Elisa Izaurralde (1959–2018)

Elisa Izaurralde, Director of the Department of Biochemistry at the Max Planck Institute for Developmental Biology in Tübingen, passed away on April 30 at the age of 58 as a consequence of a rapidly advancing cancer. She was a very passionate and indefatigable scientist who contributed greatly to our understanding of basic mechanisms of gene expression and to RNA biology. Her death marks an irreplaceable loss to the international RNA community.

Elisa was born and grew up in Montevideo, Uruguay. She would later recall how she knew very early on that science, and biology in particular, was what she wanted to study and to work on. However, choices were limited as the military dictatorship swept Uruguay in the early seventies, especially for a young woman who married a political activist on graduating from high school. So, as part of an entourage of South American political refugees, the 17-year-old Elisa left the country and began a new life in Geneva. She learned French, studied biochemistry and molecular biology at the University of Geneva, and then joined the laboratory of Ueli Laemmli as a PhD student. Elisa had found her calling.

After studying the organization and structure of chromatin in the Laemmli group, Elisa moved to the EMBL and the laboratory of Iain Mattaj, where her interest in RNA took off. During her postdoc (1990–1996), she identified the nuclear cap-binding complex (CBC) and described the fundamental role of CBC in pre-mRNA splicing and nucleo-cytoplasmic export of U snRNAs. At this time she formed lasting friendships with other postdocs and students in the group, in particular Isabel Palacios, Artur Jarmolowski, and Puri Fortes. They still recall Elisa in those long days of Xenopus oocyte injections as a seemingly immobile body with her eyes glued to the binocular, constantly running protein and RNA gels.

This was only the beginning of Elisa's fascination for RNA. In 1996, she moved to the Department of Molecular Biology at the University of Geneva to start her own group. As a PI, Elisa made the pivotal decision to stop working on CBC and instead to explore an aspect of RNA biology about which very little was known at the time, i.e., the nuclear export of mRNAs. In Geneva, Elisa's group first identified TAP as the cellular factor that is recruited by the constitutive transport element (CTE) of simian type D retroviruses and went on to show that this is indeed the major mRNA export factor in mammalian cells. It was also in Geneva that Elisa started a fruitful collaboration with Matthias Wilm, a mass spectrometrist at EMBL who was to become one of her most trusted friends. When Elisa was recruited back to EMBL in 1999, first as a group leader and later as the acting head of the Gene Expression Unit, the time was ripe to characterize the mRNA export factors that she had already identified, in terms of their cell biology but also at the structural level.

It was the perfect place at the perfect time, as Elisa entered into very strong collaboration with Elena Conti and Michael Sattler in the Computational and Structural Biology Program. During this period, Elisa also started to work on nonsense-mediated mRNA decay, elucidating many of the molecules and mechanisms that underpin this surveillance and regulatory pathway in mammalian cells. A major breakthrough was a collaborative effort with Hervé Le Hir, Lynne Maquat, and Melissa Moore that led to the seminal discovery of the exon junction complex (EJC). With her characteristic efficiency, it took Elisa less than two weeks, together with Hervé, to carry out the oocyte injection experiments that led to the discovery of the 24-nucleotide protection accompanying spliced mRNAs in the cytoplasm. Overall, Elisa's work at the EMBL was driven by her fascination with the mechanisms of transport and metabolism of mRNAs, which in turn prompted a further interest, that of their structural biology.

In 2005, Elisa joined the Max Planck Institute for Developmental Biology as Director of its Department of Biochemistry. Here, she could set up the infrastructure and logistics to tackle projects with a wide range of approaches from biochemistry and cell biology to X-ray crystallography and NMR. Her move to Tübingen also marked a shift in research direction, namely to the study of the small regulatory microRNAs (miRNAs) that had just been discovered and shown to silence mRNAs. This switch to miRNAs testified once more to her competitiveness and readiness to accept a new challenge: in this case the mechanistic aspects of miRNA repression. In the early years of the new millennium this was a largely uncharted area and controversies existed as to whether they target the translation process or rather induce mRNA deadenylation and decay. Elisa's group, working on both aspects of the repression, quickly became one of the drivers of miRNA research, filling many of the existing gaps and identifying new players in the miRNA game. Her research

was particularly important for defining the role of the GW182 protein in the repression. GW182, acting downstream from the Argonaute-miRNA complex (miRISC), recruits two complexes with deadenylase activity, PAN2/PAN3 and CCR4/NOT, the latter also being involved in translational repression. Elisa documented the interactions not only biochemically but also by solving the high resolution X-ray structures. Her team established the structures of several CCR4–NOT subcomplexes and also structurally documented how proteins other than GW182 (such as Nanos) recruit CCR4–NOT to mRNAs and regulate their activity.

Equally important was Elisa's work on a group of proteins, referred to as decapping activators, which orchestrate recruitment of decapping enzymes and facilitate remodeling of initiation complexes at the 5′-terminal cap. Elisa's biochemical and structural work provided new insights into the function of these proteins, demonstrating also that some of them interact with the CCR4–NOT complex and are important for miRNA-mediated repression. Based on her work on CCR4–NOT and decapping activators, it became clear that miRNA-mediated regulation, particularly the steps downstream from GW182, shares many features with other cellular pathways controlling the fate of mRNAs. One aspect of the decapping activator proteins that fascinated Elisa was their domain organization, particularly the presence of long disordered regions that mediate interactions between individual activators and support phase transitions and granule formation. Elisa's structural work has unraveled how the short liner motifs (SLiMs) present in disordered regions contribute to many protein–protein interactions essential for the regulation of translation and mRNA catabolism. With her typical energy, in her last years, Elisa was in the process of setting up the infrastructure and expertise to use cryo-electron microscopy and to expand further the impressive methodological portfolio of her group.

Elisa received many awards and honors in recognition of her work, including the Friedrich Miescher Award of the Swiss Society for Biochemistry, the Leibnitz Prize of the German Research Foundation, and the Ernst Jung Prize for Medicine. She was a member of the European Molecular Biology Organization (EMBO) and of the Leopoldina German Academy of Sciences. Elisa was also a very active member of the scientific community at large, serving on many international scientific advisory boards and panels, including the ERC Advanced Review Panel and the Board of Directors of the RNA Society. She also served on the editorial boards of many journals. In 2005 Elisa joined the editorial board of *RNA* and, since 2011, was an associate editor of *RNA*. She published seventeen of her papers in *RNA*, greatly contributing to the success of this journal. Indirectly, she probably contributed to many other papers in the journal, as she was a generous source of high-quality antibodies and other tools for many RNA researchers.

Elisa's dedication to science and the breadth of her research on mRNA metabolism and post-transcriptional regulation is legendary, as was her courage and readiness to take on new challenging projects and new technologies. Her work made a tremendous impact on the whole RNA research community. She was a talented communicator and a welcome speaker at dozens of meetings that she attended or organized. Elisa was very critical about her own research and also had the courage to openly criticize others, for the sake of science. Political correctness was alien to her. She cared both about science and about people, particularly those at early stages of their scientific careers. After moving to Tübingen and acting as Managing Director of the MPI for several years, Elisa also organized the International PhD Program and the Research School and enlivened the lives of students on the Tübingen campus. She coordinated these programs right to the end. Dozens of master's students, PhDs, and post-doctoral fellows passed through Elisa's laboratory over the years. Many are now managing their own independent groups, hopefully passing on the endowed enthusiasm and scientific rigor of Elisa.

Elisa was fully devoted to science. In the past few years, however, she also revived old interests and started new ones like dancing salsa with the Spanish-speaking community in Tübingen, hiking in the Swiss mountains, reading science fiction books, and lately also practicing meditation. Perhaps not surprisingly, considering her early life during the Uruguayan political upheaval, Elisa was a very private person, often with a somewhat enigmatic smile on her face. In writing this obituary, we were not sure whether to emphasize her reserved personality or whether to hint at the depth below the surface. We chose the latter, because we hope that readers of the *RNA* journal will remember Elisa not only as a world-famous scientist and somewhat frightening figure sitting in the first row of RNA meetings, and as the fiercely competitive, exceptionally rigorous, efficient and outstanding scientist that she was, but also as a human being, a dear friend, and a cherished person in our community.

Note: Elisa did not want flowers and wreaths. To honor her memory, donations to programs that fund and promote the education of girls are welcome, as this is what she strove to achieve, for herself and for others.

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