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

The accurate regulation of intracellular calcium is extremely important in pancreatitis. Indeed, the physiological release of proteases from the pancreas needed for digestion depends on increases in intracellular calcium, but excessive calcium concentration triggers pancreatic cell death by intracellular activation of those proteases. In this work, we genetically analyzed STIM1, an important protein in calcium regulation in the pancreas, in 2000 patients suffering from pancreatitis. We analyzed the calcium homeostasis of the different mutations observed in patients, and we focused on one that could be important for the development of the disease according to its location in the gene (E152K-STIM1). We applied different strategies to evaluate its importance, including computational, microscopy and biochemical techniques, both in cell lines and cells coming from patients. Our results indicate a newly described feature of this protein whereby it affects intracellular calcium stores, rather than extracellular calcium entry, by inducing changes in another key protein involved in calcium regulation called SERCA. Overall, the excessive increase in calcium within the cells bearing this specific mutation in STIM1 triggers cell death and could be the cause of the pancreatitis observed in patients.

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

I can mention two specific challenges. Firstly, this was a project in which researchers from ten different locations worked together. Everyone contributed to the manuscript by bringing their scientific expertise. Therefore, it was a challenge to manage all the timings and particularities of each researcher. I want to highlight that all the authors of the article were willing to help at any time. Secondly, in a specific period, the team decided to split the work into two manuscripts: One ‘genetic’ (see Masson et al., 2019 preprint, doi:10.1101/691899) and one ‘functional’ (this article). The changes needed regarding the focus of the work, and our will to strengthen the experiments to analyze the mechanism of action observed, delayed the publication of the manuscript for some time. I have to say, I am really happy to publish this manuscript in Journal of Cell Science as it is an excellent journal in which many papers concerning STIM1 homeostasis were previously published.

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

I didn’t have one particular ‘eureka’ moment. As I explained before, many different scientific experts in their respective fields contributed to the manuscript. So I felt several little ‘eurekas’: when results from cytosolic calcium microscopy were similar between fibroblasts from patients and cell lines; when Fabrice Antigny observed the same results from the point of view of the endoplasmic reticulum; when Wesley Brooks’s team observed a change of the E152K mutation that potentially lead to conformational changes in the protein; when Peter Stathopulos and Mitsuhiko Ikura obtained functional differences in the EF-SAM domain from wild-type and E152K STIM1; when the expression of...
the mutated STIM1 triggered higher endoplasmic reticulum refilling by increasing SERCA activity; when, in Juan Llopis’s lab, we discovered a conformational change in SERCA when STIM1 is mutated; and many examples like these ones.

Why did you choose Journal of Cell Science for your paper?
Journal of Cell Science has covered historic findings regarding calcium homeostasis. Among its publications we can find excellent works trying to elucidate the importance of STIM1 interaction with other proteins and organelles since the discovery of this protein in 2005.

Have you had any significant mentors who have helped you beyond supervision in the lab? How was their guidance special?
In this regard, I want to thank Olivier Mignen not only for his supervision in the lab but also for his scientific and personal mentorship. I felt that he always considered me as a partner and not a postdoc fellow, and we faced many challenges together for which we gave the best of ourselves.

Tell us something interesting about yourself that wouldn’t be on your CV
My strongest abilities are those related to team working. In my career, I had to deal with different scientific fields, different laboratories and different points of view of what science is. Hence, I have a wide and open-minded scientific view that helps me to see a problem to solve from different angles, having in mind the intrinsic characteristics of the laboratory. I am also an empathic person, which helps me be a teacher who tries to stimulate the scientific curiosity of the students in my lessons, focusing on what they need to know for their future.

Reference