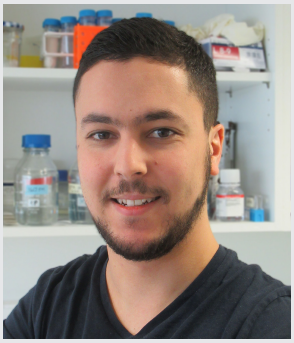
MEET THE FIRST AUTHOR



Lies Chikhaoui

***Meet the First Author(s)* is a new editorial feature within *RNA*, in which the first author(s) of research-based papers in each issue have the opportunity to introduce themselves and their work to readers of *RNA* and the RNA research community. Lies Chikhaoui is one of the three co-first authors of this paper, "Oppositional poly(A) tail length regulation by FMRP and CPEB1," along with Jihae Shin and Ki Young Paek. Lies is a PhD student in Kiran Padmanabhan's lab at the Institute for Functional Genomics of Lyon (ENS Lyon). He studies pathways that regulate dynamic mRNA processing using 4th generation direct RNA sequencing.**

What are the major results described in your paper and how do they impact this branch of the field?

FMRP (fragile X mental retardation protein) is an RNA binding protein essential for normal cognitive development. My colleagues at UMass Med School found it interacts with the cytoplasmic poly(A) polymerase GLD4. Loss of FMRP in HEK293 cells in their experiments led to overall poly(A) lengthening. Using direct RNA nanopore sequencing to quantify tail length, my analysis showed that in the cortex of FMRP knockout mice, mRNAs had both longer and shorter tails, suggesting that FMRP has an additional previously unappreciated role in poly(A) tail dynamics.

What led you to study RNA or this aspect of RNA science?

While working on circadian transcriptomes in collaboration with the lab of Dr. Yutaka Suzuki, I realized that direct RNA sequencing could fairly accurately determine poly(A) tail length in intact mRNAs without any processing. Therefore, we approached the Richter lab to use the FMRP study as a test bed.

During the course of these experiments, were there any surprising results or particular difficulties that altered your thinking and subsequent focus?

FMRP knockdown experiments in HEK cells revealed that the protein primarily played a role in poly(A) tail lengthening (using TAIL-seq, an alternative method for tail length determination). Surprisingly, in the mouse cortex, FMRP deletion revealed a regulatory role in tail length determination, with some mRNAs gaining stretches of A's while others ended up with shorter poly(A) tails.

What are some of the landmark moments that provoked your interest in science or your development as a scientist?

One of the key events that has had a major impact in my young career was an accidental loss of samples. At the beginning of my PhD, I visited the lab of Dr. Yutaka Suzuki in Japan with the aim to perform ChIP-seq and to learn bioinformatic analyses methods. The samples were damaged during shipping and this stopped my plans dead in their tracks. Instead, a secondary project involving direct RNA nanopore sequencing took off (because the samples survived!), and I have spent the last two years applying this powerful technique to biological problems, including the one on FMRP.

What are your subsequent near- or long-term career plans?

While I was still at university I decided to get some research experience—a year before most of my classmates. At that time, I was absolutely sure that I wanted to do academic research, and I thought it was time to see what the big bad wolf looked like before I started my career, so I went to get some experience in industry. I realized that in fact R&D is just a continuation of what we do in academia, with an incredible amount of knowledge generated by researchers, turned into applications by companies. This experience changed my view of science, and my career plans with it.

From these experiences, I feel I want to follow the path of science down to application, namely to grow and take full advantage of the freedom that a PhD offers, to develop my critical thinking skills in the free and stimulating environment of academia, and then try to have a more direct and concrete impact on people's lives by putting these skills to use in R&D.

I feel that I have taken full advantage of the scientific freedom that an academic environment offers to grow and mature as a scientist. I am now turning to the second stage of my career plan: apply these skills to the benefit of the community. In this regard, I think nanopore tech will serve this purpose greatly as I would like to find game-changing applications.

What were the strongest aspects of your collaboration as co-first authors?

Each one of us brought a different set of skills to interrogate the same scientific problem, and the net result is that we have identified a previously unknown regulatory role for FMRP. This publication for me is the best illustration of how collaboration takes science up to the next level. Each of us had an area of expertise that allowed us to work efficiently on the problem, and we were helped along by experience of the conductors, Dr. Padmanabhan and Dr. Richter.