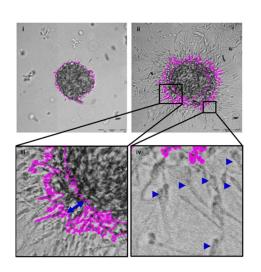
PROJECT TITLE:

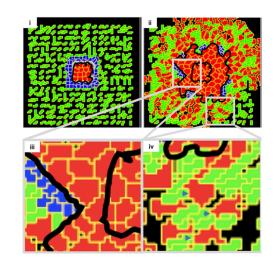
INVESTIGATING THE DYNAMICS OF RESISTANCE TO CHEMOTHERAPY IN CANCER USING EXPERIMENTAL AND COMPUTATIONAL APPROACHES



SUPERVISORS:

Ramray Bhat
(Molecular Reproduction, Development and Genetics)

Mohit Kumar Jolly
(Centre for BioSystems Science and Engineering)

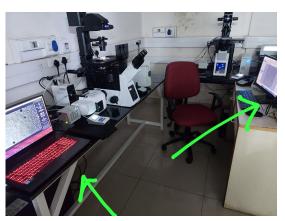


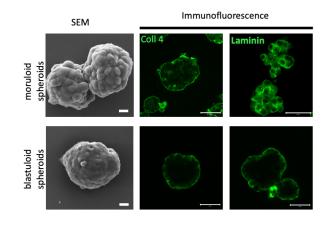
PROJECT QUESTION: Do spatial ordering of tumor cell populations and their cooperativity-competition dynamics explain resistance to chemotherapeutics? How does the architecture and mechanical properties of the tumor microenvironment influence chemoresistance?

LEARNING OPPORTUNITIES FOR THE PROSPECTIVE STUDENTS

EXPERIMENTAL

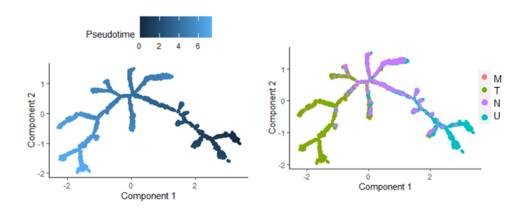
2D and 3D cultures
Organoid and tumoroid cultures
Confocal and epifluorescent microscopy
Time lapse imaging
Electron microscopy
Molecular cloning and cell biological assays
Animal experiments
Interface with clinicians





COMPUTATIONAL/THEORETICAL

Computational modeling of regulatory networks
Nonlinear dynamics
Multi-scale spatiotemporal modeling
Population dynamics/ecological modeling
Single-cell RNA-seq data analysis
Inferring cell-state transition trajectories
Spatial transcriptomic data analysis
Interface with clinicians



EXISTENT PROGRESS IN COLLABORATION



Contents lists available at ScienceDirect

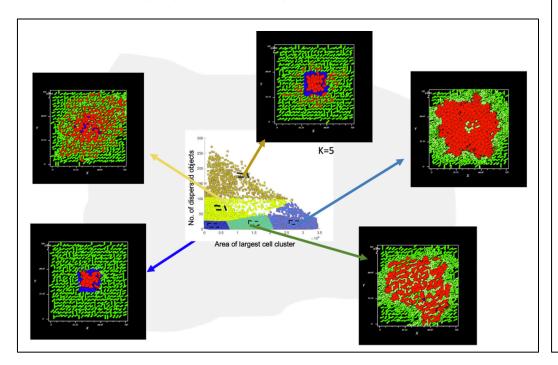
Journal of Theoretical Biology

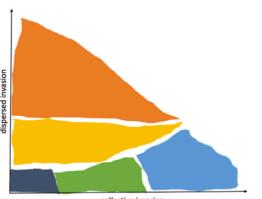
journal homepage: www.elsevier.com/locate/yjtbi

Matrix adhesion and remodeling diversifies modes of cancer invasion across spatial scales

D. Pramanik a,b, M.K. Jolly b,*, R. Bhat a,*

^b Centre for BioSystems Science and Engineering, Indian Institute of Science, Bangalore 560012, India

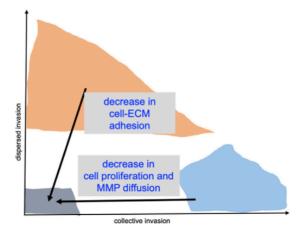




collective invasion

Papillary collective invasion: Strong cell-BM adhesion High cell proliferation

Low MMP-TIMP cooperativity



Dispersed invasion:

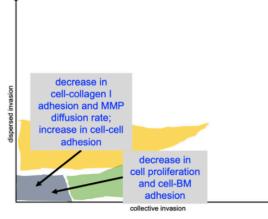
Strong cell-ECM adhesion Weak cell-cell adhesion Low dependence on cell proliferation

Multimodal invasion:

Strong cell-Collagen I adhesion Weak cell-cell adhesion Low dependence on cell proliferation High MMP diffusion

Bulk collective invasion:

Strong cell-Collagen I adhesion High cell proliferation High MMP diffusion



^a Department of Molecular Reproduction, Development and Genetics, Indian Institute of Science, Bangalore 560012, India

RELEVANT PROGRESS FROM THE EXPERIMENTAL GROUP

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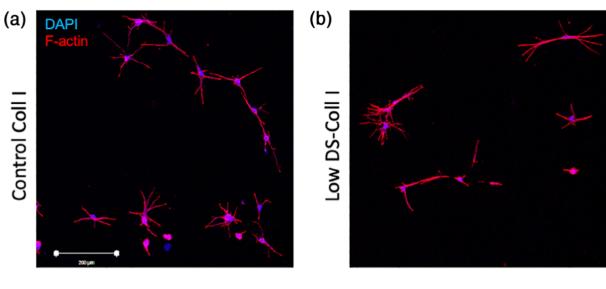
ORIGINAL ARTICLE

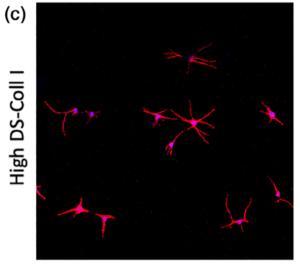


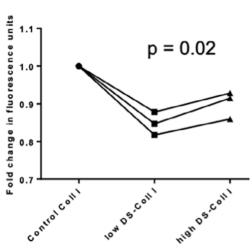
A biphasic response of polymerized Type 1 collagen architectures to dermatan sulfate

Konkada Manattayil Jyothsna¹ | Purba Sarkar² | Keshav Kumar Jha^{1,3} | Lal Krishna A. S.¹ | Varun Raghunathan¹ | Ramray Bhat² ©

Demonstration of reactivity of cancer cell interactions to varying ECM architectures







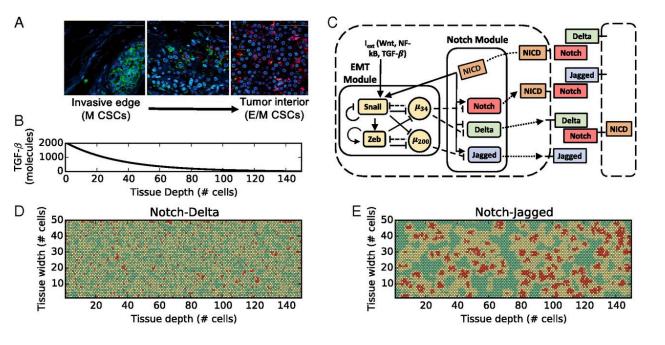
RELEVANT PROGRESS FROM THE COMPUTATIONAL GROUP



Toward understanding cancer stem cell heterogeneity in the tumor microenvironment

Federico Bocci^{a,b,1}, Larisa Gearhart-Serna^{c,1}, Marcelo Boareto^{d,e}, Mariana Ribeiro^c, Eshel Ben-Jacob^{a,2}, Gayathri R. Devi^{c,f,3}, Herbert Levine^{a,g,h,3,4}, José Nelson Onuchic^{a,b,h,i,3}, and Mohit Kumar Jolly^{a,3,5}

⁸Center for Theoretical Biological Physics, Rice University, Houston, TX 77005; ^bDepartment of Chemistry, Rice University, Houston, TX 77005; ^bDepartment of Surgery, Division of Surgical Sciences, Duke University School of Medicine, Durham, NC 27710; ⁶Department of Biosystems Science and Engineering, ETH Zurich, 4058 Basel, Switzerland; ⁶Swiss Institute of Bioinformatics, 1015 Lausanne, Switzerland; ⁶Women's Cancer Program, Duke Cancer Institute, Durham, NC 27710; ⁹Department of Bioengineering, Rice University, Houston, TX 77005; ⁸Department of Physics and Astronomy, Rice University, Houston, TX 77005; ⁸Department of Biosciences, Rice



Multi-scale models to explain spatial patterns of cancer cell heterogeneity

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NAR Cancer, 2021, Vol. 3, No. 3 1 https://doi.org/10.1093/narcan/zcab027

A mechanistic model captures the emergence and implications of non-genetic heterogeneity and reversible drug resistance in ER+ breast cancer cells

Sarthak Sahoo^{1,2}, Ashutosh Mishra^{1,2,†}, Harsimran Kaur^{1,†}, Kishore Hari¹, Srinath Muralidharan³, Susmita Mandal¹ and Mohit Kumar Jolly ^{©1,*}



Combinatorial therapies to tackle side-effects of drug-induced switch to a resistant state