**2018 IMAG Futures Meeting – Moving Forward with the MSM Consortium (March 21-22, 2018)**

*Pre-Meeting Abstract Submission Form*

*\*Please submit to the NIBIB IMAG mailbox (*NIBIBimag@mail.nih.gov*) by* ***January 8th, 2018***

*\*Save your abstract as “MSM PI Last Name \_ 2018 IMAG Futures Pre-Meeting Abstract”*

**PI(s) of MSM U01: Xiaobo Zhou and Yunzhi Yang**

**Institution(s): UThealth at Houston & Stanford**

**MSM U01 Grant Number: 3U01AR069395-02**

**Title of Grant:** Systems Modeling Guided Bone Regeneration

**Abstract**

**Which MSM challenges are you addressing from the IMAG 2009 Report and how?**

<https://www.imagwiki.nibib.nih.gov/content/2009-imag-futures-report-challenges>

(indicate which challenge (#) you’re addressing)

(#5) We are starting to focusing on a big challenging that how to systemically modeling tumor evolution based on single-cell genomics. Various mutation events occurred in the process of tumor formation. Single-cell genomic data will guide us to develop patient-specific tumor model for revealing mechanisms and potential treatment strategies.

**Are you using machine learning and or causal inference methods and how?**

Yes, we are using machine learning to learn parameters in our models.

We are designing a binary linear programming (BLP) approach by combining Gibbs structural sampler with binary linear programming-based discrete modeling to infer signaling pathway network with time-series RNA-seq data.

**Please briefly describe significant MSM achievements made (or expected).**

1. We constructed a multiscale systems model to simulate the BMSC lineage commitment under cytokine treatments (BMP2, IGF1) at both molecular and cellular levels. The multiscale model integrated our experimental data of various scales to represent a coordinated system. We also evaluated the significance of involved parameters to model output through global sensitivity analysis. We validated our model with an independent set of experimental data, and consequently proposed a convincing mechanism to explain the outcomes of combined treatment with specific growth factors.

2. We established a 3D mechanistic hybrid multi-scale model (HMSM) for systematically understanding the immunity leading to castration-resistant prostate cancers (CRPC). In our HMSM model, we infer the cell-cell interaction and connected cytokines from our RNA-Seq data generated under various co-culture conditions. Based on the inferred cell-cell interaction networks, HMSM model simulated tumor growth, immune infiltration, and angiogenesis with in an integrated 3D space, which included tumor spaces and lymph node. After optimized with the dynamic cell population data quantified from our mice model, HMSMS is capable of predicting the optimal treatment strategies for CRPC.

**Please suggest any new MSM challenges that should be addressed by the MSM Consortium moving forward.**

 How can systems modeling address drug resistance and recurrence in clinic studies? How to consider mutations in systems modeling to simulate clinical treatment? How to incorporate single cell sequencing and epigenetics regulation in systems modeling?

**What expertise are on your team (e.g. engineering, math, statistics, computer science, clinical, industry) and who?**

*Please list as “Expertise – Name, email”*

 *Engineering - Peter Yang (**ypyang@stanford.edu**); Math - Xiaobo Zhou(**xiaobo.zhou@uth.tmc.edu**) / Hua Tan (**hua.tan@uth.tmc.edu**); Computer Science - Zhiwei Ji (**zhiwei.ji@uth.tmc.edu**) / Guangming Zhang (**guangming.zhang@uth.tmc.edu**) ; Clinical - Weiling Zhang (**weiling.zhao@uth.tmc.edu**)*

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