

RETROSPECTIVE

Paolo Sassone-Corsi (1956–2020)

Groundbreaking molecular biologist and epigeneticist

By **Eric Verdin**

Paolo Sassone-Corsi, eminent molecular biologist, died unexpectedly at the age of 64 on 22 July in Laguna Beach, California. Paolo made seminal contributions in the fields of transcriptional regulation, epigenetics, circadian biology, and metabolic regulation, and he pioneered the discovery of key links between these disciplines.

Born in Naples, Italy, in 1956, Paolo devoted himself to science and discovery from an early age. At just 12 years old, he founded an amateur astronomy club with his brother Emilio in Naples. (Ten years later, the two brothers published a paper on the bands of Saturn.) Although he retained his passion for astronomy, Paolo decided to focus his graduate studies on yeast biology; he received his Doctorate in Biological Sciences in 1979 from the University of Naples Federico II. The university would honor him as a most meritorious alumnus in 2016.

During a postdoc under the mentorship of molecular biologist Pierre Chambon at the Institut de Génétique et de Biologie Moléculaire et Cellulaire (IGBMC) in Strasbourg, France, Paolo was drawn to the basic mechanisms of transcription. He contributed key work on promoters, enhancers, and transactivating factors as well as the identification and characterization of a promoter sequence of the adenovirus major late gene that became known as the TATA box, a hallmark regulatory element of most eukaryotic genes. He then moved to the Salk Institute for Biological Studies in San Diego, California, where he studied the intracellular pathway leading to the activation of the proto-oncogenes *c-fos* and *c-jun* and demonstrated their mechanism of action in the regulation of transcription; he showed that *c-fos* and *c-jun* interact with each other, and he identified the regulation of *c-fos* by cyclic adenosine monophosphate (cAMP).

In 1989, Paolo established his first independent laboratory at the IGBMC, where he rapidly progressed to the level of director of research at the Centre National de la Recherche Scientifique. During this

period, he identified a previously unknown messenger in the cAMP signaling pathway—the cAMP-responsive element modulator (CREM)—and characterized its role in spermiogenesis and germ cell apoptosis. The identification of a distinctive circadian fluctuation of CREM expression in the pineal gland led Paolo and his team into chronobiology, a fitting reconnection with astronomy, as this field of biology explores the consequences of Earth's rotation and the 24-hour cycle of light and darkness that it imposes on all living organisms.

In 2006, the University of California, Irvine (UCI) recruited Paolo and his wife, prominent neurobiologist Emiliana Borrelli. Paolo was hired as a distin-



guished professor and led the Department of Pharmacology for 5 years. He then founded the Center for Epigenetics and Metabolism, an interdisciplinary center reflecting his increasing interest in metabolism and circadian biology in relation to epigenetics. Paolo's singular understanding of transcriptional regulation led to a series of additional groundbreaking discoveries, including the dissection of transcriptional and epigenetic mechanisms that regulate circadian rhythms and an explanation of how they respond to metabolic states. He was first to demonstrate that the key oscillating transcription factor CLOCK is a histone acetyltransferase, and he characterized how the deacetylase SIRT1 and fluctuations in concentrations of nicotinamide adenine dinucleotide and its reduced form participate in the control of circadian rhythms. Through these pio-

neering studies, Paolo became a leader in the fields of circadian rhythms, epigenetics, and metabolism.

Having worked in similar fields, I came to know Paolo at scientific meetings and through service on advisory boards, visits to UCI, and collaborative efforts. I will remember him for his beautiful lectures, his charm, his warmth, the twinkle in his eye when he would gently tease you, his passion for science, and his love and pride for his students and postdocs. More than anything, many of us will remember his zest for life, food, wine, and science and his incredibly generous hospitality. Paolo and Emiliana excelled at organizing memorable meetings. Their biannual Epigenetic Control and Cellular Plasticity International Symposium was known not only for the caliber of its science but for Paolo and Emiliana's warmth and hospitality. They had moved to UCI in hopes of living somewhere climatically and geographically similar to their native Italy. In the process, they brought a big slice of Italy and its dolce vita to California for everyone to enjoy. Paolo made all of us, his guests, feel truly special. His pride and joy in wanting to share with me a beautiful sunset at the Pelican Inn in Newport Beach remains to this day a special moment with a cherished colleague and a friend.

Paolo's creativity, originality, scientific courage were recognized by his election as a fellow of the American Association for the Advancement of Science (AAAS, the publisher of *Science*) in 2014, as well as numerous awards. He received the Grand Prix Lilliane Bettencourt in 1997 and the Grand Prix Charles-Léopold Mayer de l'Académie des Sciences in 2003. He also served on various scientific advisory boards and journal editorial boards.

The scientific community has lost in Paolo a trailblazing scientist, a superb and generous colleague and mentor, and a witty, adventurous, and warm friend. Paolo is survived by Emiliana and his brothers Lucio and Emilio Sassone-Corsi. For all of us who counted Paolo as a close friend, his early departure is hard to accept. Our loss is balanced only by the gratitude we feel for having had the chance to cross paths with and draw inspiration from this brilliant, generous colleague.