

FIRST PERSON

First person – Osvaldo Contreras

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. Osvaldo Contreras is first author on 'Cross-talk between TGF- β and PDGFR α signaling pathways regulates the fate of stromal fibro-adipogenic progenitors', published in JCS. Osvaldo is a postdoctoral scientist in the laboratory of Enrique Brandan at Departamento de Biología Celular y Molecular and Center for Aging and Regeneration (CARE-ChileUC), Facultad de Ciencias Biológicas, Pontificia Universidad Católica de Chile, Santiago, Chile, investigating skeletal muscle tissue-resident mesenchymal progenitors in health and disease.

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

Our study focuses on understanding the behavior of scar-forming cells in skeletal muscles during regeneration and repair. These cells – often called fibroblasts and/or tissue-resident mesenchymal stromal cells (MSCs) or FAPs – are multipotent progenitors with essential roles in tissue repair and homeostasis in several tissues. We studied two main signaling pathways (TGF- β and PDGFR α) involved in skeletal muscle maintenance and regeneration. We found that both signaling cascades interplay in controlling the biology of the scar-producing cells during tissue damage, and determined that both PDGFR α and TGF- β crosstalk in stromal cells. Importantly, we used several *in vitro* approaches and different *in vivo* models of muscle injury, to address how both pathways regulate FAP differentiation into myofibroblasts that later drive tissue fibrosis and malfunction during pathology or disease. Our study is very interesting and provides new evidence on FAP biology, which, remarkably, is not well understood given the importance of scar formation in several tissues in pathology, disease and aging. From a broad perspective, as pointed out from one of our reviewers, our work is of general interest since the cellular and molecular mechanisms that regulate MSC differentiation into myofibroblasts are not yet well understood. Ultimately, by understanding the complexity of stromal biology and the role of PDGFR α and TGF- β upon damage and fibrotic conditions, we can develop novel therapeutics for the treatment of several scar-forming pathologies.

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

One of the major challenges our project faced was the fact that we were unable to work with pure stromal cells (or FAPs) in Brandan's lab. This was due to a lack of expertise and materials to isolate and work with these cells at the beginning of this project. To overcome this, I traveled during my PhD to Fabio Rossi's lab in the Biomedical Research Centre at the University of British Columbia, Vancouver, Canada. Fabio's lab is known to be one of the pioneering ones studying these cells in muscle biology during



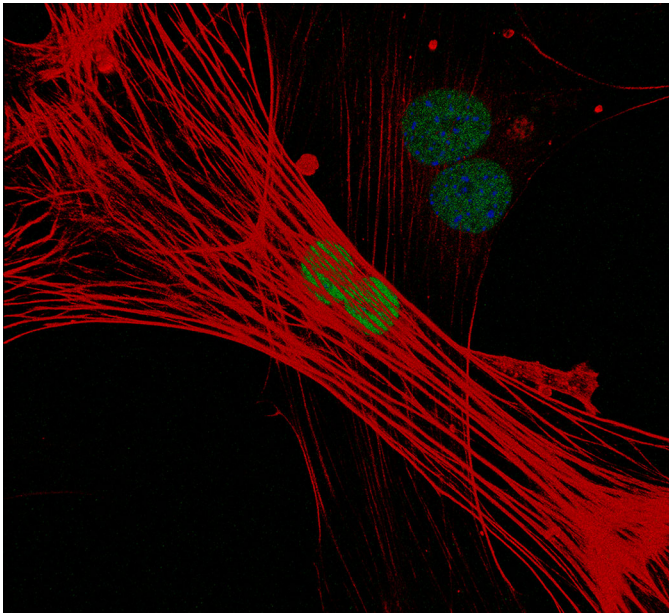
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health and disease. There, I was able to solve the puzzle and to polish our project. Hence, I think one of the better ways of facing challenges is true and strong collaborative work. One should ride on the shoulders of giants and recognize the importance of that.

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

I recall that this project had several eureka times. First, I remember when we found out that TGF- β signaling downregulates PDGFR α in skeletal muscle stromal cells. The second big eureka moment was the first time I isolated pure FAPs in Fabio Rossi's lab and reproduced the preliminary results of this project. This achievement makes me feel very proud of the ideas and results from my lab back in Chile. The third was when we observed that stromal PDGFR α expression was endogenously repressed after damage in skeletal muscle. I think the fascinating and unique experience of being a scientist is that, almost every month or so, we can have an eureka moment in the lab, which makes hard times easier to bear and helps us stay motivated.

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3D confocal image showing mesenchymal FAPs isolated from the $PDGFR\alpha^{H2BEGFP}$ knock-in mice using fluorescent-activated cell sorting. The fusion protein H2BEGFP (green) is visualized in the nuclei (blue) and α -smooth muscle actin (red) stress fibers are shown across the cells.

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

Journal of Cell Science was my first option to submit our paper to. This is because I like the clear editorial process, the journal policies and the quality of manuscripts the journal publishes. Besides, I like the drive and commitment to a better science of The Company of Biologists as, for example, they promote early-career scientists via ‘First Person’ interviews, help to build a better and open community (see, e.g. preLights), organize workshops and support young scientists through traveling fellowships, among others. I think one way one can contribute to this is publishing with them. Finally, I think our findings and results fit well with the journal’s aims and scope. It’s important to mention that seminal work by A. Uezumi and colleagues on the role of skeletal muscle mesenchymal progenitors and their participation in fibro-fatty deposition during Duchenne muscular dystrophy was also published in Journal of Cell Science (Uezumi et al. 2011).

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

I have had several influencers and scientific mentors during my lab life to whom I’m deeply thankful. Dr Noelia Escobedo guided my first steps in developmental biology at the bench during my undergraduate studies in Juan Larrain’s lab. Lately, Enrique Brandan, my PhD supervisor, trusted in my ideas and projects and, more recently, gave me the necessary freedom a PhD student needs in order to succeed in academia. Besides the members of the lab, I cannot forget the influence of my faculty professors Katia Gysling, Rafael Vicuña, María Estela Andrés and Alejandra Álvarez, among others; who helped me with my career development. I also would like to mention Marine Theret and Hesham Soliman, both co-authors of this study, for their experimental support and ideas. Finally, I think the best mentors a scientist has are the students, co-workers and lab

mates. From sharing, you learn many things, get motivated and new ideas are born. That is something you can’t have by yourself, inside your own box.

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?

My grandparents and parents have had a huge influence on my scientific path. I recall watching the TV programs Animal Planet and the National Geographic channel for hours with them. In addition, I remember discovering things in the field (one of my grandpas was a farmer) and found myself doing a couple of experiments with tomatoes, insects and birds. Counting them and looking at their differences fascinated me during my childhood. I was captivated by and fell in love with the scientific illustration and explanation of biological phenomena, such as reproduction and human physiology, in seminal biology books by Vilee and Solomon that my mum bought during my first scholar years. During my last school years, I was deeply moved by animal phenotypic variance and hominid evolution.

Who are your role models in science? Why?

My main and fundamental role models in modern science are Galileo Galilei, Charles Darwin and Alfred Russel Wallace. Their contributions to our understanding of the natural world are remarkable given the fact that, back then, the three of them faced political, religious, economic, scientific and personal challenges to openly disseminate their ideas and theories to the world. The famous naturalist Alexander von Humboldt and his travels along South America also influenced my desire to become a biologist. They were not only smart people in the right moment but also scientists with determination, passion and commitment. All necessary skills to address fundamental scientific questions.

What’s next for you?

I enjoy being a scientist and curiosity drives me. I wanted to pursue a career in academia and hope to have my own research group in the future. I’ll be moving from my country next year to work as a postdoctoral scientist with Dr Richard Harvey at the Victor Chang Cardiac Research Institute in Sydney, Australia, where I’m going to study heart development and repair. I’m super excited about having the opportunity to learn new things from a different field!

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

I love the mountains and oceans and, therefore, like to spend my weekends and free time rock climbing and surfing with friends. I also like talking with people, reading, eating, biking, whatnot. I also enjoy hanging out with my friends and family. Everything nature- and travel-related always motivates me, and – let me say – my family thinks that I’m a crazy human being because I never stop.

References

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