

Eran Meshorer: getting a chromatin perspective

Eran Meshorer is exactly where he wants to be: in the midst of molecular neuroscience, chromatin, and stem cell biology.

Many children want to be astronauts or pilots when they grow up. Not Eran Meshorer. He wanted to be a musician. But at University, Eran discovered a greater passion, biology, and ever since he's been following a carefully composed career.

Meshorer's graduate studies with Hermona Soreq at the Hebrew University in Israel gave him a good grounding in molecular neuroscience (1, 2). Then, seeking to explore new horizons, he joined Tom Misteli's laboratory at the U.S. National Institutes of Health, where he studied the chromatin changes that accompany embryonic stem cell differentiation. His work showed that transcription is global across the genome in pluripotent

embryonic stem cells, but becomes more restricted to lineage-specific genes as the cells commit to more specialized fates (3, 4).

Having now returned to the Hebrew University to set up his own laboratory, Meshorer is studying chromatin rearrangements in stem cells. He eventually hopes to embark upon a synthesis of his two fields of expertise, looking at chromatin changes that underlie learning and memory (5). Eran kindly unraveled himself from his chromatin studies and took the time to discuss with us the career path he's taken so far, and his future plans.

FATHER FIGURE

As a child, what did you want to be when you grew up?

I have to say that when I was a child, I didn't think for a minute that I would become a scientist. I literally grew up across the street from the Weizmann Institute in Israel, and I was exposed to science at home because my father worked there; he headed the animal department and was

very involved in research. But even though science was always in the background, I don't think it was my dream. I wanted to be an artist or a musician.

My father plays the violin, and classical music was always there at home. I wouldn't say I became my father, but it's obvious to me that my love for both science and music comes directly from him. Those are probably my two great passions in life.

Do you have formal training in music?

Yes, but I gave up on the dream of being a professional musician when I joined the army. In Israel, everyone has to spend three years in the army at age 18. There's a special program in the army for talented musicians that allows you to join the army as a musician—they basically give you a day job with a lot of free time so you can continue working on music. I was offered this option, but I decided not to do it because I guess I wanted to "be like everyone else." Before I joined the army, I could spend eight hours a day playing, but afterwards, when I tried to go back to it, I found it wasn't for me anymore.

I do pick up the guitar every now and then at night after the kids go to bed, and I play. The good thing about the classical guitar is that it's a very soft instrument. You can play at midnight and the neighbors won't care. That helps me squeeze it in with my other hobbies: biking, basketball, and cooking.

A CLEAR PLAN

At what point did you discover your interest in biology and research?

After my time in the army, I traveled in South America and the United States for about six months, then came back to start at the Hebrew University. I took biology because I felt it was the most interesting subject to study. Fortunately, music and science are in the same campus, so that first year I played the classical guitar at the music academy, and I took biology classes across the street. But after a while



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I had to choose between the two. By this time I knew I wasn't going to become a professional musician, so I chose to continue with biology.

Even at that point, I didn't think a career in research was my destiny. That only became clear to me later, when as an undergrad I joined the laboratory of Hermona Soreq—who later became my PhD advisor. That's where my passion started.

What intrigued you most about the subjects you studied in Dr. Soreq's laboratory?

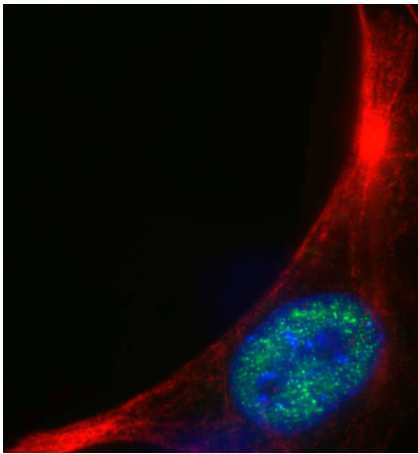
I can't even say. As an undergraduate and then later on during my PhD, I studied animal models of traumatic stress and psychological stress in the nervous system. I was studying alternative splicing in the brain, which is how I fell in love with neurons. In fact, I'm still very much interested in molecular neuroscience, even though I decided to completely switch fields as a post-doc.

Did you have a specific goal of exposing yourself to new material when you switched fields as a post-doc?

Yes, definitely. I always had in mind that I might go back to neuroscience, but when I was finishing my PhD, it was clear to me that at this stage in my career, I wanted to do something else.

I was very much attracted to the chromatin field, epigenetic regulation, and stem cells. So I decided to switch gears and try

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How do neurons make memories? RNA PolII staining (green) shows sites of active transcription in an ES cell-derived neural progenitor (identified by red nestin stain).

and combine chromatin and stem cells in my post-doctoral studies. I really chose stem cells as a system to study chromatin rather than as a system to study stem cells, because I was looking for a system where I could find very conspicuous differences in chromatin between differentiated and undifferentiated cells. I figured that, in terms of chromatin structure, there should be pronounced changes between pluripotent stem cells and differentiated cells. Ultimately, I chose to differentiate the embryonic stem cells into neurons because neurons were familiar turf for me.

That was the idea I had when I went to Tom Misteli's laboratory for my post-doctoral work. When I got there, no one was working on embryonic stem cells—or any type of stem cells, for that matter—so I was really starting from scratch. But I knew that if I wanted to study chromatin I needed to do it on the proper system, and Tom's laboratory would be a great place to do that. Of course, there is the appeal of stem cells, and I'm very glad I did it because I became a stem cell researcher, which is an added benefit.

THE PERFECT PLACE

Are you interested in stem cells as a useful system for studying chromatin structure, or for the study of stem-ness? Initially, I think I was interested in stem cells because they are a good system to

study chromatin. But once you begin studying stem cells, you inevitably become interested in the big picture: what's their secret? What's so special about them? I'm looking at this from a chromatin perspective, but I'm very interested now in stemness questions. Some of my laboratory's projects are aimed at looking at stochastic events of stem cell populations and what makes stem cells differentiate or de-differentiate. But overall, I think the laboratory is more inclined to focus on chromatin than on embryonic stem cells. We have more projects looking at chromatin in other cell types than we have doing nonchromatin work on embryonic stem cells.

I feel that with my two different backgrounds of molecular neuroscience and chromatin in stem cells, I've really been preparing myself to study epigenetic phenomena in the central nervous system. I want to look at learning and memory from a chromatin perspective. This is something that I've been thinking about at a low simmer for quite a while, but it's becoming increasingly clear that it's something I'm very interested in studying. It may take us some time to get around to doing the actual experiments, but I've started writing about it, to show that I am thinking about it.

What's the biggest challenge you've faced in your career so far?

I think the biggest challenge was really moving to the States for my post-doctoral work and having to adapt to the new environment. I had two children at the time, and one was less than a year old. That first year was pretty hard for my family, but after that we sort of landed on our feet—the next three years were calmer and quieter. We finally moved back here to Israel so I could start my laboratory, and of course that was also stressful, but I sort of just closed my eyes and did it. Looking back, I think my first year in the States was much tougher than

these first few months back here. I think it was particularly easy because I came back to the same institute where I grew up as a student, so I knew everyone, and it was like coming back home.

Where do you see yourself ten years from now?

My wife did a coaching course recently and she asked me the same question a few weeks ago, so that's actually been on my mind recently. I think I'm exactly where I want to be now, and I think I'm exactly where I want to be ten years from now, only I'll be ten years older and more well known [laughs]! There's basically no other place that I would dream to be. I would just hope to get better at what I do, to have people complete good doctorates in my laboratory, and find out new things about chromatin and stem cells along the way. **JCB**

"Science and music are my two passions in life."

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Meshorer juggles hobbies and artistic pursuits with the demands of a career in research.