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: David Basanta & Conor Lynch
Institution(s): H. Lee Moffitt Cancer Center & Research Institute
MSM U01 Grant Number: 5U01CA202958
Title of Grant: Multiscale Modeling of Bone Environment in Metastatic Prostate Cancer

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)

You may insert images by copying and pasting below

We are addressing several of the MSM challenges including #3, #8, #9, #11, and #18 with our largest effort pertaining to #9 and #18. The project is proceeding along the lines we proposed in our grant wherein experimental data is used to motivate and parameterize a mathematical models that test novel hypotheses regarding macrophage polarization in bone repair and homeostasis after a fracture. These outputs are then tested in vivo. Our results have provided us with novel insights into macrophage and bone biology that impact our understanding of normal and pathological processes such as bone injury and bone metastatic prostate cancer, the latter being the primary target of our project.

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

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Not at the moment but flow cytometry data is being used to characterize the phenotypes of the myeloid cells involved in bone repair. We anticipate that collaborating with our MSM colleagues that have expertise in machine learning we could identify relevant patterns of macrophage polarization that are indicative of how cancers are progressing in bone or responding to treatment.

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

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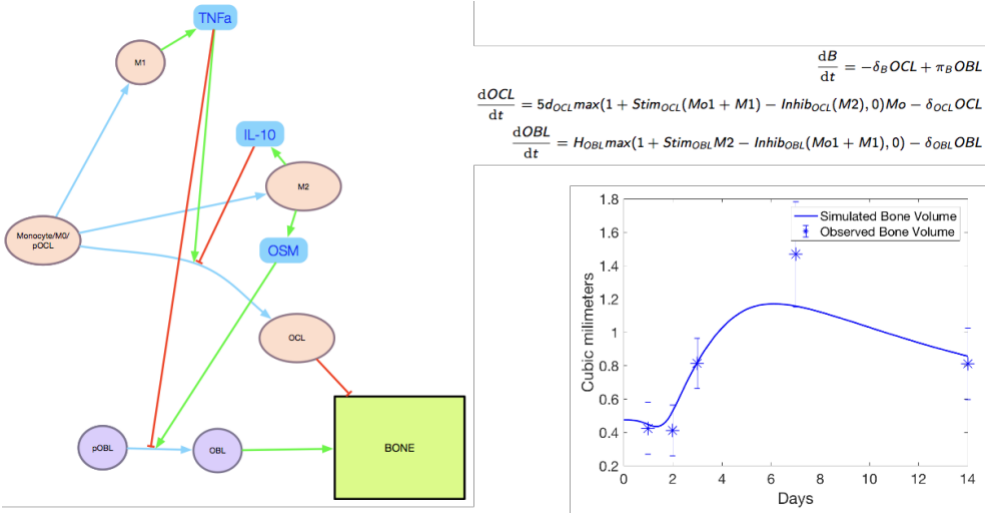
The integration of experimental data with mathematical modeling has allowed us to uncover new biology pertaining both the role of macrophages in the recovery from fractures to the establishment of a 'vicious cycle' in the early stages of prostate cancer metastases in the bone through the interactions between tumor and stroma. We are currently working on enriching our mathematical models with macrophages (at the cellular level, including M0, M1 and M2 phenotypes) as well as several signaling molecules involved in the differentiation and work of macrophages and other bone-resident cells involved in homeostasis and repair. Compared to other organs, little is known about the role of

macrophages in the bone, and even less in the context of cancer. Thus we are laying the groundwork for bone repair with the aim of improving the realism in the model in the case of metastatic cancer. Through the integration of modeling and experiments we have elucidated a number of hypothesis. One such example can be seen in this figure were we explore four different minimal models (of which we only show here one, on the right panel) that could explain M1/M2 impact on bone formation. Using experimental data which we fit into one single ODE (first one in the left), we use the remaining equations to predict osteoclast and osteoblast populations fluctuation over time. We are using a systematic approach to test many of these hypothesis to uncover enough bone biology to motivate our computational bone ecosystem approach.



Please suggest any <u>new MSM challenges</u> that should be addressed by the MSM Consortium moving forward.

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1. How to best balance the simplicity that models should bring with the complexity of biology through a rational integration of biological data and hypothesis in multi-modeling frameworks.
2. Models that facilitate the design and application of single or multiple treatments in adaptive therapy based clinical trials.

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

Please list as "Expertise – Name, email"
GU oncology – Julio PowSang, MD, julio.powsang@moffitt.org
Pathology - Jasreman Dhillon, MD, jasreman.dhilon@moffitt.org

Bone biology - Conor Lynch, PhD, conor.lynch@moffitt.org
Mathematical Biology – Alexander Anderson, PhD, alexander.anderson@moffitt.org
Computational Biology – David Basanta, PhD, david@cancerevo.org
Mathematical Biology – Etienne Baratchart, PhD, Etienne@cancerevo.org
Macrophage biology – Lochen Hao,