© 2020. Published by The Company of Biologists Ltd | Journal of Cell Science (2020) 133, jcs256644. doi:10.1242/jcs.256644

FIRST PERSON

First person – Mohammad Yunus Ansari

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. Mohammad Yunus Ansari is first author on 'Mitochondrial dysfunction triggers a catabolic response in chondrocytes via ROS-mediated activation of the JNK/AP1 pathway', published in JCS. Mohammad Yunus is a Research Assistant Professor in the lab of Tariq M Haqqi, at the Department of Anatomy and Neurobiology, Northeast Ohio Medical University, USA, investigating the mechanism of regulation of mitochondrial function in articular cartilage and its role in cartilage homeostasis in health and disease.

Mohammad Yunus Ansari

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

Mitochondria perform many key functions in the cell, notably oxidative phosphorylation, which generates the energy required for cellular functions. Energy production in mitochondria is a tightly regulated process, and any damage to mitochondria disrupts this process and results in excessive production of oxygen free radicals, which are harmful to the cell in many ways. In this study, we show that mitochondrial function is impaired in the osteoarthritis (OA) cartilage of human knee, which is associated with the excessive production of inflammatory mediators that play a critical role in the pathogenesis of OA. Using different approaches and pharmacological induction of mitochondrial damage, we show here that mitochondrial dysfunction promoted cartilage degradation through the increased production of oxygen free radicals, which induced the activation of a transcription factor that is involved in the regulation of cytokines and cartilage matrix degrading proteases.

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

To show mitochondrial function impairment and increased production of free radicals in human OA cartilage, the major challenge was to study depolarization of mitochondria and to determine the reactive oxygen species (ROS) levels in chondrocytes (the only cell type present in cartilage), while they are sitting in their native environment. To overcome this challenge, I prepared thin sections of human OA cartilage and stained them with JC-1 dye, before performing confocal microscopy to observe either red and green fluorescence from JC-1 dye, depending on the mitochondrial membrane potential. Similarly, we stained the human OA cartilage with ROS-sensing dyes and found increased production of ROS in OA cartilage. This strategy, although successful in the end, required a lot of effort and optimization. Using this approach, we showed that there is extensive mitochondrial damage and significantly impaired mitochondrial function in human OA cartilage.

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

Chondrocytes live in cartilage, which is an avascular tissue, and until recently it was believed that mitochondria do not have much of a role in chondrocyte biology. For me, the most striking result was the loss of mitochondrial membrane potential in the damaged areas (the area that showed cartilage matrix degradation) of human OA cartilage. This strengthened our hypothesis that mitochondrial dysfunction is associated with OA pathogenesis.

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

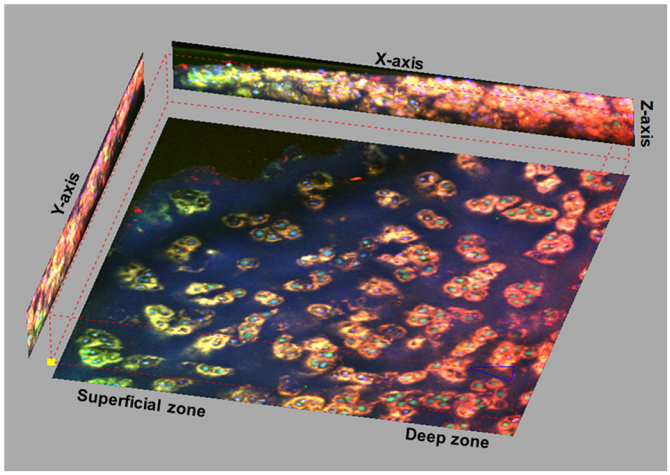
I wanted my paper to have a wide audience. My research field is osteoarthritis, but I wanted my work to be visible to the people outside the osteoarthritis field too. JCS is a long-standing and highly reputed peer-reviewed journal with a wide audience from almost every field in the biological sciences. Therefore, we chose to submit our research to JCS, and I am very happy that our research work made it through the peer review process and finally got accepted in JCS.

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

Yes!!! I have more than one mentor who taught me, helped me, guided me, and always motivated me. The spark of science in me changed to a full fire during my Master studies at the Department of Biotechnology, Aligarh Muslim University. I did my PhD with Dr M. S. Shaila, at the Indian Institute of Science, who taught me how to focus on my project. Dr Shahid Jameel, my first postdoctoral supervisor at the International Center for Genetic Engineering and Biotechnology, New Delhi, taught me that a person from a different field comes with a different perspective,

Mohammad Yunus Ansari's contact details: Department of Anatomy and Neurobiology, Northeast Ohio Medical University, 4209 State Route 44, Rootstown, OH 44272 USA.
E-mail: mansari1@neomed.edu

Journal of Cell Science (2020) 133, jcs256644. doi:10.1242/jcs.256644



Mitochondrial depolarization in human OA cartilage. I stained unfixed, fresh, thin sections of human OA cartilage full of live chondrocytes, the only cell type present in the cartilage, with JC-1 dye, which changes its fluorescence color (from red to green) when there is a loss of mitochondrial membrane potential. The image was captured by confocal microscope and I discovered that mitochondria in chondrocytes in the surface region that was exposed to synovial fluid, which is rich in cytokines and other inflammatory mediators, were heavily damaged compared to the mitochondria in chondrocytes present in the deep zone of the cartilage.

and two minds from different fields of expertise look at the same problem in different and unique ways. Joining Dr Haqqi's lab at the Northeast Ohio Medical University was a milestone in my career. He gave me the opportunity and freedom to explore different pathways and to study their association with the pathogenesis of OA. I wish all young and enthusiastic scientists had the chance to meet mentors like Dr Shaila, Dr Jameel and Dr Haqqi in their careers.

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?

Finding answers to questions that haven't even been asked yet and exploring the possibilities of what we can do with our scientific knowledge has always inspired me. For example, the thought that the human body has a trillion cells and all of them share the same genome, but still the body has different organs with unique functions. What makes every part of the body unique? What decides the shape of our body parts? What decides the size of our body parts? There are so many of these questions that we have not even asked yet.

Who are your role models in science? Why?

My role model is Muhammad (pbuh). He said, "There is no disease that God has created, except that He also has created its treatment". This always gives me hope, encourages me, motivates me, and tells me never to give up.

What's next for you?

I am looking for an independent faculty position in academia and to develop an internationally recognized research program. My long-term research interest is to explore the regulation of mitochondrial function in chondrocytes and its role in OA pathogenesis.

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

I love photography. Whenever I have time, I love to do macro photography and my favorite subject is snowflakes. So far, I have captured photographs of more than 20 shapes of snowflakes. I also have a yellow belt in kung fu.

Reference

Ansari, M. Y., Ahmad, N., Voleti, S., Wase, S. J., Novak, K. and Haqqi, T. M. (2020). Mitochondrial dysfunction triggers a catabolic response in chondrocytes via ROS-mediated activation of the JNK/AP1 pathway. *J. Cell Sci.* **133**, jcs247353. doi:10.1242/jcs.247353