APPLIED MATHEMATICS COLLOQUIUM:
Applied Mathematics Seminar Series

Date:
11/4/2022

Time:
3:00 PM - 5:20 PM

Location:
SSB 170

Roberto Alonso Matilla
Physical Modeling to Optimize Design of Theraupetic T cells,
Department of Biomedical Engineering
University of Minessota

About The Speaker:

Alonso-Matilla holds a B.S. degree in Industrial Engineering from the University of Valladolid (Spain), and a Ph.D. in Mechanical and Aerospace Engineering from the University of California San Diego. He was a postdoctoral researcher in Chemical Engineering at Columbia University, and he is currently a postdoctoral researcher in the Department of Biomedical Engineering at the University of Minnesota, where he is studying the biomechanics of cancer and immune cell migration during cancer progression. His primary research interests lie in the intersection of biophysics, cancer and immunology. Combining mathematical modeling, computer simulations and experimental approaches, Alonso Matilla aims at extending the existing base of scientific knowledge and applying fundamental and applied science to address major cancer research problems with the aim of finding novel solutions to treat cancer.

Abstract:

Many solid tumors exhibit an immunologically cold tumor microenvironment, characterized by very limited distributions of cytotoxic T cells, limiting the success of cancer immunotherapies against this type of tumors. Despite recent progress in understanding amoeboid-mesenchymal migratory balance, it remains largely unknown how T cells mechanically move through tumors and what factors set migration speed and directionality. We are applying a novel approach, involving mathematical modeling, computer simulations, live cell imaging and genome engineering to push the frontiers of T cell migration and elucidate the physical principles and molecular components that modulate T cell migration capabilities. We aim to identify how these molecular regulators can be perturbed to enhance cell migration, and ultimately engineer and design therapeutic T cells to a cellular state of maximal tumor infiltration and migration. Our model results predict that T cells might employ a hybrid adhesion-based, bleb-based migration mechanism for optimum cell motility, predict that higher extracellular matrix stiffnesses hinder bleb-based T cell migration and identify the existence of an intermediate level of membrane-cortex adhesion and cortical contractility for optimum cell migration. The developed mathematical framework, driven by data on immune cell migration combined with key experiments suggested by model results is helping us gain a new physical perspective of the mechanisms underlying single T cell migration that hopefully will change the way we design stroma targeting and T cell therapies for enhanced T cell migration capabilities. In my talk, I will also discuss traction force production of cell protrusions on compliant substrates, and show that alterations in cell adhesion levels, actomyosin activity and extracellular matrix rigidity can cause nontrivial cell traction force changes and modulated cell migration capabilities.

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