


Dan Salah Tawfik (1955-2021)—A giant of protein evolution

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It was with great sorrow that we have learned of the untimely death of our friend, mentor, collaborator, and hero, Dan Tawfik. Danny was a true legend in the field of protein function and evolution. He had an incredibly creative mind and a breadth of knowledge—his interests spanned chemistry and engineering to genetics and evolution—that allowed him to see connections that the rest of us could not. More importantly, he made solving biochemical mysteries fun: He was passionate about his work, and his face lit up with joy whenever he talked about scientific topics that excited him (of which there were a lot). Conversations with Danny made us all smarter by osmosis.

Danny's own evolution in science began with physical organic chemistry and biochemistry. His PhD at the Weizmann Institute of Science, awarded in 1995, was on catalytic antibodies under the supervision of Zelig Eshhar and Michael Sela. It was followed by a highly productive period at the University of Cambridge's Centre for Protein Engineering, first as a postdoctoral fellow with Alan Fersht and Tony Kirby, and then as a senior researcher. Among his many achievements during his time in Cambridge was the demonstration that off-the-shelf proteins—the serum albumins—could rival the best catalytic antibodies in accelerating the Kemp elimination reaction due to non-specific medium effects. This work was an early example of unexpected catalytic promiscuity, and it sowed the seed for Danny's later fascination with “esoteric,

niche enzymology” that went far beyond convenient model systems.

It was also in Cambridge where Danny first realized the power of the then new field of directed evolution, both for biotechnology and for elucidating evolutionary processes. He and Andrew Griffiths pioneered emulsion-based *in vitro* compartmentalization. The idea of controlling biochemical reactions in separate aqueous droplets inspired emulsion PCR and next-generation sequencing technologies, whereas Danny used it to solve a long-standing problem in directed evolution; *in vitro* selection techniques had always been good at identifying ligand-binding proteins, but compartmentalization finally enabled the directed evolution of ultra-fast catalysts.

Danny returned to Israel in 2001 to join the faculty of the Weizmann Institute of Science where his scientific trajectory further evolved, diverged, and even “drifted”. He developed new methods for enzyme engineering and applied his evolutionary insights into *de novo* protein design efforts. In this context, Danny's interest was always focused on *how* proteins evolve, particularly the connection between promiscuity, conformational diversity, and evolvability. His depth of understanding underpinned both applied research, such as engineering enzymes to detoxify nerve agents, and fundamental research, such as the evolution of enzymes from non-catalytic scaffolds.

Through it all, Danny retained his sense of joy and wonder at the “beautiful aspects of Nature's chemistry”. This includes his discovery of an exquisite molecular specificity

mechanism mediated by a single, short H-bond that enables microbes to scavenge phosphate in arsenate-rich environments. In recent years, he deciphered the biosynthetic mechanism of dimethyl sulfide, “the smell of the sea”, and homed in on the interplay between the evolution of an enzyme, its host organism, and environmental complexity. His insights into how the first proteins emerged caused tremendous excitement in the field. He established the roots of two common enzyme lineages, the Rossmann and P-loop NTPases, as simple polypeptides, and suggested ornithine as the first cationic amino acid. Prior to his death, he published the results of another tour de force: evidence that the first organisms to utilize oxygen may have appeared much earlier than thought.

His work impacted many research fields, and he won many significant awards. Most recently, Danny was awarded the EMET Prize for Art, Science and Culture (2020), informally dubbed “Israel's Nobel Prize”. He was an active and valued member of the EMBO community, having been elected in 2009, and, until his passing, served on the Editorial Advisory Board of *EMBO Reports*.

Danny was also a superb science communicator. Both his research articles and reviews are a joy to read. What stood out just as much as his brilliance was his personality, as he embodied the Yiddish concept of being a true “mensch”. Danny was humble, was down-to-earth, and treated all his colleagues—including the most junior members of our research teams—as equals. He championed the careers of others, both

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DOI 10.15252/embr.202153256 | EMBO Reports (2021) 22: e53256 | Published online 27 May 2021



Figure 1. Dan Salah Tawfik (1955–2021).

Photo courtesy of Prof. Joel Mackay, The University of Sydney.

those who worked directly for him and those who were lucky enough to be “just” his friends and collaborators. He believed in us even when we did not believe in ourselves, and he was always there to answer questions both scientific and professional. While he loved to share his own ideas, he would be just as excited about ours. Despite his own busy schedule, he always found the time to help others. He was also excellent company, with a great, very dry, sense of humor, and endless interesting stories, including from his own colorful life. In the days after his untimely death, an often-repeated phrase was “he was my best friend”. Danny’s

former group members have gone on to be highly successful in both industry and academia, including more than 15 former doctoral and postdoctoral researchers who are now faculty. The network of researchers Danny has trained, mentored, or influenced is broad, and this legacy is testament to his qualities as both a scientist and a person.

Danny was born in Jerusalem to an Iraqi Jewish family, and his Arabic Jewish identity was important to him. He believed strongly in coexistence and peace, and very much valued the Arabic part of his heritage. In his own words: “I am an Israeli, a Jew, an Arab, but first and foremost a human

being”. He would often speak of the achievements of his children with immense pride. Danny also had a passion for being outdoors, especially climbing and hiking—when the best discussions were often to be had (Fig 1). One of the easiest ways to persuade him to come for a seminar, a collaborative visit, or a conference was to have access to high-quality climbing in the area. He passed away in a tragic rock-climbing accident, doing what he loved most outside of science. Our thoughts are with his partner Ita and his children, and we join the much broader community of friends, collaborators, and colleagues whose hearts are broken by his sudden loss.