

monkeys which includes the snub-nosed monkeys discussed above) with the fossil record, as well as information on palaeoenvironments and current social organisation and behaviour, to investigate any genetic and environmental factors driving the differences of social structures between these primate species (Science (2023) 380, <https://doi.org/10.1126/science.abl8621>). Colobine monkeys residing in colder regions, such as the snub-nosed monkeys (*Rhinopithecus*), tend to live in larger groups with complex social structures. In agreement with this current observation, the researchers found that cold events, like the late Miocene cooling and Pleistocene glacial periods, selected genetic changes to dopamine and oxytocin pathways that favoured the switch from groups with one male and multiple females to more complex multilayered societies.

Adapting to change is also an important issue for today's primate species, seeing as they are facing rapid anthropogenic disruption of their natural habitats, especially through deforestation in the tropics (Curr. Biol. (2017) 27, R573–R576). The more than 100 lemur species in Madagascar are one biodiversity hotspot that is now at risk. Elsewhere, iconic species including all three species of orangutan (genus *Pongo*) are also listed as Critically Endangered (Curr. Biol. (2019) 29, R225–R227).

The new treasure trove of genome data offers opportunities for conservation research as well, such as recognising genetic diversity bottlenecks. In their broad study of the genomes of 233 primate species, researchers could find no correlation of low genetic diversity with increased extinction risk, confirming that it's not the genes that have caused the currently precarious situation of primate species. Still, the genomes do enable conservation experts to look out for any vulnerabilities arising.

Uniquely, the main reason why hundreds of primate species are now at risk of disappearing is found in the global success of one primate species, namely our own, making it our prime responsibility to ensure their survival.

Michael Gross is a science writer based at Oxford. He can be contacted via his web page at [www.michaelgross.co.uk](http://www.michaelgross.co.uk)

## Q & A

### Shai Shaham

*Shai Shaham is the Richard E. Salomon Family Professor at The Rockefeller University. He received his A.B. degree from Columbia University, and a Ph.D. from MIT, where he studied programmed cell death. Following postdoctoral work at UCSF, working on yeast nuclear import and *Caenorhabditis elegans* neurodevelopment, he joined the Rockefeller faculty in 2001. His group has pioneered the use of *C. elegans* to study glia–neuron interactions, uncovering novel principles of nervous system development and function. He and his colleagues also continue to study programmed cell death, discovering a prevalent morphologically conserved form of cell death termed linker cell-type death (LCD). Recently, his lab described a new mechanism by which neurons and other morphologically complex cells are dismantled.*

**What drew you to science?** I cannot remember a time when I was not fascinated by science. My mother is a human cytogeneticist and my father was an astrophysicist; metaphase chromosome spreads and equations relating to stellar evolution were a common fare growing up. When I was five years old, I was returning home from school one day, walking on the gravel path that runs through the valley of the cross in Jerusalem, when I unexpectedly saw my father running towards me with a piece of darkened film in his hand. He said that we should hurry back home because a solar eclipse was imminent. Sitting in our back yard, staring through the film at the disappearing sun and witnessing the ensuing unnatural darkness was an experience I still vividly remember. I was in awe not only of the phenomenon, but also of the fact that my dad knew it was going to happen. I think that day probably played a significant role in my eventual resolve to become a scientist.

**Why study glia?** I have always been captivated by the “road not taken” and, as a postdoc, I spent a lot of time trying to imagine a difficult research



question that I could envision studying for years to come. I stumbled onto glia while reading about cell death in the nervous system. At the time (mid 1990s), I knew next to nothing about these cells, and soon discovered that they were generally not well understood by anyone. Why was this the case, especially given that glia and neurons are equally abundant in vertebrate nervous systems? After spending a couple of years reading papers and talking to colleagues, I realized that the answer was inherent to what it is that glia do. Following their initial description in the 19<sup>th</sup> century, evidence suggested that glia function as support cells, supplying neurons with survival signals in the form of nutrients and growth factors. Although a few neurobiologists suggested that broader roles were possible, experimental support for this view was limited, and the prevailing thought, even until recently, remained that dynamic signaling was the purview of neurons. Ben Barres, a luminary in glia research, pointed out to me many years ago that the trophic roles of glia were actually the key obstacle to fully understanding what else these cells might do, because inhibiting or manipulating glia usually results in the demise of their associated neurons. Therefore, even if we wanted to study glia–neuron interactions separate from survival, we could not, because the neurons are gone. This problem piqued my scientific curiosity, spurring me to think of a way out of this “Catch-22”.

**Why *C. elegans*?** After settling on the question of glia, my next step was to come up with an approach to tackle the thorny issue of neuron survival. As a graduate student in Bob Horvitz's lab at MIT, I studied programmed cell death in *C. elegans*, identifying caspases as mediators of apoptosis. After a few years researching nuclear transport in yeast with Ira Herskowitz at UCSF, I returned to worms to complete a postdoc with Cori Bargmann. My work with Bob taught me that, in *C. elegans*, cell death was largely a cell-autonomous process regulated by a cell's lineage and not by its neighboring cells. I reasoned, therefore, that if worms had glia, these would be unlikely to control neuron viability. When coupled with the 'awesome power' of worm genetics, this predicted absence of trophic interaction could come in handy for uncovering genes and pathways directing glia–neuron communication unrelated to cell survival. Indeed, Cori's work and that of others on the worm nervous system would serve as a model for how to proceed.

**But do worms even have glia?** Sam Ward and John White, two revered *C. elegans* neuroanatomists, had referred in their seminal papers to six mesodermally derived nervous-system-associated cells as glia, and Bill Wadsworth had published a foundational paper on what he termed worm 'neuroglia' that guide axon outgrowth. But did they really show that these were glia, and what exactly are glia anyway? From immersion in the literature, I distilled two characteristics that were common to all glia: they physically touch neurons, and they are not neurons themselves. In addition, most glia are of neuroectodermal origin (although some, like microglia, are not). Inspecting the catalogue of *C. elegans* cells, it became immediately obvious that 50 of the 959 somatic cells in the hermaphrodite of the species fit all three criteria, and six conform to the first two. Other cells also fit the bill, but have additional functions outside the nervous system, and were put aside. When I opened my lab at Rockefeller, we used a reporter labeling two of the 50 cells (the only such reporter available at the time) to isolate these cells for transcriptome and genomic

studies, which identified additional markers for the various glia, and we began ablating them. The prediction that these cells are not required for neuron survival was quickly verified. And to our delight, in the absence of glia, neurons did not function properly to mediate behavior, suggesting other important roles. We succeeded in finding an *in vivo* setting in which we could study glia–neuron interactions without fear of neuronal loss. We now know that there are many functional and molecular similarities between these cells and vertebrate glia. The early hope of marrying the technical prowess of the worm with this difficult-to-answer question about what glia do has become a reality. Over the past 20 years, our work has dovetailed nicely with a surge in glia research across model systems. The expanding community of glia researchers studying these cells in *Drosophila*, zebrafish, mice, and other settings is tight knit, very supportive, and single-mindedly dedicated to revealing the mysteries of these cells. It is a rare privilege to be part of this effort.

**How important is scientific collaboration?** I believe there is always some tension between a scientist's drive to experience the thrill of discovery, and the realization that most of us cannot accomplish much without the help of others. Yet I don't think these are mutually exclusive. In my experience, engaging with other scientists and being generous with your discoveries will usually pay off sooner or later. I grew up in two remarkably collaborative and supportive scientific communities — *C. elegans* biologists and glia researchers. From its very beginnings, the *C. elegans* field engaged in large-scale projects that had immediate impact on all community members. The compilation of the genetic map of the worm, the determination of its full cell lineage, the reconstruction of its nervous system, the toolkit for generating transgenic worms, and the sequencing of its genome are all excellent examples. These projects set the tone for conduct in the field, and collaboration was the norm. I started my path in worm biology as an undergraduate in Marty Chalfie's lab at Columbia. When Marty's lab later demonstrated that

GFP could be used to label *C. elegans* cells, I remember how the vectors the lab generated spread like wildfire across the community. I found a similar ethos among glia researchers. Both communities are composed of doggedly determined scientists — often fighting against the grain — who believe strongly in their mission. It is a great feeling to know that so many people have your back.

**Who were your scientific influencers?**

About 20 years ago, I returned home in the evening to relieve our babysitter, a lovely older Yemenite Jewish woman whom the kids adored. I began making dinner and, as she was leaving, she asked about the food I was preparing. I recited the recipe (probably something involving pasta, knowing my kids and my own culinary abilities), to which she responded with a saying from the Mishna, a collection of discussions about Jewish customs and ethics: "From all my teachers have I become wiser". I feel the same way about my scientific influencers. I have picked up nuggets about how to conduct research and how to ask interesting questions from many, both those I met only in print and those I met in person. In some complicated way, which I don't quite understand, their advice, together with my own experiences, has shaped my scientific outlook.

**What is an impactful lesson you've learned?**

I think we live in very exciting times: thousands of researchers are tackling problems in every aspect of biology, tens of thousands of papers are published every year, and our understanding of nature is rapidly accreting. Science is also no longer the purview of the very few and is practised in an ever-growing community. Yet these remarkable advances can be intimidating to those starting a career. A new assistant professor might wonder whether all the interesting problems to study have already been 'taken'. This was certainly something I had concerns about. I discussed the issue with a fellow postdoc in the Herskowitz lab, Linda Huang (now at UMass, Boston), who later bought me a book by the noted neuroscientist Santiago Ramon y Cajal, titled *Advice for a Young Investigator*. Chapter 2, 'Beginner's Traps', was particularly revealing. Here,

Cajal tackles an apparently common complaint from the “newly graduated: ‘Everything of major importance in the various areas of science has already been clarified.’” This would not have been of note, except for the fact that the book was first published in 1899! That the same sentiment existed before modern biology, chemistry, and physics were even conceived is truly inspiring. To me, this sentence is a way to peek into the future and keep motivated, knowing that interesting and exciting discoveries are always out there.

#### How then does one find new ideas?

I do not believe that there are hard and fast rules that will guarantee discovery: after all, the list of major advances that followed a chance observation by a prepared mind is a long one. Yet I think there are some things to consider. In Chapter 2 of Cajal’s book, he also discusses a trap which he refers to as “undue admiration of authority”. Science rewards those who have made discoveries with professorships, prizes, and leadership positions. It is important to realize, however, that those who have acquired these titles do not necessarily have all the answers. Indeed, progress frequently comes not from experts, but from outsiders who approach questions without prior knowledge. There is no better example of this than the molecular biology revolution, heavily influenced by outsider physicists including Delbrück, Gamow, Crick, Benzer, and many others. In my own lab, several exciting advances were initiated by students and postdocs advocating for experiments that I was convinced would never work... Who to consult, then? I have found that older papers, often predating the invention of molecular methods, are a treasure trove of thought-provoking ideas. For example, the Sulston *et al.* paper describing the embryonic cell lineage of *C. elegans* is replete with one-sentence observations and statements, each of which has launched entire research careers. Several of Cajal’s hypotheses, over 100 years ago, about the roles of astrocytes in the nervous system were rediscovered independently in recent years and are studied today. Luria and Delbrück’s serious contemplation of non-genetic modes of inheritance foreshadowed current interest in epigenetics. When science moves

rapidly from one hot topic to the next, some ideas are forgotten. Thus, paradoxically perhaps, digging up long-abandoned ideas is a great way to pursue new and creative research.

**Finally, any thoughts on scientific training?** The path of most biologists these days is fairly narrowly prescribed: attend graduate school following undergraduate studies, seek a postdoc (usually in a different area of research), apply for faculty positions, and move up the ranks to tenure. I followed this track. But I have learned over the years that the road to discovery can favor those who navigate more unusual paths. And by unusual, I really mean unusual. One colleague whose work I greatly admire was a construction worker before serendipitously deciding to attend graduate school. Another spent many years in industry before turning to academia, and yet another trained for the ballet. I have come to believe that the path is less important than the content. When I first started thinking seriously about science I was in a position where, as my amazing physician wife once remarked about her early training, I didn’t know what I didn’t know. I was unaware of the existence of entire fields of research. With time, I could say with more confidence that I know what I don’t know. These stages of learning have been codified, I believe, in the standard education path, where graduate school provides the first real opportunity to broaden familiarity with the vast science that is out there. Alternative paths inherently imbue their pursuers with the instinct to look well beyond what they are familiar with and may therefore counterintuitively speed up the initial stages of learning. These days I feel there are some things I actually do know, at least in some depth, but these are generally few and far between and this is great, because science is about learning; and how exciting it is that there is so much more left to learn!

#### DECLARATION OF INTERESTS

The author declares no competing interests.

Laboratory of Developmental Genetics, 810 Weiss Research Building, The Rockefeller University, 1230 York Avenue, New York, NY 10065, USA.  
E-mail: [shaham@rockefeller.edu](mailto:shaham@rockefeller.edu)

## Quick guide Sea robins

Corey A.H. Allard<sup>1,3</sup>, Amy L. Herbert<sup>2,3</sup>, David M. Kingsley<sup>2</sup>, and Nicholas W. Bellono<sup>1,\*</sup>

**What are sea robins?** Sea robins are an extremely unusual group of fishes with a host of dramatic adaptations suited for life on the sea floor. Sea robins belong to a family of ray-finned fishes called Triglids, which inhabit diverse habitats ranging from shallow salt marshes to deep oceans around the world. Most Triglidae fish are benthic specialists that spend much of their time on the ocean bottom where they hunt in the sand for fish, crustaceans, and other invertebrates. To facilitate their benthic lifestyle, sea robins have evolved a number of bizarre traits, the most iconic of which are their six leg-like appendages (Figure 1).

**Wait, what are fish legs?** Sea robin ‘legs’ comprise the first three fin rays (lepidotrichia) of each pectoral fin. In most fish, pectoral fins are webbed to facilitate efficient and effective swimming. Similar to other fish, newly hatched sea robins have webbed fins that they use to swim and hunt throughout the water column. Remarkably, later during ontogeny the first three fin rays begin to separate from the rest of the pectoral fin to result in three individual appendages on each side (Figure 1). Leg development is accompanied by skeletal changes and extensive modification of the musculature and nervous system. Each leg contains two segmented chains of bone (hemitrichia) which slide against one another to bend the leg while sea robins ‘walk’ along the sea floor. There are no tendons in the legs themselves, and instead all motion is actuated from the base by specialized musculature in the pectoral girdle. Intriguingly, this metamorphosis coincides with a shift from a planktonic lifestyle in the water column to a benthic existence at the bottom of the ocean.

While fish legs may seem strange, they are not unique to sea robins. Indeed, they are also found among other families of fishes that are part of the Scorpaenoidea superfamily that includes

