Co-funded by the Erasmus+ Programme of the European Union

Meet a *Sci*-Star: Jenifer Croce

Jenifer Croce is a CNRS researcher at the Institut de la Mer in Villefranche-sur-Mer. She has been working there since 2009 and is a PI with the Laboratoire de Biologie du Développement de Villefranche-sur-Mer (LBDV). Jenifer has spent her whole career researching sea urchins, specifically looking at their development and at animal evolution. DigitalMarine interviewed her to ask about the sea urchin model, her career, and advice for young researchers.

What is your area of research and interest in biology, and what is your specialty?

I came into biology with a fascination for developmental biology - how a single cell (an egg) can give rise after a certain time to a multicellular organism, a 3-D-organized organism that is completely functional. I have also started more recently to become interested in animal evolution - how all of these different body plans we see in animals came to life and evolved through time. Developmental and evolutionary biology are the two main topics of my research and my speciality is evo-devo, so for me the two are combined, because to answer some evolutionary questions you have to dig into developmental biology processes. I have more experience in Devo, and I've been accumulating experience in Evo over the past five years or so. As an anecdote, I once presented myself to the CNRS in a developmental biology section and the reporter said "that was a very interesting presentation from a person whose work is so linked to evolution". I thought to myself "I've never thought of evolution before, how can this person think of evolution when I present my work?" There are a lot of people who think that when you work with sea urchins, you work with evolution only, but I see sea urchins as a useful model to address questions both in developmental biology and evolution, as well as in ecology, toxicology and cellular biology.

An adult sea urchin (photo credit: Jenifer Croce)

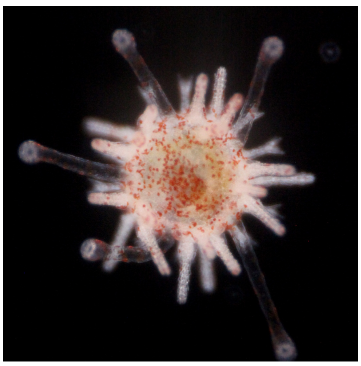
Why did you choose sea urchin as an experimental model, and what kind of advantages do you see in this model?

When I finished my undergrad I had the option to work in two different labs for my PhD that used either mice or sea urchins, and honestly I didn't want to work with mice, so I decided to go with sea urchins. I had the opportunity to work here in Villefranche already for my PhD. It is close to the sea and close to my hometown so I have to say that it was a hot choice, but it quickly also became a scientific choice. The fact is that sea urchins develop from a single cell to a larva, meaning an organism that is fully functional, *in only two days*. The larvae can feed, they have an immune system, muscles that function, and a nervous system. That means you can go through a lot of developmental biology questions in a really short period of time. That makes a big difference when you're digging into the properties of certain genes and proteins, as in only two days you can start having results. Also, sea urchins are, like us humans, deuterostome animals, meaning that they share several distinct cellular and molecular features with us. So, if we investigate specific processes in sea urchin development, it can likely provide clues about the same processes taking place in humans. These have been my main scientific reasons for staying with sea urchins. I did both my PhD and my postdoc working on these animals, and I am also now still working on sea urchins - my whole career has been looking at sea urchin development!

What new insights may you expect by characterizing molecular actors involved in the regionalization of the sea urchin embryo?

As previously pointed out, sea urchins are deuterostomes and as such they share with humans a lot of their cellular and molecular toolkits and properties. The main goal of my research is to characterize these toolkits and their interactions to provide key insights into the mechanisms underlying embryo regionalization and development. My idea is that these findings, obtained through fundamental research, may in the long term, like previous discoveries from sea urchins did already, provide the scientific community with material for human, cancer, and stem cell research, ways of identifying candidates to improve their approach, define better ways to produce organs from stem cells, or produce more appropriate medicine for tomorrow.

I've been looking at developmental biology questions using sea urchins for the past 20 years, and while the focus of my research has been on the regionalization of the embryo and the specification of the germ layers, I'm also interested now, in the context of evolutionary questions, in adult development, which comes much later in time. As I've said, in two days with sea urchin embryos the germ layers are formed, patterned and so on, but I'm now also interested in investigating the development of the adult nervous system, which comes into play around 5-6 weeks post-fertilization. As of today, the molecular knowledge of the adult nervous system of sea urchins is rather poor. Because of this lack of information, it's very difficult to reconcile the characters of the nervous system of the last common ancestor of the deuterostomes. By defining the characteristics of a sea urchin adult nervous system, we aim to contribute to this large and long-standing question and participate more globally to the question of the evolution of the nervous systems in bilaterians. That's why we've decided very recently to start a new research project that is less focused on the first two days of development but more on the weeks of development of sea urchins.



A sea urchin juvenile (photo credit: Laurent Formery)

What are the significant advances made by the sequencing of the different echinoderms?

The sequencing of the genomes of different echinoderms (including sea urchins and sea stars) has brought several advances. The first provided us with a tool to move a lot more quickly in our analyses. For instance, having access to the genome of a sea urchin species enabled us to rapidly identify whether our genes of interest were present in our animal models or not. It also enabled us to perform a lot of OMICs analyses like transcriptomic analyses and to thereby identify at which particular stage(s) of development our genes of interest were expressed. Likewise, they enabled the survey of regulatory components, the components that lead to the expression of a gene at a specific stage and in a specific tissue. The second would be towards the evolutionary questions where they allowed to look at the evolutionary history of proteins, through their presence, their sequence and in the long run their function. In my opinion those are the two main advances that have come from having access to genome information.

If you had to give one example, what would you select to show how the sea urchin model has enabled notable advances in the understanding of embryonic development?

It's really complicated to pick only one! Sea urchins have been used for more than a century now in biological research, and that's why picking just one is hard. There have been so many advances over this time, in fertilization for instance, in chromosomal inheritance, in nucleus fusion during fertilization, and more recently thanks to a worldwide effort in sea urchins – not just the species we work with in Villefranche but sea urchins as a whole, as a community – in the establishment of gene regulatory networks (GRN). Establishment of a GRN means that people have dug into the genome, picked up all the transcription factors, and started bulk functional analyses, since, thanks to modern techniques, functional analyses can be performed on sea urchins, which is a very powerful tool. They have since knocked down one gene and looked at how this loss of function impacted the expression of the other genes and the development of the embryo, and by these means they determined which genes interact with which other ones. A tremendous amount of work has been done and I think that is one of the most important recent advances the sea urchin has contributed to in biological research.

What are the current bottlenecks of the sea urchin as a model?

The main one as of today is the lifetime - I mean, it would be wonderful if we could have mutant lines of sea urchins in the lab. We have managed to complete the life cycle of the sea urchin we work with in the lab from fertilization to gravid animals and to reduce the amount of time between the two to a few months… but it still takes at least 9 months between fertilization and the next generation. That's better than what it was in the past, but it's still very long, so creating lines of mutants remains very tricky. Also, there are some species for which the CRISPR-Cas9 technique is available, and people have created F0 mutants with knockdown of certain genes; however, putting in some kind of GFP or fluorescent marker to trace some specific structures like it has been done in other organisms hasn't been done yet in sea urchins. This would be a tremendous advance and will open a new world of research once lines maintenance could then be achieved.

Do you remember a funny experiment or a fun event with echinoderms?

At some point I was a TA (teaching assistant) at Woods Hole, Mass. for the embryology course. It's the time where you are with a lot of students at different points in their career, and for me it was about showing them what one can do with sea urchins and let their imagination run free. So I told the students here we have sea urchin eggs and sperm, what kind of scientific question would you like to explore or kind of experimental approach would you like to try out? Two students came to me and said "well, we want to try electroporation. Since in tunicates we can electroporate DNA into the eggs and get a fluorescent output later in the embryos and the larvae, we would like to try to do the same in sea urchins". I told them "well, if you want you can give it a try, but different labs have been trying for years and it's never worked, so I don't think it's gonna work." The students told me "we don't mind, we want to try", but guess what… *it did work!* It's the only time that I've seen a sea urchin egg electroporated with DNA and that provided a fluorescent output! I've tried again at home, it didn't work, I know other people who have tried since then, it didn't work, so I don't know what happened that day! Even worth the DNA that was electroporated was not even a sea urchin DNA but a DNA from the ascidian tunicate *Ciona intestinalis*, nonetheless somehow it worked!

What do you think is the future of sea urchins as models?

I think it still holds a lot of scientific possibilities, but I think it's going to be used more as an evolutionary model instead of a developmental biology model. I'm not sure whether it's because we've done everything we could on sea urchin embryos or because the field of developmental biology is less attractive and exciting for students and for people in general. I hope the future will tell me I'm wrong, but I see it being perceived as more interesting for evolutionary questions, as much as other echinoderms actually. Starfish, sea cucumbers, crinoids, there are a lot of people starting to work on these animals as well to make comparisons with sea urchins and come up with evolutionary information regarding echinoderms in general.

A sea urchin larva with four arms (photo credit: Laurent Formery)

Could you say a few things about the sea urchin community?

Oh, it's a wonderful community! We have what we used to call the Sea Urchin Meeting every 18 months, which brings together all of the people from around the world using sea urchins as a model. Recently the meeting has been opened up to people working with other sea invertebrate animals like hemichordates and others. Yet since we're a relatively small community, the meeting only compiles about 120 to 180 people from year to year. Having evolved in this community for the past 20 years I feel like everybody is supportive, everybody is kind, and I would say that compare to other communities, although this is based on what people have told me since I haven't been in other communities, it's a friendly community. It's comfortable and good to be a part of it.

What are your personal experiences that you would qualify as the most important of your scientific career?

For me it has been the people I've worked with and the people I've met through my career. I've had the extraordinary chance to interact with wonderful people who have accepted to be my mentors, so my PhD mentor and my postdoc mentor. I started working with sea urchins during my PhD in Villefranche. There I was supervised by Christian Gache who opened my mind to

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fundamental research and developmental biology questions. During my stay in his laboratory, we had the opportunity to host an American scientist, David McClay, who also uses sea urchins to address biological questions. At the time, like most French students, I wasn't able to say a single sentence in English, my English was so bad, but my PhD advisor Christian Gache took me under his wing and said "don't worry, I'm gonna talk to Dave and tell him you want to do a postdoc with him and see how it goes". Thanks to Christian, I have no clue what he said, but Dave came back to me and said "Jeni, I'll go back home, I'll see what I can do and I'll send you an email". Two months later and even though I hadn't defended my PhD yet, I got an email saying there was a postdoc fellowship opportunity for me in his lab if I wanted it! The two together, Christian and Dave, they both have been the most important people in my scientific career, along though with some other people I have met during my PhD and HDR defenses and during my CNRS recruitment interviews.

Why do you do your job, and what advice would you like to give to students or young colleagues?

Oh, I do my job because I love it! My main advice to students and young colleagues is to be passionate. It's a long shot and it's gonna be difficult, but if you are passionate and you know that it's what you want, go for it. Also don't listen to people who tell you it's too difficult, if you're sure you want it then go for it! If you have doubts and are not sure, think again and then decide, because you will encounter a lot of difficulties.

Another thing I would say to students is to pay attention to what you're learning in the lab, but also pay attention to what your supervisor does, because if at some point you're gonna become a supervisor, then you're not gonna do what you used to do in the lab. I love my job, I love working with sea urchin larvae, but now that I'm a supervisor I have to do a lot of work on my computer and a lot of meetings, and to me it's less pleasant. At the same time, I love exchanging with people, with students, with other researchers, having those kinds of connections. When you become a supervisor you also have a lot of administrative responsibilities and it's a lot of work. Especially managing people, it's quite something else, and I really think it has to be taken into consideration when going into research and wanting to become a PI.

I know some people who did a PhD and really loved working at the bench, and they decided instead to go for a research engineer position which exists in France. In that job it's all benchwork and you don't have to worry about writing papers, writing grants, but you're mostly doing research that has been thought of and brought to you by someone else. When I have students, I tell them to think about this kind of things when considering what they want to do as a job later on, and if they want to stick to benchwork, they should look at postdocs that would train them in specific techniques that they would specialize in. This would also be a good idea if you want to go into the private sector instead of the public sector. If you really want to be a PI and teach at a university, please take this into consideration and start teaching during your PhD. It's not an easy task to think about where you want to go as a student, but it is really an important step.

Contact Jenifer @
jenifer.croce(at)
imev-mer.fr