(09.04.24) Farah Daou interview

The article **"Unraveling the transcriptome profile of pulsed electromagnetic field stimulation in bone regeneration using a bioreactor-based investigation platform"** has been recently published in the May 2024's issue of the prestigious scientific journal *Bone*. One of the authors, alongside with lecturers Lia Rimondini and Andrea Cochis - full professor and associate professor of Applied Medical Technical Sciences at Università del Piemonte Orientale -, is **Farah Daou**, student of Food Health and Longevity UPO's PhD. A peculiar part of Dr. Daou's work – the Biorender photography of the bone model at the centre of the project – earned the honour of the front cover of this leading publication in the pathophysiology of skeletal tissues.
We have met Dr. Daou at CAAD, the Center for Autoimmune and Allergic Diseases in Novara, and asked her to tell us about the background behind this great success.

SS: Dr. Farah Daou, thank you for receiving me. We are here for a very relevant occasion, since you deserved the cover of *Bone*, the important scientific magazine. So, the first question after saying thank you for being here, is: "Who is Farah Daou, and how and why she is here in Novara? What is her job?"

FD: My name is Farah Daou, I am from Lebanon. I did my studies in Lebanon, so I have a Bachelor's degree in Clinical Laboratory Sciences and a Master's degree in Bio-analytical Toxicology. During my master's studies, I discovered that research is probably the best way to learn, because it's not conventional at all. I quickly set myself a new goal: I want to do a PhD.
Life just surprises you all the time and I ended up here in Novara thanks to Professor Annalisa Chiocchetti and Professor Lia Rimondini; it's not so easy for a person coming from a developing country to be given a chance. They gave me a chance to come here and I arrived as a scholarship fellow, so not even as a PhD student. During the first few months, Professor Rimondini asked me if I wanted to apply for the PhD position open in her lab and this is how I am now pursuing my PhD in Bone Tissue Engineering.

SS: How did you feel to set your world and life upside down, changing country? How do a town like Novara and a country like Italy look to your eyes?
Have you ever been here before, or was it your first time? Please, tell me about the impact.

FD: Since I arrived in Novara - you know, I unfortunately come from a country of conflict -, the first thing I noticed is that people here live in peace. I just appreciated this peace a lot and that's why I was like… *I really want to live here, I find myself here*. When I was in Lebanon, I felt that the environment was a little bit stressful for me, maybe I am not strong enough to handle all what was happening around me. So, coming here really helped me on my personal level and on the professional level too: I did research when I was in Lebanon during my master's studies, but it had nothing to do with the research here. Also, I am really thankful to Professor Rimondini because we are in a lab in which she pushes us to go to conferences, to go to summer schools, to participate to a lot of activities… just to give an example, last summer I went to a summer school related to wine production, organized by Università Cattolica del Sacro Cuore. I applied, I got accepted and Professor Rimondini didn't say no. So, on the professional level too, this atmosphere helped me a lot.
I'm saying this after three years in Italy. In the beginning, things were not very easy for me: I arrived in a new country, I had to learn a new language and change the field of studies. I arrived in Italy knowing the basics of the Italian language, because I studied a little bit of Italian by myself.

SS: I think it's a kind of trauma, because, you know, a different language… and also English is not so popular here, out of the scientific community.

FD: What helped me to improve my Italian was volunteering with the Community of Sant'Egidio. I arrived in May 2021, and in June I started learning Italian with the volunteers of the Community of Sant'Egidio and, at the end of June, I started volunteering by serving food to poor people. Being around people who do not know English means that the communication can only be in Italian. This not only improved my Italian, it also helped me to integrate in the society and maybe, yes, the fact that people outside the scientific community don't know a lot of English is also the reason why my Italian improved.

SS: Please, tell me about your path till this point, this very important point, and so what did you do and how did you start the work that brought you to the cover of *Bone*?

FD: This is also something that probably scientists know about, but I hope people who are not scientists will read this interview. We published this paper now in 2024, but this work really started almost two years back. When I arrived, I wrote a research proposal, definitely like all PhD students; we then received a new project, and this was related to creating an ***in vitro* investigation platform that mimics bone tissue**. Having better tools to perform experiments in the lab can help us to reduce the number of animals used in research. Usually, we do tests in lab (*in vitro*), then (*in vivo*) with animals and then we move to humans. So, this movement from *in vitro* to *in vivo* is not very efficient (because *in vitro* experiments do not replicate the complexity of organisms), which makes the movement from *in vivo* to clinical studies also not very efficient. This project aimed to use **3D models instead of 2D models**, which means that we are working in an architecture similar to the body and with, let's say, mechanical stimuli, because we are not in a static state, we are always in movement: everything in our body, from blood to interstitial fluid, is in constant movement.
So, we tried to create this system and these two years, before being able to run experiments, have been a journey of optimization. How can we put stem cells in the scaffolds? How can we feed these stem cells (what type of nutrients we want to supply the cells with)? Is it better to feed them with a differentiation medium (that pushes stem cells to transform to bone cells) or with a regular medium? After doing all of these, let's say, trial and error things, we moved to the final experiment that allowed us to dig deeper by doing transcriptomic studies, etc. and we published the paper.

SS: Another purpose of this interview, my job, is to communicate this great work and the deep sense of itto people who don't deal with science every day. Basically, if I understood well, you are finding a way to – we can say – not experiment on animals, but to **create an artificial bone that works like a proper bone**, and that's a turning point. So, how did you feel when you realized that it was actually working? If you want to talk to me about some technical phases in which you actually said: “Okay, this artificial thing that I did is working and it can be put into a person”.
I'm obviously simplifying…

FD: I'll explain to you the other side of the project, but before I'll give you an example. It's going to be a long answer, but just to make things clearer for everyone. So, the thing is that now the main studies are done on cells in 2D culture, let's say, and they test, for example, cancer, okay? They test drug 1 versus drug 2, and they check in this 2D environment where drug works better, okay? Then, based on these experiments, they move to animals, things don't work out, or maybe they work out, but animals are very different from humans, so that's why it's a long journey.

SS: When you say animals, for example, in your specific work, which kind of animals?
FD: This is also another big topic. I've never done animal studies, but my knowledge is based on what I read in articles. When it comes to bone and cartilage regeneration, we cannot work with small animals like mice or rats.
That's why usually bigger animals are needed: goats, sheep, etc. Here, we still don't have the facility to do animal studies on big animals, so mainly studies are done on smaller ones like mice. So, in our

study, we aimed to produce this *in vitro* platform that mimics bone tissue in order to study a treatment for bone regeneration, and this treatment is very interesting for clinicians, because it is not an invasive treatment, so people will not be taking a pill, they will not be exposed to injections, it's just simply an apparatus that you put outside of your body and that produces electromagnetic fields.
Clinicians discovered that… you know what? If we put these electromagnetic fields where bone is damaged, this helps bone to heal. But they still don't know how, like, what's happening, what signaling pathways, what molecules are being produced by cells, so this is not known yet. The second missing factor about the use of this apparatus is that there are no clinical guidelines, which means that as an orthopaedist or physiotherapist, you can decide the treatment based on your experience, so it's not like… okay, if I am a female at this age (before or after menopause), having this condition, and I have a fracture, how much should I be exposed to these electromagnetic fields? Two hours a day for two weeks? Four hours a day for one week? There are no clinical guidelines.
You need more experiments to know the signaling pathways and to have clinical guidelines.
So, if you notice that our work is a bit complex, that's why. Although maybe for some people it's just a cover image, **this cover image on *Bone* journal** is really the integration of a lot of experiences, the coming together of a lot of collaborators, because here at UPO, in our group, we work with biological evaluations, we are not engineers.
So, engineers in **Politecnico di Torino** are those who designed the bioreactor that provides mechanical stimuli similar to those of the bone tissue. We have also the **Hypatia Research Consortium in Rome**, that was able to 3D print a 3D model that looks exactly like the trabecular bone in our body by having a random architecture.
And we also have the collaboration of **IGEA,** an Italian company that produces this apparatus for clinicians. It produced an apparatus that is compatible with our system, so we could use it and test it in the lab. So maybe, as I told you, for some people it's just an image, but for us it is really much more.

SS: If we talk about material, what this artificial bone is made of?

FD: Okay, so there are a lot of materials that are currently being used, like titanium, we all know about titanium, that is used to restore bone, and there are other innovative materials. Until now, these innovative materials haven't reached the clinics. We have been trying to use a material that is FDA approved for medical devices. That's why our scaffolds are made up of **polylactic acid (PLA)**. It is a polymer. The advantage of this polymer is that it is as strong as bone.
And the second advantage of polylactic acid is that it degrades, so it is removed out of the body as fast as new bone is being produced by our body. This is the aim: when you want to put something that helps bone to regenerate, you want this something to go away, being replaced by a real bone.
A polymer, speaking in popular language, is a very big thing that is made up of small things that repeat each other, and it's how it looks like. Something that can be printed in 3D, very light, resistant, not so heavy to wear. Exactly, and you know what, I can send you a photo of the scaffold, so that maybe you can show to the readers.

SS: When were you informed that *Bone* dedicated the cover to your work? Tell me how it happened, please.

FD: So, I finished the first part of my lab work in the morning, and Professor **Andrea Cochis**, who is also another responsible of us as a group, he was like: **"Did you check *Bone* journal?"**
I was like: "What do you mean?" and I opened it: "Oh my god! This is the figure that I created on BioRender!", and he knew from another professor that by chance was checking *Bone* journal, and saw our figure actually posted on the front page.
I told you, it was such a great achievement for all of us, because it gives satisfaction not only to us, but all our collaborators.

Our collaborators were happier than us. This is the good part of the process; on another hand, also money counts, because you also need a lot of funds to do significant research. We and our partners invested in this project, but this kind of return… I think it's very important. So, it was a surprise, basically. Research is also becoming very competitive; science joined all other fields, we know that we're doing a good job, but we know that there are bigger institutions who are doing much better, because they have more facilities, more resources.
That our work stands out is something that is really appreciated, especially in UPO, because UPO is a young university, and it is great for us to be able to show our work, and to really show the progression we are doing in a short period of time. I think this also because the university supports us a lot. Here in **CAAD**, where we are now, we have a two-photon microscope, which is one of the most important microscopes, it's a cutting-edge technology. We can do all omics studies, (transcriptomics, proteomics, metabolomics, etc.) so university is trying as much as possible to support us, just with the little that it has got, it's just.
I also want to thank Professor **Lia Rimondini**, as well as other Professors like **Annalisa Chiocchetti** and Professor **Andrea Cochis**, who are very active when it comes to applying to European projects, and bringing funding into the university. Now, we as a group, the Innovation Laboratory, we don't have an issue when we want to buy reagents, but this was not the case when Professor Rimondini started her laboratory, and the same for Professor Chiocchetti.
Now, our laboratory has four European projects. Two of them are "Marie Curie", so this should be respected, but it is the effort of Professor Rimondini and Cochis who want to push the laboratory in innovation, but also the university, because, let's say, when we have funding, we are able to purchase new instruments. Recently, we were able to get the scanning electron microscope (SEM), which really helps us in our work.
We also have a nano indenter, so, all of these instrumentations make our university rich, because they are not for us, they are for everyone. Just like we use the facilities of other groups, but they are the groups that were able to purchase them, and this environment, the fact that here in University there is no competition, but collaboration between labs and professors, this really helps.
One example is that recently I had an issue with designing an experiment.
Everyone is willing to help you, so this is such an amazing environment for science in general. We not do things alone.

SS: What's the relation between science and communication in your work?

FD: About writing, I want to tell you something; for me writing is very important. For me it's like a therapy, you know, like letting things out, and if you would like to add also this to the article, I'm totally fine, because I really encourage students who feel that they can write, to use a platform that is free for everyone, it is called Medium. I used to have a blog on Medium, maybe three years ago, and now I decided to start it again, and the idea that I started with, because I decided to publish one blog per month, the idea of this blog is that I'm going to use an image I took in the lab, so using the scanning electron microscope, fluorescent microscope of my cells, with the scaffolds, with whatever, and this image is going to inspire me to write something.
This is not only for me to write, but also for people to see the beauty of science, for them to see the amazing images that we take, because for us we've been doing this for… let's say a few years now, so it's not impressive to see a cell attached to a scaffold, but for others it's astonishing. So the first blog post that I published, was an image of the scaffold, a part of my polylactic acid scaffold, one part that is embedded with a lot of cells, one on top of the other, and this image inspired me to write about the PhD journey, because people think that… you know, like you're here, you come, you just click a few buttons, do a few things, and… boom! you found a treatment, you discover something. No, it's not like that.
It's a very long journey, and I honestly believe only people who are strong enough to continue can actually do it. There are a lot of challenges, and there are a lot of things that you have to manage,

because you start working on a project that can be new to you, just like in my case, but there is all the work in the background, from ordering reagents – we are not a big university where we have a lab manager ordering for us – so you have to learn how to use the ordering system of UPO. You have to think about attending conferences, improving your skills, then you have to follow master's students, teach them what you learned, help them correct their thesis, so that's why at the end of the journey, you are literally like this scaffold, because then you have all of these things to manage, plus writing your thesis, so it is, let's say, a tiring or a challenging journey, but a beautiful one, just like the photo that I published in the blog post.

SS: We can say that, with your work and efforts and commitment, you are building the perfect bone and the strong bone that can hold the effort of the journey, basically, it can permit you to walk till the very end of the path. To the finish line.

FD: Yes, I like this description, that's absolutely right. Yeah, and that's how I would like to narrate this experience, because I think it's the proper metaphor for the journey, for the work, and also my personal experience.

Link to the article, readable on ScienceDirect:
https://www.sciencedirect.com/science/article/pii/S8756328224000541?via%3Dihub

Farah's article on Medium blog
https://medium.com/@farahdaou/a-story-through-a-picture-capturing-the-phd-journey-e28feb91a218