© 2019. Published by The Company of Biologists Ltd | Journal of Cell Science (2019) 132, jcs238634. doi:10.1242/jcs.238634

FIRST PERSON

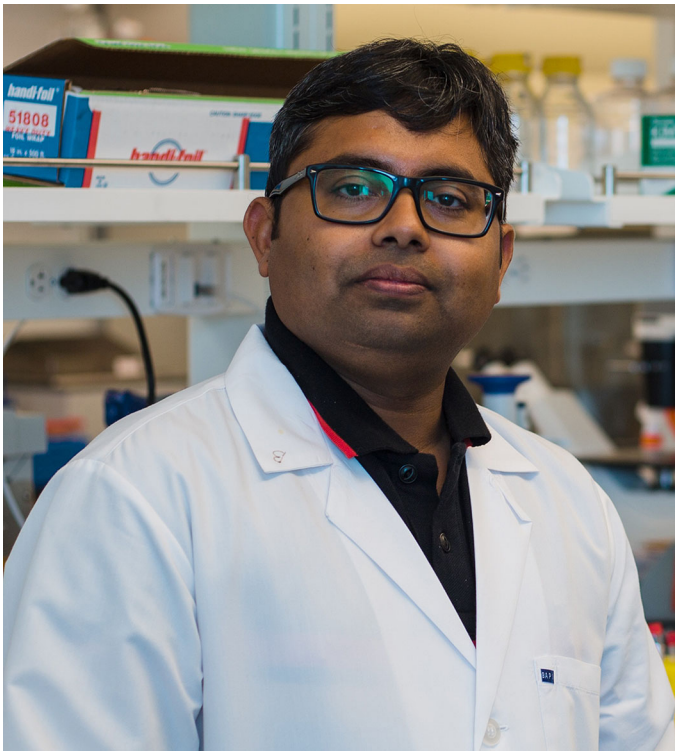
First person – Bapi Sarker and Amrit Bagchi

First Person is a series of interviews with the first authors of a selection of papers published in Journal of Cell Science, helping early-career researchers promote themselves alongside their papers. Bapi Sarker and Amrit Bagchi are co-first authors on 'Longer collagen fibers trigger multicellular streaming on soft substrates via enhanced forces and cell–cell cooperation', published in JCS. Bapi is a Postdoctoral Research Associate in the lab of Amit Pathak at Washington University, USA, designing tissue engineering scaffolds that can mimic native extracellular matrix, working to understand cell–cell and cell–matrix interactions in complex 3D microenvironments. Amrit is a PhD student in Amit Pathak's lab, investigating the biophysics behind substrate topography-influenced directed collective cell migration.

Amrit Bagchi

How would you explain the main findings of your paper in lay terms?

BS: Collective migration of epithelial cells is a hallmark of tissue remodeling, wound healing, and tumor invasion. In solid epithelial tumors, metastasis begins with the invasion of tumor cells into the surrounding stroma followed by migration toward the blood stream. While epithelial cells migrate in sheets on 2D substrates, they often form finger-like structures and migrate like streams in fibrous 3D microenvironments. It has remained unknown whether these finger-like structures form because of the fibrous architecture of the surrounding matrix and whether this is regulated by matrix stiffness. To address this question, we developed a novel hydrogel that enables us to tune the stiffness of hydrogel and coated collagen fiber architecture, independently. We observed multi-cellular finger-like structures emanating from the epithelial monolayer on both soft and stiff hydrogels coated with long collagen fibers. However, this streaming of cells was more pronounced and persistent on softer gels. We observed that the tip cells in the multicellular fingers aligned long collagen fibers on soft gels and used them as tracks to migrate. On the other hand, no streaming occurred on short collagen fiber-coated gels. This study reveals a stiffness-modulated effect of collagen fiber length on multicellular streaming of epithelial cells that could help us to better understand the effect of the surrounding tumor microenvironment on tumor cell invasion.

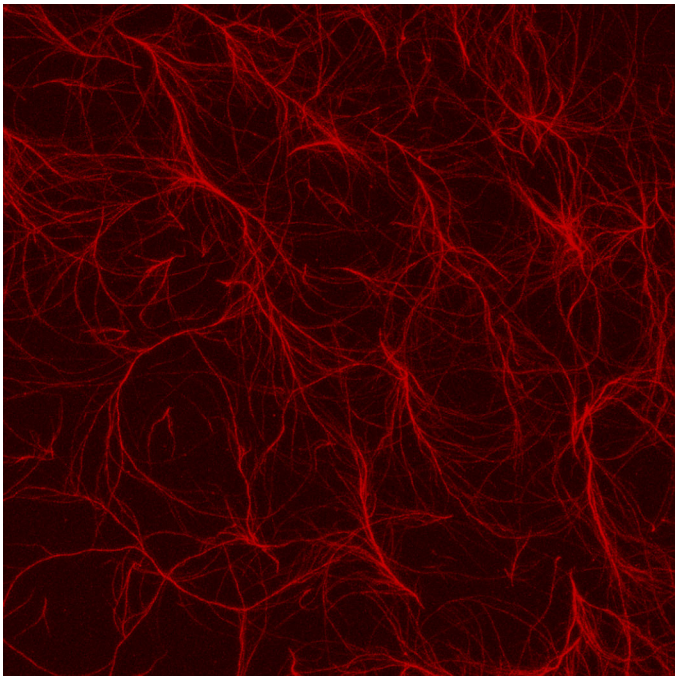


Bapi Sarker

Bapi Sarker and Amrit Bagchi's contact details: Department of Mechanical Engineering & Material Science, Washington University, 1 Brookings Dr., Saint Louis, MO 63130, USA.
E-mail: bapisarker@daad-alumni.de; amrit@wustl.edu

AB: Collective migration is one of the modes which cancer cells utilize to metastasize from a primary site. This mode of migration is both dependent on the stiffness of the tissue as well as the fibrous architecture around the tumor. Often, stiffer tissues as well as fibrous environments promote invasive behavior from the primary site, leading to higher chances of secondary tumor sites. However, it's not known whether these two signals in conjunction would promote invasive phenotypes. Our goal was to delineate the effect of these two factors. To that end, we designed a gel system where both stiffness of the substrate and the coated collagen fiber architecture could be controlled independently of each other. In this setting, we carried out collective migration experiments of breast epithelial cells. Surprisingly, we found that collective streaming at the

Journal of Cell Science (2019) 132, jcs238634. doi:10.1242/jcs.238634



Fluorescently labeled collagen type I (0.1 mg/ml) on aldehyde-functionalized polyacrylamide gel (120 kPa).

monolayer edge was more pronounced on softer substrates having longer collagen fibers when compared to every other condition, including stiff substrates with longer fibers. This is quite contradictory to non-fibrous modes of invasion where higher stiffness will cause more invasive phenotypes. Thus, this study reveals an inverse stiffness-dependent effect of collagen fiber length on invasive streaming of epithelial cells.

Were there any specific challenges associated with this project? If so, how did you overcome them?

BS: The biggest challenge of this project was to develop a polyacrylamide (PA) hydrogel that could enable fiber formation when coated with collagen-I. In the conventional approach of collagen coating on PA hydrogel, a heterobifunctional crosslinker, Sulfo-SANPAH is used. This approach does not allow collagen fiber formation because it blocks lysine residues, which are required for formation of collagen fibrils. Therefore, we were looking for a collagen-conjugation approach that keeps the lysine residues unblocked. We solved this problem by introducing primary aldehyde groups to the polymeric network of PA, knowing that primary aldehyde groups form covalent bonds with N-termini (ε-amino groups) of protein.

AB: Challenges were in developing the tools for characterizing migration, traction and stresses. Most of the tools were custom built. I had to follow the theory behind them and then build them. It was a steep and fast learning curve but a lot of fun. I really enjoyed learning on the go.

When doing the research, did you have a particular result or 'eureka' moment that has stuck with you?

BS: Achieving the tunable collagen-I fiber architecture on PA gel by chemical modification of PA gel was definitely a eureka moment for us, which has stuck with me for a while. We believe that this aldehyde-functionalized PA gel (PAaf) is a big contribution to the field of mechanobiology.

AB: While analyzing the data, I observed that cells, when presented with both high stiffness and long collagen fibers, couldn't sustain streaming. Later on we proved, with velocimetry analysis and molecular biology, that collective streaming on fibrous substrates is stiffness sensitive. This was another eureka moment for us.

"We believe that this aldehyde-functionalized PA gel is a big contribution to the field of mechanobiology."

Why did you choose Journal of Cell Science for your paper?

Journal of Cell Science is a high impact, renowned and reputable journal in the field of cell biology. We chose this journal because we wanted to reach a broad audience of cell biologists.

Have you had any significant mentors who have helped you beyond supervision in the lab? How was their guidance special?

BS: My postdoc advisor, Amit Pathak, was very supportive in all aspects of research. We had very frequent meetings discussing problems and generating ideas to solve the problems. He always supported my research ideas. My PhD advisor, Aldo R. Boccaccini, always advised me how to expose my research works to the broad scientific community. He gave me the huge opportunity of attending conferences and doing manuscript reviews. He gave me freedom in research, especially in collaborative works with interdisciplinary research groups. My Masters' advisor, Ruhul A. Khan, is a great motivator who encouraged me to pursue my career in science. I am very grateful to all of my amazing colleagues for their great support and company, which helped me to overcome the stresses caused by living a long way from my home, family, friends, and relatives in Bangladesh.

AB: My PhD advisor, Amit Pathak, for giving me this opportunity to collaborate with my colleague, Bapi, for this project. I was given a lot of freedom to pursue my thought process, and our deliberations were very insightful. My Masters' advisor, Shamik Sen, for his guidance in research and key career decisions. Carsten Ehrhardt and Kaushik Chatterjee, for giving me early exposure to research during and after my undergrad. My family for selflessly caring for me and letting me follow my aspirations.

"While the last century was the century of physics, this century is going to be all about how well we understand our biology using these physical laws and leveraging this knowledge for our wellbeing."

What motivated you to pursue a career in science, and what have been the most interesting moments on the path that led you to where you are now?

BS: I am always enthusiastic when exploring new things. My Masters' advisor, Ruhul A. Khan, encouraged me to do research. I continued my research with him for a year after completing my research project. He encouraged me to apply for PhD scholarships.

Journal of Cell Science (2019) 132, jcs238634. doi:10.1242/jcs.238634

I got a prestigious doctoral scholarship from the German Academic Exchange Service (DAAD), which defined my career. I came to know the beauty of tissue engineering approaches, and I decided to try to make some contributions to this emerging field.

AB: The fact that an entire physical existence can be explained by rigorous mathematical laws really gets me. While the last century was the century of physics, this century is going to be all about how well we understand our biology using these physical laws and leveraging this knowledge for our wellbeing. Mechanobiology is a field that is heavily invested to this end, and I hope to make a significant contribution in it.

Tell us something interesting about yourself that wouldn't be on your CV

BS: I love traveling. Traveling all of the countries on earth is my dream. I am also enthusiastic about hiking.

AB: I'm a sports enthusiast, I love playing soccer, cricket and table tennis. I also love to sketch and play an Indian percussion instrument called a tabla.

Reference

Sarker, B., Bagchi, A., Walter, C., Almeida, J. and Pathak, A. (2019). Longer collagen fibers trigger multicellular streaming on soft substrates via enhanced forces and cell–cell cooperation. *J. Cell Sci.* **132**, 226753. doi:10.1242/jcs.226753