main campus at Washington DC on April 1st-2nd, 2015.** It will consist of panel presentations and in-depth discussions by leading scholars and researchers. The workshop will be focused on reviewing progresses and identifying challenges and opportunities in integrative additive biomanufacturing and tumor engineering. Panelists will consist of leading investigators and junior investigators as well as early career investigators. The panel discussion will be led by a session chair and documented by a scribe. The scribe will
be responsible for developing session report based on the discussions. The session report will be further extended into a white paper that will be submitted to funding agencies such as NIH and NSF for consideration.

The Workshop will have four sessions including invited presentations, followed by in-depth panel discussions. A perspective paper will be developed during and after the workshop and will be published in a perspective journal.

**Agenda (Tumor Engineering Workshop) (April 1st, 2nd, 2015 at NIH Main Campus)**

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**Session**

Day 1-April 1st (Wednesday)

- **8:30 am—Workshop Opening**

  --Welcome, Initial Guidance—Kaiming Ye, Professor and Department Chair, Binghamton University, State University of New York (SUNY)

  --Remarks

  - Dr. Pramod Khargonekar, Assistant Director, Directorate for Engineering, NSF
  - Dr. Dinah Singer, Director, Division of Cancer Biology, NIH/NCI
  - Dr. Athanassios Sambanis, Program Director, NSF/CBET
  - Dr. Larry Nagahara, Associate Director, Division of Cancer Biology, NIH/NCI

- **9:30 am-11:30 am  Session 1: Tumor-on-A-Chip** (Session Discussion including Pre-organized overview presentation focusing on discussing barriers, key solutions to
address gaps in knowledge, and road map to advance the field; followed by presentation from two or three panelist to support and supplement the overview presentation. Inputs will be sought from the larger workshop attendees after the presentations. Expected Outcome: framing topics and recommendations for the initial roadmap report and reporting back to the large workshop for finalizing the roadmap report.)

- **Topics**—integrating tumor tissues into microfluidic systems, micro-total analysis of oncology, high-throughput and real-time (4D) pharmacological screening, biofabrication of tumor-on-a-chip, bioreactor for growing and maintaining tumors-on-chips
- **Panelists**—Kam Leong (Duke) (*Session Chair*), Daniel Haber (Massachusetts General Hospital), Mina Bissell (Lawrence Berkeley National Laboratory), Philip LeDuc (CMU), Peter Searson (John Hopkins), Melkoumian Zara (Corning), Gretchen Mahler (Binghamton University), Utkan Demirci (Stanford), Gordana Vunjak-Novakovic (Columbia), and Bahareh Behkam (Virginia Tech).

- **11:30 am-1:00 pm** Lunch Break

- **1:00pm-3:00pm: Session 2: Biomanufacturing including 3D Printing of Multiple Tissues Integrated Physiological Tumor Models** (*Session Discussion including Pre-organized overview presentation focusing on discussing barriers, key solutions to address gaps in knowledge, and road map to advance the field; followed by presentation from two or three panelist to support and supplement the overview presentation. Inputs will be sought from the larger workshop attendees after the presentations. Expected Outcome: framing topics and recommendations for the initial roadmap report and reporting back to the large workshop for finalizing the roadmap report.)

  - **Topics**—Biomaterials for 3D tumor printing, multi-scale and complexity of tumor tissues, vascularization of tumor tissues through 3D printing, validation of 3D printed tumor tissues. long-term culture of 3D tumor tissues
  - **Panelists**—David Kaplan (Tufts) (*Session Chair*), Wei Sun (Drexel), Lance Munn (Massachusetts General Hospital), Melody Swartz (Chicago), Guohao Dai (RPI), Seung-Schik Yoo (Harvard), Valerie M. Weaver (UCSF), Esmaiel Jabbari (South Carolina), and Edna Cukierman (Temple U)
• 3:00 pm-3:20 pm Coffee Break

• 3:20 pm-5:20 pm **Session 3: Noninvasive Characterization of 3D Printed Tumor Tissues** (Session Discussion including Pre-organized overview presentation focusing on discussing barriers, key solutions to address gaps in knowledge, and road map to advance the field; followed by presentation from two or three panelist to support and supplement the overview presentation. Inputs will be sought from the larger workshop attendees after the presentations. **Expected Outcome:** framing topics and recommendations for the initial roadmap report and reporting back to the large workshop for finalizing the roadmap report.)
  
  o **Topics**—noninvasive characterization of mammary tissue development and tumor progression in 3D printed tumor tissues, label-free tracking the response of tumor tissues to drugs and stimulate, and biomechanics of tumor tissues and their noninvasive characterization
  
  o **Panelists**— Claudi Fischbach-Teschl, (Cornell) (Session Chair), Parmela Kreeger (U. Wisconsin), Paul Janmey (U Penn), Robert J. Gillies (Moffitt Cancer Center), Maja Oktay (Einstein College of Medicine), Cheng Dong (Penn State), Bruce Tromberg (UC Irvine), and Gang Bao (George Tech).

• 6:00 pm-8:00 pm Informal Dinner (Location: TBD)

**Day 2 (April 2nd) (Thursday)**

• 8:00 am – 10:00 am **Session 4: Multiscale Tumor Computational Modeling** (Session Discussion including Pre-organized overview presentation focusing on discussing barriers, key solutions to address gaps in knowledge, and road map to advance the field)

  o **Topics**— multiscale modeling of 3D tumor models, simulating tumor heterogeneity
  
  o **Panelists**—Thomas S. Deiboeck (Harvard-MIT) (session chair), Doug Lauffenburger (MIT), Bumsoo Han (Purdue), Paolo Provenzano (U. Minnesota), Viek Shenoy (U. Penn), Paul Macklin (U Southern California), Jordan Miller (Rice U), and Ming Zhan (Methodist Hospital research Institute, Houston).
• **10:00 am-10:20 am** Coffee Break

• **10:20 am-12:20 am** Team Discussion in session breakout rooms (Each team will provide topics and recommendations to the larger workshop, as well as the outlines for the workshop report and the white paper, Chair and scribe will draft inputs from the team members and frame the discussions at subsequent larger workshop)

• **12:20 pm-1:20 pm** Lunch

• **1:20 pm-3:20 pm** Large Workshop Group Discussion (Chair of each sessions presents the findings for additional feedback, leads discussion, identifies interfaces with the other session team, and finalizes plans for each team)

• **3:20 pm Adjourn** (Draft the workshop report and white paper within a month after the workshop)

For each session, 3-4 session panelists will be invited to present 10-12 min each to initiate and stimulate a panel discussion. Session Chairs will communicate with session team members to prepare overview presentation before the workshop. The Scribe of each session will document and finalize the panel discussion. A final report and white paper will be developed by all participants.

**Confirmed Government Attendees:** Rosemarie Hunziker (NIH/NIBIB), Joseph Mosca (NIH/NIBIB), Piotr Grodzinski (NIH), Joe Akkara (NSF), Friedrich Srienc (CBET/NSF), Keith Roper (NSF), Leon Esterowitz (NSF/CBET). More Program Directors from NIH, NSF, DARPA, FDA, ..., etc. will join the workshop.