

## Elena Galea (1962–2023)

By Douglas L. Feinstein

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**M**aría Elena de la Trinidad Galea Rodríguez de Velasco (Elena Galea as we knew her), Research Professor at ICREA (Catalan Institution for Research and Advanced Studies) and the Institute of Neurosciences and Department of Biochemistry and Molecular Biology, Universitat Autònoma de Barcelona (UAB), died unexpectedly on 23 January 2023. Elena received her PhD in Biology in 1990 from the Department of Physiology at the Universidad Autónoma de Madrid, where she worked under the mentorship of Carmen Estrada looking at cerebral vascular responses. She then carried out a postdoctoral fellowship in the Department of Neuroscience at Cornell University Medical College in New York, under the directorship of Donald Reis. It was at Cornell I first met Elena, which led to life-long collaborations and a deep friendship. At that time, methods for quantifying mRNA levels were being developed, and together we devised ways to quantify astrocyte mRNAs.

Elena's work on cerebral vasculature provided a smooth transition into nitric oxide (NO) research. We were fortunate that Carl Nathan, studying macrophage NO production, was at Cornell and helped us to characterize inducible NO synthase (iNOS) in astrocytes, leading to Elena's 1992 *PNAS* paper. That led to a series of papers describing the regulation of astrocyte iNOS expression, her cloning of the *INOS* (also known as *NOS2*) mRNA from astrocytes, and confirmation that it is expressed in astrocytes as well as microglia. Elena remained at Cornell for several years, collaborating with Eugene Golanov to examine intrinsic mechanisms underlying neurogenic protection from hypoxia and ischemia, focusing on activation of the fastigial nucleus and endothelial cell responses.

Elena spent 7 years living in the upper East Side of Manhattan, attending concerts at Lincoln Center, strolling through art galleries in Greenwich village, and relaxing in Central Park. She was a connoisseur of exotic cuisine, always ready to head to an Ethiopian restaurant; and was famous for her home-made gazpacho.

In 1998, she became Assistant Professor of Anesthesiology at the University of Illinois in Chicago (UIC). This was due in part to her work with NO and ischemia, and to collaborations



with Dale Pelligrino at UIC. To run an independent lab, mentor her own students, and write her own grants was an important step in her career. Dale was interested in the effects of estrogen on brain inflammation and endothelial cell NO, and the use of various anti-inflammatory agents to reduce ischemic damage. At that point, several observations came together that may have sparked Elena's interest in Alzheimer's disease (AD). She had previously shown that noradrenaline potently inhibited astrocyte iNOS; then Michael Heneka joined the lab and showed that lesions of noradrenergic neurons exacerbated neuropathology in mouse models of AD. It was also when the target of non-steroidal anti-inflammatories, which reduced astrocyte activation as well as the risk of AD, was identified as the peroxisome proliferator-activated receptor- $\gamma$  (PPAR $\gamma$ ). Together with Michael, myself and later Pierre Lacombe in Paris, Elena began to study the neuroprotective effects of selective PPAR $\gamma$  agonists in mouse models of AD, multiple sclerosis, and X-linked adrenoleukodystrophy.

In 2004, Elena joined the Institute of Neurosciences at UAB. There she continued to study astrocytes, focusing on their plasticity during disease. Together with Roser Masgrau, she created AstroLab, collaborating with local and national neuroscience labs to examine CREB-dependent transcriptional changes due to traumatic brain injury. Elena became a member of the Barcelona cultural scene, starting 'Serendipity', a group with shared interests

in local gastronomy and music, and where she hosted jazz sessions for young musicians. She also found time to get involved in social work, helping with the education of low-income children in the neighborhood.

In 2012, Elena did a 1-year sabbatical in Bradley Hyman's lab at Massachusetts General Hospital and Harvard Medical School in Boston. Along with Eugene Stanley, she used multi-photon microscopy and cranial windows to image astrocytes in transgenic AD-type mice and showed that the well-known tiling distribution of astrocytes in healthy mice is maintained in plaque-bearing AD mice, indicating that astrocytes do not migrate towards plaques – a common misconception until then. As in New York, Elena enjoyed Boston's museums; classical concerts; strolling through the Commons; and watching sunsets over the Charles.

Returning to UAB, she began studies of astrocyte mitochondrial function, concluding that astrocytes were oxidative and not merely glycolytic, as generally viewed. This led to her thought-provoking opinion paper questioning the use of the terms 'neuroinflammation' and 'glia'. She was also a key driving force, along with Carole Escartin, Alex Verkhratsky, Michael Sofroniew, and Alberto Serrano Pozo, for a multi-authored 2022 consensus paper published in *Nature Neuroscience*, which made recommendations for astrocyte nomenclature and discussed research challenges posed by these cells.

Elena was passionate to apply systems neuroscience and machine learning approaches for understanding astrocyte–neuron interactions, and during her final years in Spain she renamed her lab to 'Systems AstroLab' and founded Clisyne, the Clinical System Neuroscience Network, bringing together AD and astrocyte researchers, bioinformaticians and computational neuroscientists. She strongly believed that astrocytes could compute, and should be integrated into Systems Biology, as she claimed in 2020.

Throughout her career, Elena supported the career development of young investigators, sharing her global vision of neuroscience, helping them to recognize current and future challenges to astrocyte research, and encouraging them to question even accepted dogmas. We honor her scientific rigor and legacy; she was an exemplar of how science can and

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# Obituary

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should be done in the service of society. She leaves behind her collaborators, mentors, mentees, family members and friends who will miss her humor, her unique perspectives and insights, and of course her shining silver mane.

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