

FIRST PERSON

First person – Georgios Efthymiou

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. Georgios Efthymiou is first author on 'Fibronectin Extra Domains tune cellular responses and confer topographically distinct features to fibril networks', published in JCS. Georgios conducted the research described in this article while a Labex Signalife PhD Student in Ellen Van Obberghen-Schilling's lab at Université Côte d'Azur, France. He is now a postdoctoral researcher in the lab of Sophie Vasseur at the Centre de Recherche en Cancérologie de Marseille, Marseille, France, investigating crosstalk between composition and mechanical properties of the ECM and cellular metabolism in cancer.

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

Much as humans construct and reshape the environment in which they live, cells sculpt their microenvironment by producing and assembling an extracellular matrix (ECM). The ECM is a meshwork-like structure made up of fibrillar molecules, among others, that differ in size, shape and the biological signals they deliver to cells of various tissues and organs in the body. One such molecule, which is indispensable for tissue integrity, is fibronectin (FN). FN can acquire different forms, also known as 'oncofetal' variants, during development and in disease. In our study, we asked whether and how FN variants can differentially affect cell behavior and fibrillar network assembly. Despite only having slight differences in their protein sequences, these variants influenced the physical properties of the ECM such as its thickness, rigidity and fiber geometry. They also altered the behavior of the cells by tuning their consumption of nutrients, their capacity to proliferate and the extent to which they transmitted signals from the environment to the cell interior. Understanding these behaviors helps us decipher the role of these variants in health and disease.

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

In this study, I have considered myself lucky to have been able to take advantage of the enormous amount of information and resources available after more than 50 years of research on FN. A series of critical obstacles, however, had to be overcome. The first major challenge was the lack of the appropriate system and tools to compare full-length FN molecules differing only by two remarkably similar short regions. The second was the need for an unbiased method to quantify the differences we empirically observed. We tackled these challenges by generating our own tools for analysis and by undertaking an interdisciplinary collaboration to quantitatively compare what we perceived as qualitatively different among the variants.

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

Several observations related to FN B+A- were of particular interest. If I had to highlight one, that would be the 'a-ha' moment when I



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noticed the acidification of the culture medium of cells stimulated with this variant. So, logically, I doubted the finding and I convinced myself that I had made a mistake! However, after repeating the experiment multiple times and by measuring the intracellular pH, we confirmed that this variant did induce an increased concentration of H⁺ in the cells. This original finding suggests a link between the composition of the extracellular environment and the regulation of intracellular pH, and can provide a stepping stone for further research.

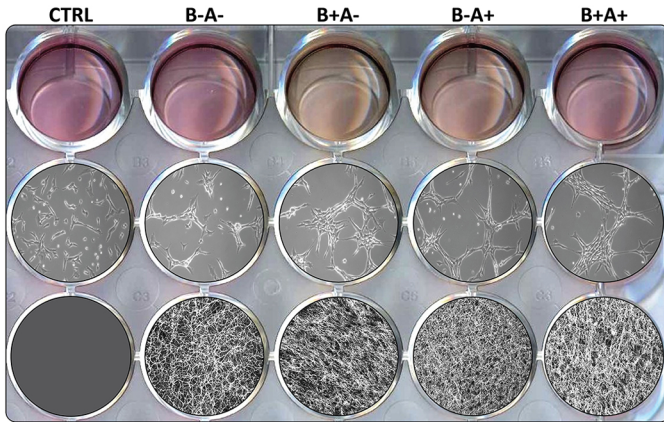
Why did you choose Journal of Cell Science for your paper?

We decided to submit our work to Journal of Cell Science because with a history of almost 170 years, it is among the most recognizable scientific journals, publishing a wide range of topics in cell biology. This way, we are reaching out to the broad readership of the journal to stress the importance of the extracellular matrix, as well as the necessity to combine different disciplines, such as biology, mathematics and machine learning in this study, to address complex questions and provide robust solutions.

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

Throughout the years, I have been mentored by people who left their imprint on me not only for being excellent scientists, but also for their remarkable character. Supervision in the lab is one thing, but

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Fn1^{-/-} mouse fibroblasts presented with soluble FN variants. These cells display different medium acidification (top), cell cohesion (middle) and matrix architecture (bottom).

help and guidance to overcome non-lab-related issues is what I have appreciated and acknowledged even more, especially during transitional periods, such as moving from one lab to another or from one country to a different one.

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?

Coming from a non-scientific family, finding answers to complex questions about life and natural phenomena was a real challenge that always stimulated me. One of the most interesting moments was when I was introduced to atomic theory as a school kid. It was a true revelation which made me want to know more about science. My choices led me to study biology at the University of Crete, Greece, where I had one of the most thrilling moments in my path: the acquisition of my first electron microscopy image of a slit diaphragm in the mouse kidney. It was an exciting result that paid off for all the efforts and the failures encountered until its achievement.

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

I write my own stand-up comedy scripts, but I am too afraid to perform in front of an audience.

Reference

Efthymiou, G., Radwanska, A., Grapa, A.-I., Beghelli-de la Forest Divonne, S., Grall, D., Schaub, S., Hattab, M., Pisano, S., Poet, M., Pisani, D. F. et al. (2021). Fibronectin Extra Domains tune cellular responses and confer topographically distinct features to fibril networks. *J. Cell Sci.* **134**, jcs252957. doi:10.1242/jcs.252957