Sydney Brenner (1927–2019)

Sydney Brenner, Nobel Laureate 2002, was born on 13th January 1927 in Germiston, South Africa and died in Singapore on 5th April 2019. His death marks the end of a golden era in molecular biology: the MRC Laboratory of Molecular Biology (LMB) obituary[1] provides a summary of his considerable achievements; as does Errol Friedberg in *Nature*[2]—who also wrote a biography on Sydney[3].

I first met Sydney Brenner in 1975 when he interviewed me for a PhD place in his lab. When I joined Sydney's lab a year later, I had the freedom to choose my own project. I chose to work on bacterial transposons, to stay close to his early work in bacteria. This work had shown that the genetic code is triplet by elegant frameshift mutagenesis[4] and led to his discovery of messenger RNA[5].

Sydney was generous with his time, but he was also very busy and often travelling. First, I sank. Then I swam. It was good for me.

Sydney shared an office with Francis Crick, who had a sign above his desk saying "Reading rots the mind"; the running lab joke was that he expected Sydney to tell him what was going on. Sydney read, knew, thought about, and talked about everything. We listened in awe as we sat in the coffee room and were captivated.

Sydney was an Enlightenment thinker who applied reason to any problem. He was focused, concise, witty, irreverent, sarcastic, honest, and completely open-minded. He enjoyed an unbridled appetite for life. He never indulged in small talk; he did, however, poke fun at human foibles. Sydney made the assumption that we also embraced the Enlightenment Proposition, and treated us as equals. He was also very generous in helping people with their careers. His intellect was formidable, but his style was also familiar to me; we were both Jewish and South African-born, both his parents and my grandparents had escaped the pogroms of Lithuania and Latvia to emigrate to South Africa; although life in Apartheid South Africa turned out to be not so sweet.

In the mid-70s Sydney's group was working on his new model system: the nematode *Caenorhabitis elegans* ('The Worm') which he had realized was a perfect system for cell and developmental biology, biochemistry and genetics.

He attracted excellent researchers, his lab produced a 3D map of the worm from EM sections and identified all the neuronal connections. They began genetic approaches working on muscle mutants, and on cell lineage studies that led to a complete description of cell fate, including developmental apoptosis, which earned him, and former colleagues Bob Horvitz and John Sulston, the 2002 Nobel Prize.

In the mid-70s another 'new thing' was recombinant DNA technology with plasmid and phage vectors, restriction enzymes and ligases. Sydney was working at the bench making phasmids—hybrid phage λ-plasmid cloning vectors—and he kept a little red book chronicling his multiple phage crosses in beautiful handwriting. I would mainly talk to him here, with a lytic phage cycle bubbling in aerated glass tubes in a water-bath beside him. Sydney also made *E. coli* double mutants that could not grow on rich medium to develop methods to prevent recombinant DNA escaping the lab. He demonstrated this by drinking it. He began an experiment in evolution growing E. coli in heavy water which ran for many years. Sydney next developed fugu, the Japanese puffer fish, showing it to have the most compact vertebrate genome then known.

Sydney advised Victor Rothschild on his venture capital biotechnology investments, where he met Sam Eletr, who co-founded Applied Biosystems, the company that automated Sanger DNA sequencing to build the machines that sequenced the human genome. Sydney invented Massively Parallel Signature Sequencing (MPSS), the first NextGen DNA sequencing technology, and developed in Sam's new company, Lynx Therapeutics.

I ran into Sydney again at a meeting at the Royal Society celebrating the 50th anniversary of the elucidation of the structure of DNA. I whined to Sydney about how horrible academic life had become with all the bean-counting and Sydney provided me with an opportunity to escape, inviting me to help develop Population Genetics Technologies, a new biotechnology company he and Sam were establishing to perform DNA barcoding for sequencing candidate genes to identify the genetics of disease predisposition and drug response.

Sydney, for the last 35 years, played a key role in the development of biomedical sciences in Singapore, where he lived for the last 4–5 years of his life and headed a lab of 20 people. He co-organised a lecture series of invited speakers covering evolution from the birth of the universe to life on Earth, published as a book last autumn[6].

He also helped establish, and was president of, the Okinawa Institute of Science and Technology Graduate University (OIST) in Japan.

There was no one quite like Sydney, he is irreplaceable. Fortunately, there are some wonderful interviews with Sydney to cherish. These include 236 2–5 minute excerpts of Sydney being interviewed by Lewis Wolpert[7]. Notable excerpts include 45/236, 231/236, and 9/236 where, discussing selecting students, he says: "…that even if a student comes to me with a First Class degree he has to prove to me he could have got a Second Class degree, if he had tried…" These are all pure Sydney. ■

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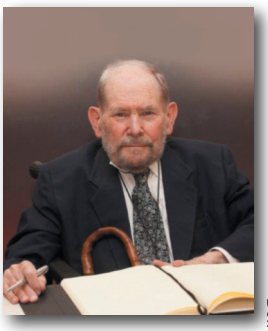

[1] https://www2.mrc-lmb.cam.ac.uk/about-lmb/archive-and-alumni/alumni/sydney-brenner/

[2] Friedberg, E. (2019) Sydney Brenner (1927-2019). Nature, **568**, 459

[3] Friedberg, E.C. (2011) Sydney Brenner: A Biography. Cold Spring Harbor Laboratory Press, New York

[4] Crick, F.H.C., Barnett, L., Brenner, S., and Watts-Tobin, R.J. (1961) General nature of the genetic code for proteins. Nature 192, 1227–1232

[5] http://web.stanford.edu/~mariamo/articles/Time/brenner1961.pdf

[6] Sim, S. and Seet, B. (eds.) (2018) Sydney Brenner's 10-on-10: The Chronicles of Evolution. World Scientific, Singapore

[7] https://www.youtube.com/watch?v=Zf13v0OEdt8&list=PLVV0r6CmEsFyxf1sRqxZgh-06WFw4zgPj