

A HEROIC VOYAGE

Sydney

Brenner's

Life in

Science

1927-2019



Agency for
Science, Technology
and Research



Cold Spring Harbor Laboratory 125
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A Heroic Voyage: Sydney Brenner's Life in Science

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Agency for Science,
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ONE OF OUR OWN

Message by Lim Chuan Poh

Former Chairman
Agency for Science, Technology and Research



Thirty years ago, when Sydney Brenner first visited Singapore, the state of research, especially in biomedical sciences, was vastly different from what it is today. Singapore's economy was structured around manufacturing, and there was little research conducted at the universities, if at all. But Dr Brenner saw the potential in our people and urged Singapore to start its own research institute dedicated to the exciting new field of molecular biology.

With the enthusiastic support of Singapore's founding fathers Mr Lee Kuan Yew and Dr Goh Keng Swee, the Institute of Molecular and Cell Biology (IMCB) was set up within two years, and thus began Dr Brenner's long association with science and research in Singapore. Within a decade, IMCB had gained international standing in the life sciences and by 2000 was recognised as the first major centre for biomedical sciences in Asia, winning the Nikkei Prize for Technological Innovation. All this took place before Dr Brenner himself was recognised with the Nobel Prize in Physiology or Medicine in 2002.

Internationally respected as one of the great statesmen of science, Dr Brenner has for decades been a trusted advisor to both the Agency for Science, Technology and Research (A*STAR) as well as the Biomedical Sciences (BMS) initiative. A relatively short 15 years after it was first launched, the biomedical sector grew five

times to reach over S\$29 billion in 2012, contributing to 5% of Singapore's GDP.

While Singapore's success in this area certainly cannot be attributed to any one person, few have been as deeply involved in raising Singapore's scientific standing as Dr Brenner. It is apt then, that Dr Brenner was the first person in our history to be made an honorary citizen, a distinction conferred on him by then President S. R. Nathan at the Istana in 2003. Dr Brenner also has an orchid named after him, the *Dendrobium Sydney Brenner*. The orchid can be found at the Singapore Botanic Gardens, which was recently listed as a UNESCO world heritage site.

But Dr Brenner's greatest legacy is perhaps the many excellent scientists he has trained, who have gone on to blaze their own trails in science and take up leading roles in academia and industry. In 2009, Dr Brenner set up the Molecular Engineering Laboratory at A*STAR with the aim of giving young researchers the independence to explore their ideas. There, researchers continue to explore interactions at the boundaries of different disciplines, just as Dr Brenner himself has done all through his extraordinary career.

It is befitting that this symposium and exhibition in honour of Dr Brenner's life and work should take place in the same year as Singapore's Golden Jubilee anniversary. Thank you Dr Brenner; we are truly fortunate to call you one of our own.

AN EXCELLENT TRAVEL COMPANION

Message by James Watson

Chancellor Emeritus
Cold Spring Harbor Laboratory



Over the course of my career, I've had the privilege of tackling some of the most fundamental questions in biology, working alongside some of the finest minds in science to solve them. In this six-decade-long quest, Sydney Brenner has been an invaluable colleague and personal friend.

My first encounter with Sydney was in April 1953, in the heady days just after our discovery of the structure of DNA. Sydney had driven from Oxford to Cambridge that cold, spring morning—just to be among the first to look at our model. We went for a long walk that day—six hours as I recall, and the first of many over the years—because there was so much to talk about.

As important as it was, the structure of DNA was just one part of the puzzle; we still needed to figure out how the RNA transcribed from DNA could be 'read' into proteins. Twenty of us, led by George Gamow, formed the RNA Tie Club, to share ideas on molecular biology. Brenner was valine, while I was proline.

And it was Sydney who eventually worked out that the genetic code was non-overlapping and degenerate, and discovered what messenger RNA and ribosomes were really doing. As if all that wasn't enough, he followed it up by establishing an entirely different kind of model system—the nematode worm—so wonderfully complex and simple at the same time.

Then there were the exciting, frenetic years of the Human Genome Project. We kept up our exchanges, with him in the UK and me in the US, doing as much science as possible while being responsible for entire research institutes.

Genomics owes a great deal to him and his ideas; not just for the worm, which is what his Nobel Prize was for, but also technologies like massively parallel signature sequencing, which allowed gene expression to be analysed on a scale few could have imagined earlier.

We both embarked on our careers in an extremely exciting time for molecular biology and have enjoyed front row seats. In 1954, Sydney and I actually drove through the eye of a hurricane while on a road trip across the US to Caltech. Then as now, I'm glad to have had such an excellent travel companion for the journey.

If you happened to be in the centre of the small town of Germiston in South Africa in 1939, you may have come across a stocky, 12-year-old boy coming out of the public library with a book that he had been allowed to borrow from the adults' section. »



An Early Start

Sydney Brenner
(third from left)
with family.
(Photo: CSHL Archives)



Corporal Sydney Brenner (second row from back, far right) at S. H. Military College in 1944, at the completion of a course module. (Photo: CSHL Archives)

“I read everything. As I say, I speak two languages: English and rubbish. I read everything but mostly I read non-fiction.”

Sydney Brenner, interview for SG50 book *Singapore's Scientific Pioneers*

» You might have also seen him about a mile away down the main street, looking for frogs in the small stream that ran between his house and the starch factory; or in his garage extracting pigments from flowers.

The budding scientist, Sydney Brenner, was no ordinary teenager. As a child, he had not only read *The Young Chemist*—F. Sherwood Taylor’s book for amateur chemists—but had already performed many of its experiments using small quantities of chemicals purchased from a pharmacy. His main interest, however, was in biology; plants and animals remained a source of fascination throughout his life. He also discovered early on that his “teachers did not know very much”, and that many things could be learnt by reading and doing.

An avid reader

Sydney Brenner was born on January 13th 1927 in Germiston to Jewish immigrants from Russia. The family lived in a few rooms at the back of his father’s cobbler shop.

When he was five, one of his father’s customers—a certain “Miss Walkinshaw”—found him reading a newspaper. Impressed, she found him a place, with fees waived,

at a private church school. At age six, he entered the local primary school two years ahead of his contemporaries, and completed the first three years of primary school in one year. Brenner began at the local high school when he was 11, and graduated just before he turned 14.

Throughout school, he continued to read voraciously and perform experiments in his garage laboratory. One particularly inspiring book was *The Science of Life*, a nine-chapter illustrated science book by H. G. Wells, Julian Huxley and G. P. Wells.

Brenner at university

By the time he finished school, he knew he wanted to become a scientist, but his family was too poor to afford a university education for him. He won a bursary from the Town Council to study medicine and began a six-year medical course in early 1942 at the University of Witwatersrand—also known as Wits University. There, the 15-year-old studied physics, chemistry, botany and zoology, commuting by bicycle and train with packed sandwiches for lunch. He was greatly influenced by Edward Roux, a lecturer in botany who

allowed him to stay on after hours to work in the laboratory. Roux was an important figure in the long struggle of the African people in South Africa and this helped to shape many of Brenner’s subsequent student activities. In the second year of his course, he moved up the hill to the medical school where he was to remain for the next nine years.

Two years into the six-year medical degree, Brenner was advised to take an extra gap year as he was too young to qualify for the practice of medicine. He grasped this eagerly.

A “heavenly” gap year

Brenner spent a “heavenly” gap year in a medical bachelor of science (BSc) course in anatomy and physiology. He was part of a group of about a dozen medical students, who worked closely with more advanced researchers in a small room in the department of anatomy.

When histologist Joseph Gillman invited Brenner to stay on for an honours and master’s degree, he accepted and supported himself by working part-time as a laboratory technician.



A “Proclamation” allowing Sydney Brenner to travel from South Africa to the UK. (Photo: CSHL Archives)



A young Sydney Brenner and his team at an anthropological site in South Africa. (Photo: CSHL Archives)

During those two years, Brenner learnt how to produce histological sections, mount them on glass slides, and stain them with various dyes. He reconstructed embryos; performed experiments on neuromuscular junctions; synthesised his own dyes; learnt mathematics; and even built ultracentrifuges.

He also began to publish. Together with mentors Joe and Teddy Gillman, the 18-year-old Brenner published his first paper in *The South African Journal of Medical Sciences* in 1945. It was on the topic of porphyrins (organic compounds) in the liver of Africans suffering from pellagra, a disease caused by chronic vitamin B deficiency. A follow-up publication appeared the same year in *Nature*.

Anthropology and palaeontology became another of Brenner's favorite activities. On weekends, he and other students in the science class went on field trips to famous South African sites, where they sifted through debris in limestone caves during the day and played poker

around the campfire at night. In 1946, an expedition to the Kalahari Desert led to a publication, "Man and the Great Kalahari", for which he was the last author.

A clarion call to do science

Around this time, Wilfrid Le Gros Clark, a professor of anatomy at Oxford University, visited South Africa and invited Brenner to apply to Oxford. Brenner was advised, however, to obtain his medical degree first, and so returned to the study of medicine in 1947, completing his medical degree in 1951.

By his own admission, Brenner was not a good medical student. Instead, he continued to spend time in the laboratories in the anatomy department, later moving with Joe Gillman to the physiology department. In 1946, he taught himself genetics, focusing particularly on cytogenetics. His MSc thesis, in fact, was on the chromosomes of the South African tree shrew, *Elephantulus myurus*. This marked the beginnings of his long involvement in genetics. He published several papers during this period, including



Sydney Brenner at a scientific meeting in Edinburgh, 1958. (Photo: CSHL Archives)

a 1947 paper—of which he was particularly proud—that showed that the microsomes of the cell were the same as the chromidial substance of the cytologist.

Brenner once said that he was "the only medical student to graduate from Wits without ever laying hands on a patient until the actual final examination". His interest lay in scientific research and, specifically, molecular biology—"which, of course, did not exist at the time," as he later mused.

Upon graduating from medical school, Brenner applied to the University of Cambridge's department of biochemistry, but did not receive a reply.

In 1952, Brenner won a highly competitive scholarship from the Royal Commission for the Exhibition of 1851, and on the recommendation of the head of Wits University, H. Raikes, went to work in the laboratory of Sir Cyril Hinshelwood, a professor of physical chemistry at Oxford University. Hinshelwood set into motion Brenner's scientific career by suggesting he work on bacteriophage resistance in bacteria. ■

“When I was younger I had another scientific hobby, geology, but it threatened to become research so I gave it up. I used to go looking for fossils and going on expeditions but it’s always been science.”

Sydney Brenner, interview for SG50 book *Singapore's Scientific Pioneers*

Becoming a Molecular Biologist

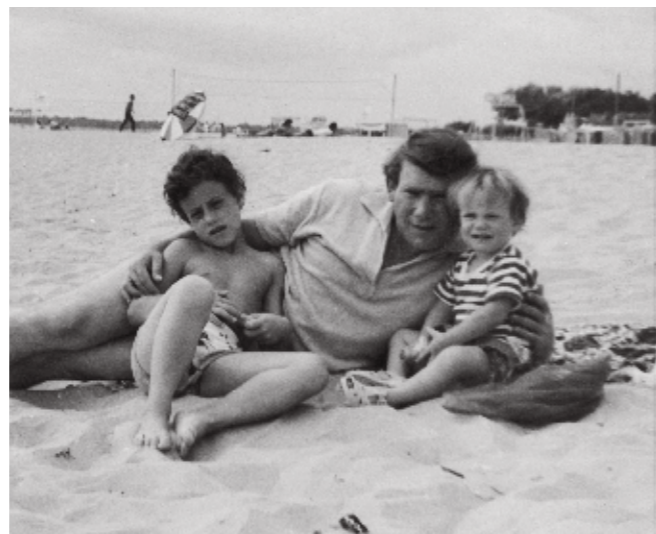


Sydney Brenner (right front, in dark shirt) at the Cold Spring Harbor Laboratory Phage Meeting in 1954. Immediately behind him are (L-R) Al Hershey (chequered shirt), Milislav Demerec and Francis Crick. (Photo: CSHL Archives)

In the 1950s Sydney Brenner's career progressed rapidly from the relative isolation of South Africa to Oxford University and the top scientific institutions in the US. »

The young Mrs Brenner (May Covitz).

Sydney Brenner with daughter Belinda (left) and Carla (right) on a beach in La Tranche-sur-Mer, France in 1962. (Photos: CSHL Archives)



Sydney Brenner was an honorary member of the RNA Tie Club, a “gentleman’s club” of scientists founded by Gamow to “solve the riddle of the RNA structure and to understand how it built proteins”. The club’s motto was “Do or die, or don’t try”. Each of its 20 members was given a woollen necktie with an embroidered helix, as well as a unique amino acid moniker—Brenner’s was valine.

Left to right: Francis Crick, Alex Rich, Leslie Orgel and James Watson in Cambridge wearing their RNA ties. (Photos: CSHL Archives)

» After some difficulties in getting a passport from the new nationalist government that had been elected in South Africa in 1948, Brenner sailed to Southampton from Cape Town in September 1952. In October 1952, post-World War II England was a grim place. Food was still rationed, and even the colleges of Oxford were not spared austerity. Brenner—and many of the other researchers—were outsiders. As he wrote in his Nobel autobiography, “In addition, I and the others were outsiders three times over; we were scientists, we were research students and we were colonials.”

However, there was an institution called Halifax House across the road from the physical chemistry laboratory where he and the other scientists could have lunch, and it was here that he met Jack Dunitz, a crystallographer, and through him, Leslie Orgel. Both were to remain lifelong friends and colleagues.

The birth of molecular biology

Dunitz had been to Caltech and knew all about the quest to reveal the structure of DNA. In early 1953, he told Brenner that two scientists in Cambridge, James Watson and Francis Crick, had solved the structure of DNA—a double helix where the two strands are held together by complementary pairing of the four bases: adenine with thymine and guanine with cytosine. On a frosty morning in April 1953, Dunitz, Brenner and Orgel drove with Dorothy Hodgkin to Cambridge to see the model in the Medical Research Council Unit in the Cavendish Laboratory.

After a short exposition of the model by Crick, the other two left and Brenner spent the rest of the day on a six-hour walk around Cambridge with Watson, talking about many things but mainly about DNA and

the importance of the structure. Brenner has often described this visit as a revelatory experience, one that had a definitive bearing on the future of his scientific life.

Marriage and family life

Brenner had met May Covitz while studying medicine at Wits in 1950. May, who was completing bachelor’s degrees in psychology and English literature, had attended a lecture given by Brenner on basic statistics.

In Errol Friedberg’s biography of Brenner, May spoke fondly of Brenner as “a combination of a clown and some sort of Greek god” and “absolutely different from anyone I had ever met”.

Shortly after graduating from Wits in 1951, May moved to London with Jonathan Balkind, her son from her first marriage, to pursue a PhD in psychology.

When Brenner moved to Oxford in 1952, he contacted May. They married in London within two months, in December 1952, and were together until May’s death in January 2010. Their children are Stefan, Belinda, Carla and Jonathan.

The road to America

In late 1953, Milislav Demerec, director of the Cold Spring Harbor Laboratory in New York, visited Hinshelwood, Brenner’s professor, in the physical chemistry laboratory in Oxford. At that time, there was a controversy about the development of resistance to drugs and antibiotics; most geneticists thought it occurred by mutation and Hinshelwood was almost alone in pursuing work to show that it could arise by adaptation. Demerec met Brenner and when he heard that Brenner was working on bacteriophage resistance and that he had shown it was due to mutation, he invited Brenner to the Cold Spring Harbor Laboratory for the summer of 1954. Demerec

helped Brenner to be awarded a Carnegie Corporation Fellowship for a four to five month visit to the United States. In July 1954, Brenner, armed with his DPhil, went to New York, while the rest of the family—May, Jonathan and Stefan—returned to South Africa.

During his visit to America, Brenner met Seymour Benzer and heard of his work on the fine structure of the gene and spent a long weekend at Woods Hole where Crick and Watson were also spending part of the summer. There he met George Gamow, a Russian-American physicist who had published a paper on the genetic code earlier that year.

Brenner attended the phage course as an auditor in Cold Spring Harbor and finally attended the annual phage meeting where he presented Benzer’s initial work on the *rII* gene. Benzer had to leave Cold Spring Harbor early because one of his children was ill, and asked Brenner to give the talk in his stead.

After the meeting, Brenner and Watson went on “an epic road trip” that took them through Boston, Massachusetts, and New Hampshire, and then to Watson’s home in Chicago, Illinois. They then continued across the US to Caltech in Pasadena, California. Along the way, Brenner met many scientists who would shape molecular biology, such as Max Delbrück, the founder of molecular genetics. Brenner ended his trip in Berkeley, California where he worked in the Virus Laboratory with Gunther Stent, another eventual lifelong friend and colleague.

Before leaving America, Brenner stopped in Washington D.C. where he met Gamow and Alex Rich and showed them the work he had done on the genetic code. On his return to England, he visited Crick in Cambridge and discussed what would later

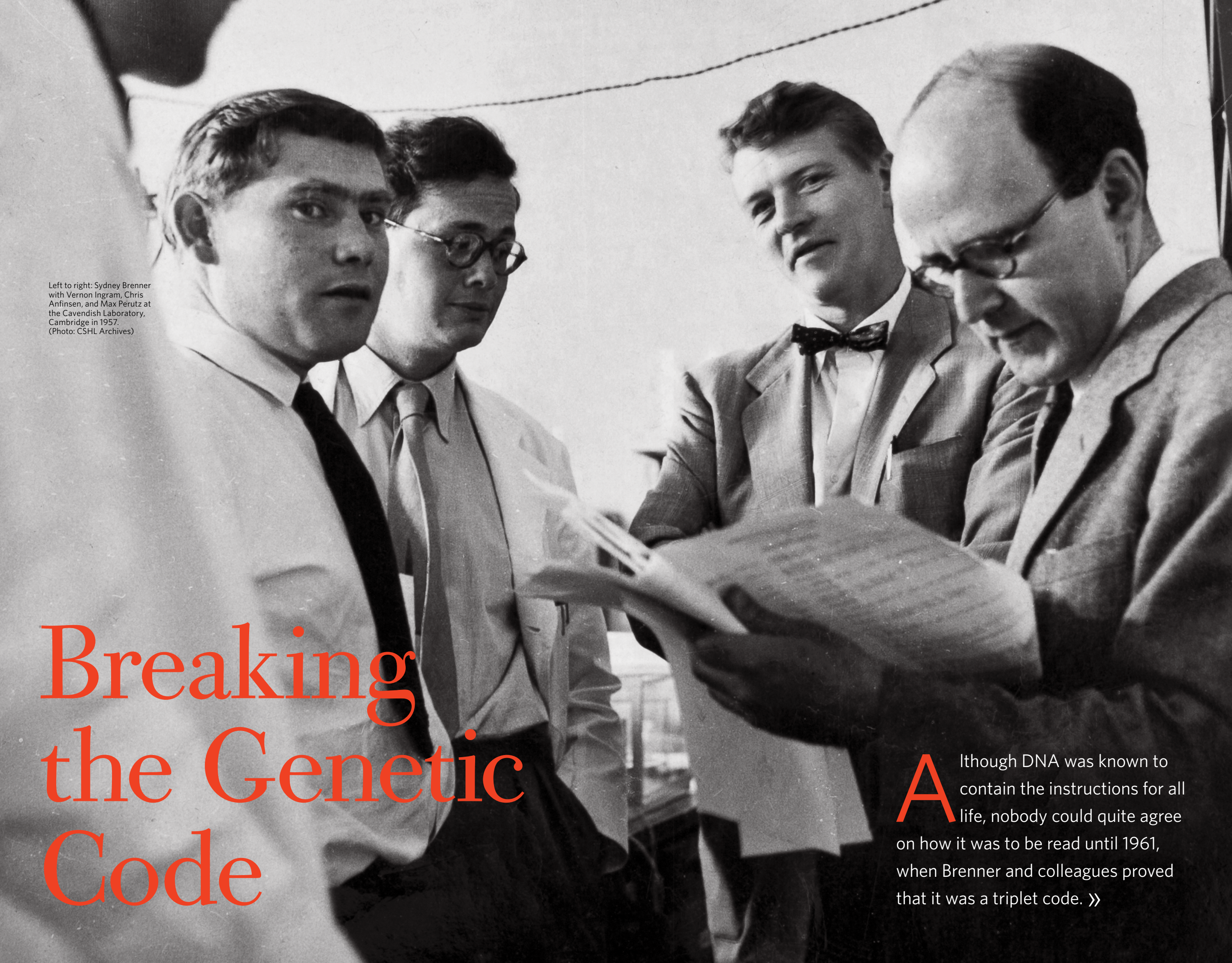
become the adaptor hypothesis. Finally, he left England for Cape Town to fulfill his obligations to the Carnegie Corporation.

Return to South Africa

On his return to Johannesburg, he set up a laboratory in the department of physiology at Wits University’s medical school. He knew exactly what he wanted to do.

Benzer’s work shattered the classical concept of the gene as a unit of mutation and recombination by showing that there were many sites of mutation in a gene and that resolution of recombination was high enough to separate adjacent base pairs. In their second paper, Crick and Watson had already proposed the essential feature of the genetic code: that the sequence of bases in DNA specified the sequence of amino acids in protein. Brenner realised that if he could find the right gene and protein he could begin to analyse the correspondence of the two sequences. In his laboratory in Johannesburg, he began to study mutations that might affect the protein coat of bacteriophage T4.

Gamow’s theoretical code, known as the diamond code, was an overlapping triplet code. Brenner realised that this hypothesis might be problematic, as it would impose a constraint on the number of dipeptide sequences, so he began to collect peptide sequences from the literature. By the end of 1954, he could provide a statistical argument to rule out overlapping codes, and with additional data was then able to obtain a proof. He circulated his findings in 1956 to the other members of the RNA Tie Club (see photo), in a note called “On the impossibility of all overlapping triplet codes”. Gamow later communicated the paper to the *Proceedings of the National Academy of Sciences*, where it appeared in 1957. ■



Left to right: Sydney Brenner with Vernon Ingram, Chris Anfinsen, and Max Perutz at the Cavendish Laboratory, Cambridge in 1957. (Photo: CSHL Archives)

Breaking the Genetic Code

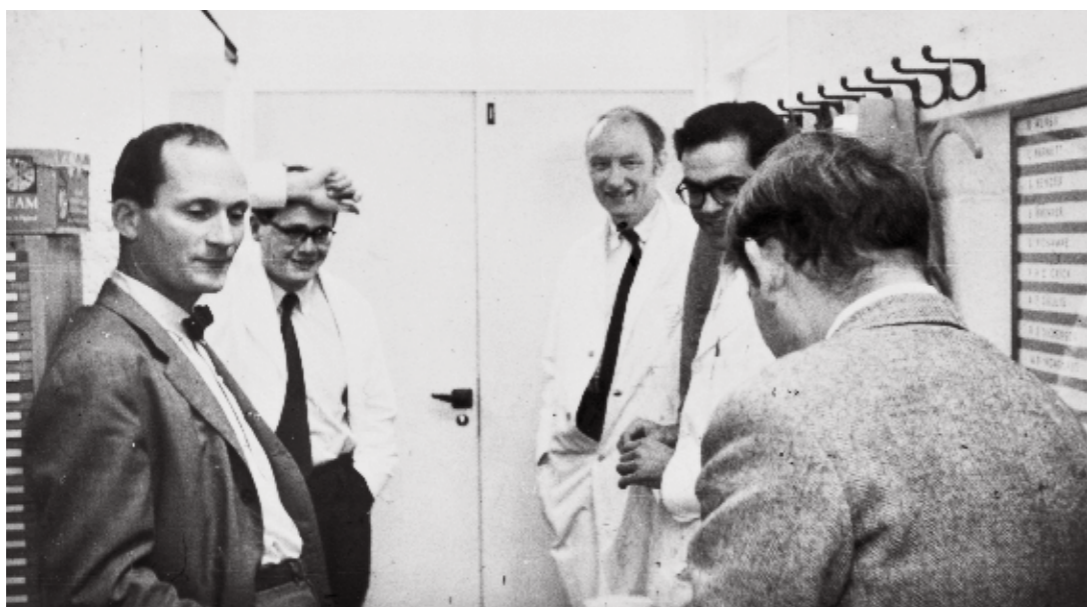
Although DNA was known to contain the instructions for all life, nobody could quite agree on how it was to be read until 1961, when Brenner and colleagues proved that it was a triplet code. »

On camera: Sydney Brenner, holding a model of a phage, alongside Raymond Baxter, host of "What is Life?", a BBC television programme. Behind them, from left to right, are models of the tobacco mosaic virus, turnip yellow virus, and DNA. (Photo: the BBC)



Jacques Monod and Sydney Brenner in 1960. (Photo: CSHL Archives)

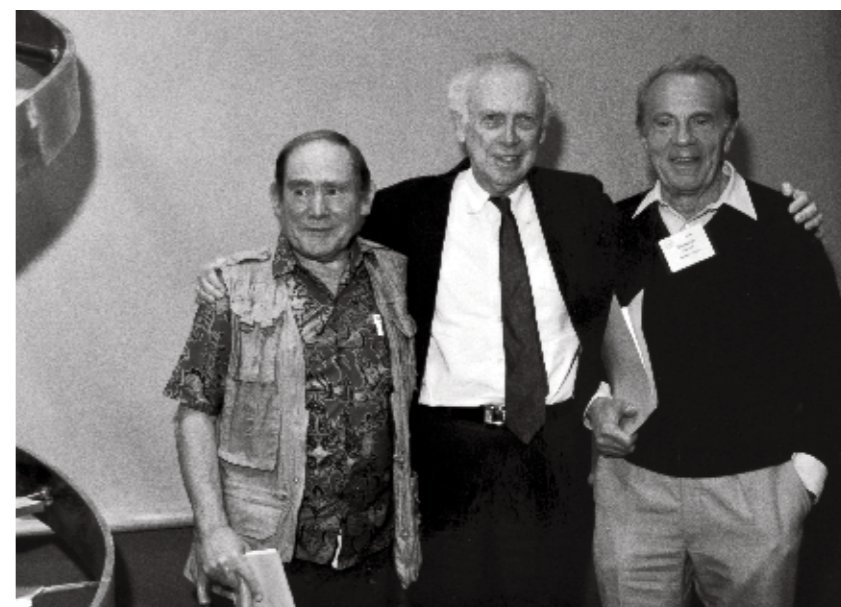
Sydney Brenner and James Watson at the Symposium on Quantitative Biology. (Photo: CSHL Archives)



Francis Crick (centre) and Sydney Brenner (far right).

François Jacob and Sydney Brenner in 1985.

Sydney Brenner with James Watson (centre) and François Jacob (right) at CSHL in 1990. (Photos: CSHL Archives)



» Following his adventure in the US, Brenner spent "a frustrating and lonely" two years in South Africa. Despite his isolation, he maintained a lengthy correspondence with colleagues such as Francis Crick and Gunther Stent. Eventually, Crick was able to secure a position for him with the Medical Research Council (MRC) unit in the Cavendish laboratory. In December 1956, Brenner left South Africa for England to join Crick in building up molecular genetics in what was essentially a laboratory for protein crystallography.

It was the start of a long fruitful intellectual collaboration with Crick; they shared an office in the MRC unit and continued to do so at its successor, the MRC Laboratory of Molecular Biology.

The next five years would see explosive developments in molecular biology.

In Cambridge

Brenner set up a laboratory in a crowded space in the basement of the Cavendish laboratory. Later, they were able to acquire more space on the Cavendish site. He continued to search for a gene-protein system in bacteriophages. He found a new method of "negative staining" for electron microscopy and used it powerfully in his work on the structural components of bacteriophages—all the while continuing to work on the genetic code.

In Gamow's code, the amino acids are recognised by "cavities" on the DNA, and thus polypeptides are assembled directly on the gene. Nobody believed in this and indeed there was considerable evidence that RNA might be involved in the protein synthesis. Cells contain large amounts of RNA in the form of ribosomes and there was clear

evidence that the ribosomes are involved in protein synthesis. But there were difficulties with this idea: ribosomal RNA has a constant base composition in many different bacteria whereas the DNA base composition varies over an enormous range. Furthermore, in the Pasteur Institute in Paris, Jacques Monod, François Jacob and Arthur Pardee working on β -galactosidase "inducibility" showed that synthesis of the enzyme starts immediately after the gene enters the cell and is shut down immediately after the inducer is removed. To explain their results, they postulated Factor X, an unstable intermediate between the gene and the enzyme.

One cold Good Friday morning in 1960, Jacob, Brenner, Crick and some other visiting scientists attended a meeting in Brenner's room at King's College in Cambridge University where he was a fellow. There

was a long discussion about the Paris experiments when Brenner suddenly leaped up, and as described by Crick and Jacob in their autobiographies, and began to talk at an extremely rapid rate. He had seen the light, remembering that a minor RNA made after phage infection had been discovered by Elliot Volkin and Lazarus Astrachan and was thought by many to be a precursor to DNA. It had all of the properties required of an intermediate and its base composition was the same as that of the phage DNA.

By that evening, Brenner and Jacob had formulated the experiment. Because Jacob was going to spend a month in Caltech in July 1960, it was decided that Brenner would join him there and they would work with Matt Meselson who had all the heavy isotopes of carbon and nitrogen to prove the existence of messenger RNA.

“I learnt very quickly that the only reason that would be accepted for not attending a committee meeting was that one already had a previous commitment to attend a meeting of another organisation on the same day. I therefore invented a society, the Orion Society, a highly secret and very exclusive society that spawned a multitude of committees, sub-committees, working parties, evaluation groups and so on that, regrettably, had a prior claim on my attention. Soon people wanted to know more about this club and some even decided that they would like to join it. However, it was always made clear to them that applications were never entertained and that if they were deemed to qualify for membership they would be discreetly approached at the appropriate time.”

Sydney Brenner, *Loose Ends* (1997)

But in Pasadena, experiment after experiment failed, as the ribosomes disintegrated in the density gradient generated by centrifuging 8 molar caesium chloride solutions for 24 to 36 hours in a high-speed centrifuge. Near the end of their visit, they went to Malibu Beach with a friend, and Brenner then realised what was needed.

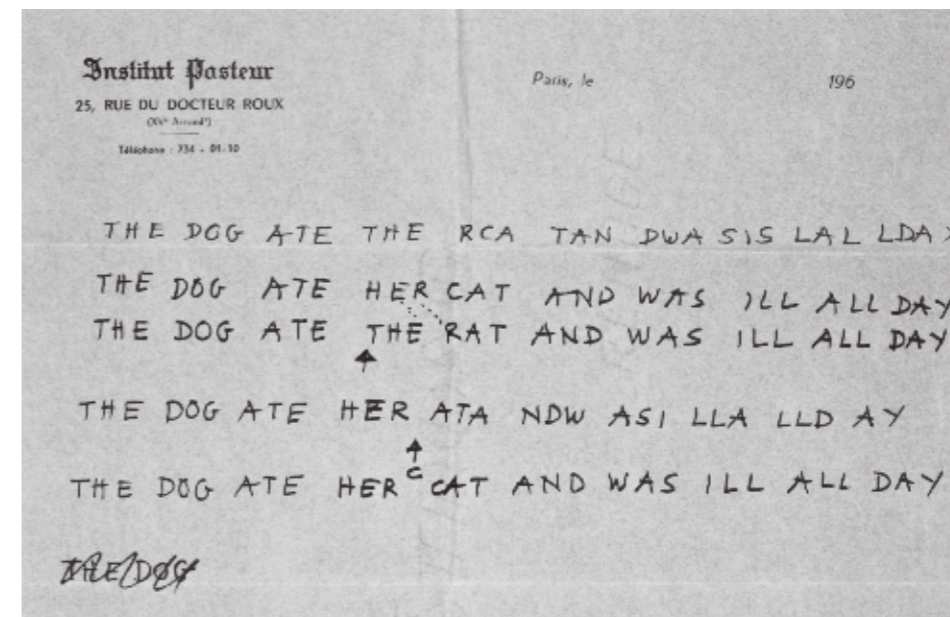
“It’s the magnesium!” he cried. He realised that the concentrated caesium salt had displaced the magnesium, which was present only at a thousandth molar. They quickly returned to the lab and did one last experiment with added magnesium. They had to endure the agony of carrying the rotor carefully from a centrifuge that had broken down to one in another lab but in the end they proved that no new ribosomes are synthesised after phage infection and that new RNA becomes attached to old ribosomes.

After performing further experiments

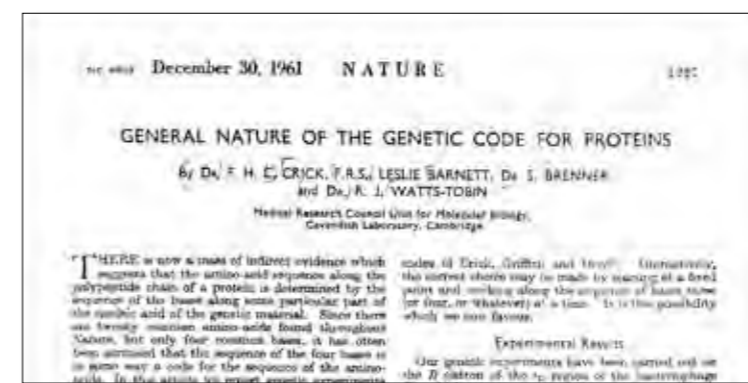
to complete the work, Brenner, Jacob and Meselson authored a paper titled “An unstable intermediate carrying information from genes to ribosomes for protein synthesis”, which was published together with a paper by Watson and his collaborators in Harvard University, who showed a similar unstable RNA revealed by pulse labelling of *E. coli*.

Frameshift mutants

In 1957, Benzer came to the MRC on a year’s sabbatical. He had been working on chemical mutagens and had constructed spectra of occurrences of the induced mutations. Proflavine, an acridine dye, had been found to interfere with phage assembly and was known to also produce some mutants. Brenner and Benzer decided to generate a set of *rII* mutants and map them. The *rII* mutants and mutants induced by other mutagens were not used until



Triplet codon word games by Sydney Brenner. (Photo: CSHL Archives)



The groundbreaking 1961 paper in *Nature*—Sydney Brenner’s second that year. (Photo: Nature Publishing Group)

Crick decided he would try to study what were called intragenic suppressors where a mutation in one part of the gene could be compensated by a second mutation in another part of the gene. He started with a set of base analogue mutants but did not find very much. However, when he used the proflavine mutants he found them abundantly in the first part of the *rII* B gene.

It was at first difficult to explain these findings but one Saturday morning in 1961, while having lunch with Crick at The Eagle pub, Brenner postulated that the proflavine mutations are of a completely different class. They could be additions and deletions of bases and correspond to the plus and minus categories that Crick had arbitrarily assigned to the mutants and suppressors. A “don’t worry” theory of how they are produced could be provided by the known intercalation of proflavine dyes into the DNA structure. Single mutations would

produce disastrous changes in the protein.

Brenner immediately went to do the experiments, showing that proflavine mutants could not be obtained in a gene that specified an essential protein for the phage. His results were published in a paper titled “The theory of mutagenesis” in 1961 in the *Journal of Molecular Biology*.

Crick and Brenner realised they could also use proflavine to decide on the size of the codon. By constructing triple mutants of the same sign, they proved that the coding unit was a triplet. Their 1961 paper (see photo), “General nature of the genetic code for proteins”, was heralded as a classic in molecular biology. Without the frame shift theory it would be difficult to explain an apparent puzzle: how pairs formed from the three mutants, A, B and C—e.g. AB or BC—are still mutant; and yet when the pairs are crossed to generate a triple, function is restored. ■

Governing board of the Laboratory of Molecular Biology (LMB), October 1967. Left to right: Hugh Huxley, John Kendrew, Max Perutz, Francis Crick, Fred Sanger, Sydney Brenner. (Photo: MRC Laboratory of Molecular Biology)

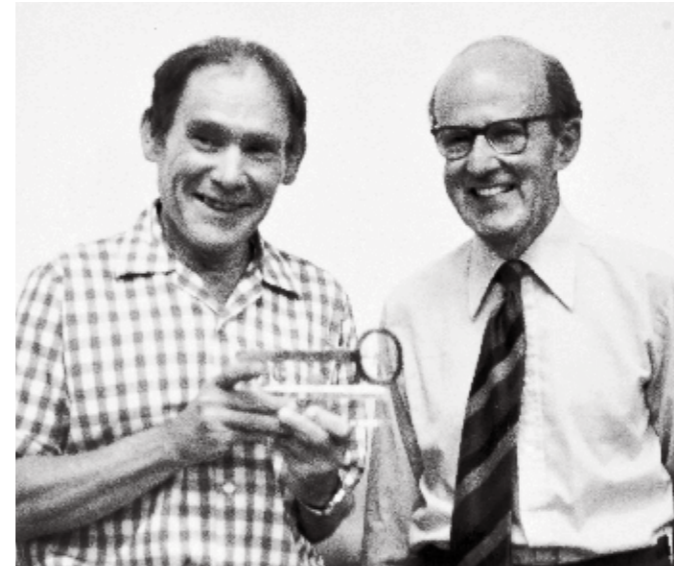
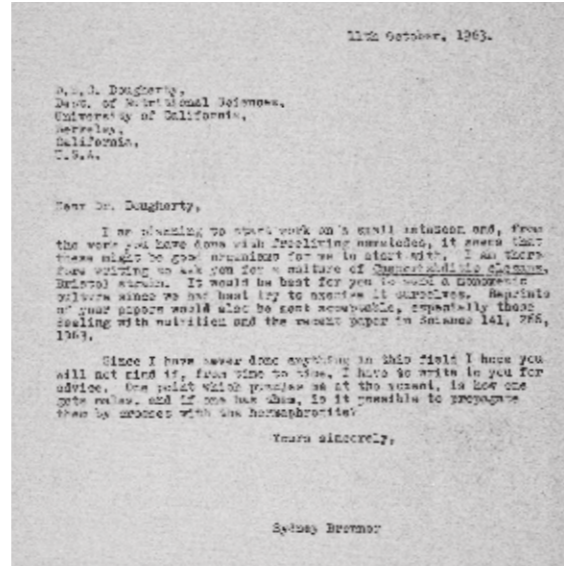
Molecular biology's golden age in the 1950s gave rise to a new era of developmental genetics in the 1960s. »

Genes, and More Genes



C. elegans under the microscope.

In a 1963 letter to *C. elegans* scientist Ellsworth Dougherty, requesting a culture of the *C. elegans* Bristol strain, Sydney Brenner asks, "One point that puzzles me at the moment is how one gets males, and if one has them, is it possible to propagate them by crosses with the hermaphrodites?" It turns out that most *C. elegans* adults are hermaphroditic and self-fertile; on occasion, a hermaphrodite yields a pure male, allowing conventional genetic analysis. (Photos: CSHL Archives)



“As a more long term possibility, I would like to tame a small metazoan organism to study development directly. My ideas on this are still fluid and I cannot specify this in greater detail at the present time.”

A 1963 letter by Brenner to LMB director Max Perutz

» 1961 was marked by the announcement by Marshall Nirenberg and Heinrich Matthaei that they had been able to programme ribosomes with a synthetic messenger RNA—polyuridylic acid—and had found that the polypeptide produced is a polymer of phenylalanine. It became clear that the code would soon be found. Brenner and Crick both decided that the central problems of molecular biology had been solved, and with the entry of many young scientists into the field, they must look for new problems.

Brenner had been impressed by the power of posing the problem correctly and having the right organism to work on. Therefore, he started to look for an experimental system that could be used to study the genes that specified the structure and function of more

complex systems such as nervous systems. Although he continued to work in what would be called classical molecular biology, by 1962 he was focussing on a small nematode worm, *Caenorhabditis elegans*.

C. elegans

He chose a small nematode with a life cycle of five days and with a fixed number of cells. His goal was to find the lineage of every cell and in particular, to determine the structure of the nervous system with electron microscopy. He also needed an organism on which he could perform genetic experiments and easily keep in a laboratory.

The Medical Research Council (MRC) supported him in this very risky project; among other things, it provided more space for the expansion of the Laboratory of Molecular Biology (LMB) in Cambridge. He started with one technician and was joined by Nichol Thomson who had been working in Lord Rothschild's laboratory. In the 1970s, his work on *C. elegans* progressed steadily but a new development in science propelled him into a totally different field.

In 1974, Stanley Cohen and Herbert Boyer reported that they had been able to clone DNA by inserting fragments into plasmid, which they could propagate in a bacterial host. There had also been considerable work done on characterising the DNA genomes of small viruses such as SV40. Amidst these developments, there were concerns about the escape of pathogens from laboratories and an increased concern that recombinant DNA, as it was called, might create completely

“I immediately took over the financial management of the laboratory and spent several years in trying to get the finances on a proper basis. These were times of hyperinflation in Britain and not enough attention had been given to the rising costs of our research. I often referred to myself as the ‘epileptic’ director.”

Sydney Brenner, Nobel Prize autobiography

new pathogens. A group of scientists in the US made a public call for a moratorium on this work. In Cambridge, Fred Sanger had begun to develop techniques for sequencing DNA and Brenner realised that this together with DNA cloning could create a revolution in biology. Brenner accepted Paul Berg's invitation in 1975 to join the Asilomar conference, which had been called to discuss the moratorium. Brenner was instrumental in getting a formal motion passed almost unanimously to end the moratorium and to explore new guidelines so that the research could proceed. He returned to Cambridge and spent a considerable amount of time on this area, first by developing safe strains, which he tested on himself, and by working to obtain more rational guidelines so that the

research could proceed more effectively. Brenner also began to actively clone genes from the nematode. His *C. elegans* research had begun to attract attention and from the mid 1970s an increasing number of young scientists came to Cambridge to join him. Many were post-doctoral fellows who, upon their return to the US, established their own laboratories doing research on *C. elegans*, making it a successful global enterprise.

The “epileptic” director

In 1977, the MRC appointed Brenner as proleptic (anticipatory) director to succeed Max Perutz when he retired in 1979. Three days before his official start date, Brenner rode his motorcycle to the police station to deliver a wallet he had found. On his way

Sydney Brenner receives the key to the LMB from departing director Max Perutz in 1979. The letters AUG, which refer to the initiator codon for protein synthesis, were inscribed on the key.

Left to right: Leslie Barnett, Francis Crick, and Sydney Brenner at a blackboard in the Laboratory of Molecular Biology, circa 1986. (Photos: MRC Laboratory of Molecular Biology)

2002 Nobel Laureates in Physiology or Medicine. Left to right: Sydney Brenner, Bob Horvitz and John Sulston.



Left to right: Queen Silvia, May Brenner, King Carl XVI Gustaf and Sydney Brenner.

NOBEL PRIZE CITATION

The Nobel Prize in Physiology or Medicine 2002 was awarded jointly to Sydney Brenner, H. Robert Horvitz and John E. Sulston “for their discoveries concerning genetic regulation of organ development and programmed cell death”.

Sydney Brenner receiving his Nobel Prize from His Majesty the King at the Stockholm Concert Hall. (Photos: CSHL Archives)



“Organisms survive on this planet, because some are able to make the complex molecules using elementary sources such as nitrogen, hydrogen and carbon dioxide, and harness the primary source of energy which comes from the Sun. Biological evolution depends on the food chain at each level—organisms survive by eating others lower in the food chain. My research depended on a chain. I began my research with *E. coli* and bacteriophage which eats bacteria from the inside. I then moved up a level, and using much the same tools began to work on nematodes which eat *E. coli* from the outside. I then worked on fish which eat worms and finally on humans who eat fish. In the end we are eaten by microorganisms and worms to start the cycle again.”

Sydney Brenner’s Food Chain of Research, for the 2014 re-opening of the Brenner Library in Singapore.

out, a car hit him. A compound fracture in his left knee took more than a year to heal; he has had to use a cane ever since.

During his directorship, the LMB continued to grow as a research institution with a unique style and performance. The LMB’s alumni now include many Nobel Laureates, including five of Brenner’s former post-doctoral fellows—John Sulston, Martin Chalfie, Bob Horvitz, Sidney Altman and Andrew Fire.

In 1983, his scientific “progeny” organised a special symposium for him. Three years later, Brenner retired as director of the LMB.

***C. elegans* postscript and Nobel accolades**

Few scientists make their mark on even one specialised field of research, but Brenner has left an indelible mark on many. In 2002, Brenner and two of his former post-doctoral fellows, John Sulston and Bob Horvitz, were jointly awarded the Nobel Prize in Physiology or Medicine for their pioneering use of the nematode worm as a model for understanding human biology.

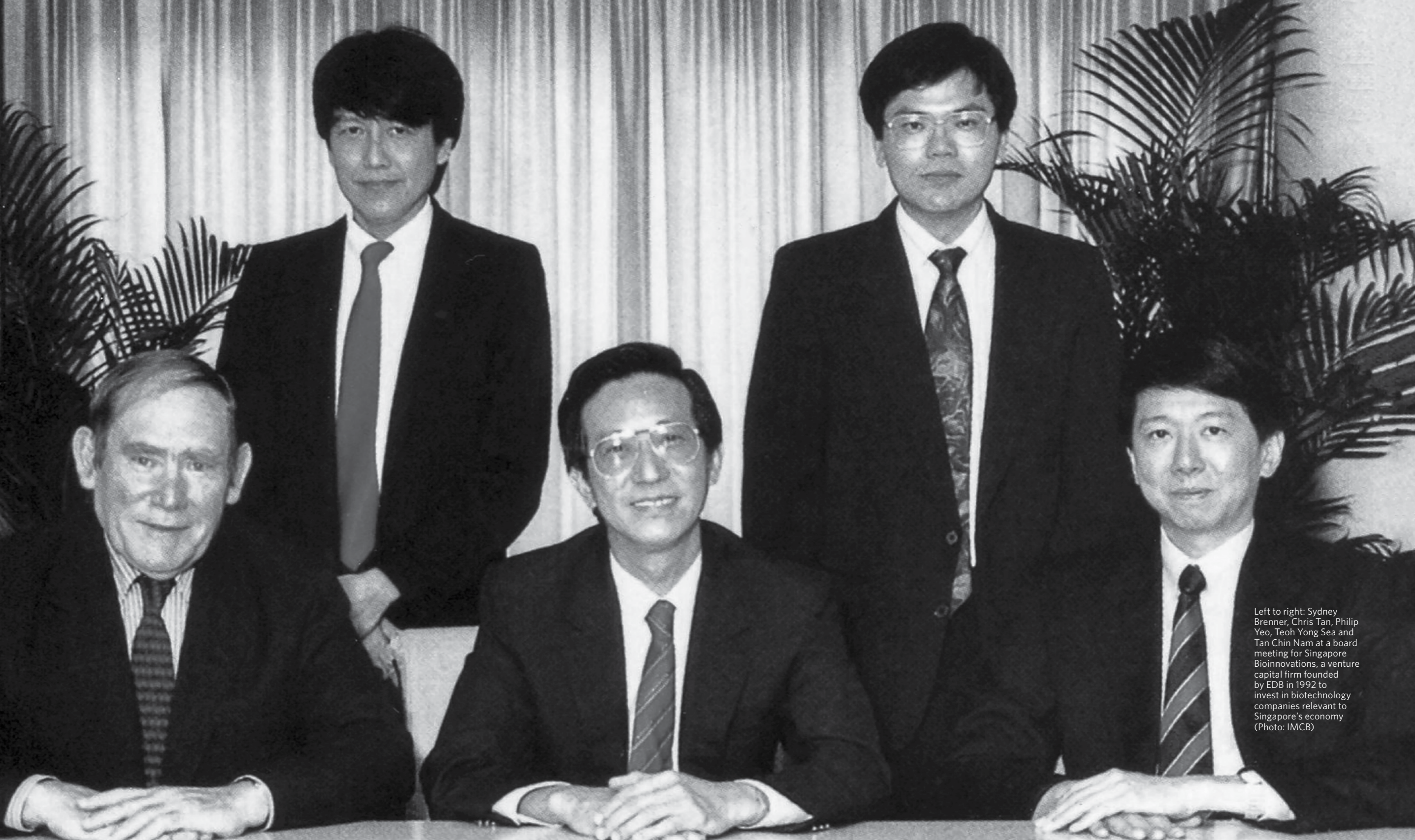
The title of Brenner’s Nobel lecture in December 2002, “Nature’s Gift to

Science”, was an homage to this modest nematode. Brenner believes choosing the right organism to study is as important as addressing the right problem.

While director, he continued his research and another project was completed and published. The work on the structure of the nervous system of *C. elegans*, which had been continued by John White and Nichol Thomson, was published as a 300-page paper in the *Philosophical Transactions of the Royal Society*. It was the product of 20 years of research, and it would take 20 more for other such projects to be initiated. Brenner likes to call it anatomy; today it has a new name: connectomics.

In 1998, thanks to a consortium of researchers in the UK and the US led by Sulston, *C. elegans* became the first multicellular organism to have its complete genome sequenced.

Brenner is nicknamed the “father of the worm”. In recognition of his pioneering role in spawning a global research community that works on *C. elegans*, two researchers in 2007 gave a closely related nematode the scientific name *Caenorhabditis breneri*. ■



Left to right: Sydney Brenner, Chris Tan, Philip Yeo, Teoh Yong Sea and Tan Chin Nam at a board meeting for Singapore Bioinnovations, a venture capital firm founded by EDB in 1992 to invest in biotechnology companies relevant to Singapore's economy (Photo: IMCB)

In 1984 Sydney Brenner visited a tiny island in South-east Asia for the first time. Since then, his enduring guidance and influence have indelibly shaped the course of Singapore's biomedical science and industry. »

Mentoring a Young Nation

Sydney Brenner scrutinising a scorpion delicacy offered by Deputy Prime Minister Goh Keng Swee (right), during Brenner's 1984 visit to Singapore. The delicacy came from a recent trip by Goh to China.



Sydney Brenner and Deputy Prime Minister Teo Chee Hean, thirty years later, at the IMCB 30th anniversary in 2015. (Photos: IMCB)



“I stressed to both Philip [Yeo] and the NSTB that the only way that biomedical research and commercial spin-offs from such research could evolve and prosper in Singapore was by establishing a single agency that oversaw all biomedical research, from molecules to mind—and nothing else.”

Sydney Brenner at the 2014 re-opening of the Brenner Library in Singapore.



The old IMCB building at Medical Drive, renamed the Brenner Centre for Molecular Medicine. (Photo: IMCB)



Biopolis, a sprawling scientific hub at Singapore's One North campus. (Photo: A*STAR)

» It all began in 1981, when Brenner started consulting for British financier Victor Rothschild's Biotechnology Investments Limited. It was Rothschild who recommended Brenner to the Singapore government, which was eager to diversify the country's economy away from low-cost manufacturing to other industries, such as biotechnology.

Brenner came to a meeting in Singapore in 1984. He later discovered that this invitation had come from Dr Goh Keng Swee, then deputy prime minister.

During this visit, Brenner met Lee Kuan Yew, then prime minister of Singapore, and wrote a short proposal to set up a research institute in molecular and cell biology to train Singaporeans at the PhD level, who could then provide the country with the necessary biotechnology infrastructure. When Lee remarked that Singapore was

a nation of technicians and not scientists, Brenner candidly replied, “Prime Minister, if you don't do something like this, you will remain a nation of technicians.” A decision was made in 1985 to create the Institute of Molecular and Cell Biology (IMCB)—a name Brenner had suggested. That year, he also returned to Singapore to give a lecture on biology under the aegis of the Lee Kuan Yew Distinguished Visitors Programme.

The IMCB was initially part of the National University of Singapore, and Brenner became the founding chairman of its scientific advisory board, a position he held until 1995. He returned several times a year to Singapore and started a laboratory in IMCB in 1990.

Fishy genetics

Brenner often recounts J. D. Bernal's comparison of scientific research to the game of chess. Most scientists play the

middle game, which is tedious, and too few have the chance to play the end game; thus the only alternative is to play the opening game. Believing that his forte lies in the opening game, in 1986 Brenner retired early from his directorship of the Laboratory of Molecular Biology to pursue a new scientific problem. He left to start a new Medical Research Council unit of molecular genetics in a laboratory in the department of medicine at Cambridge University's Clinical School. The time was ripe—with technological advances, the tools were finally available to study the genetics of everything through the sequencing of DNA. In fact, there had been several meetings on this topic and in 1985 there was a meeting in Santa Cruz to discuss the project of sequencing the human genome. He became a strong supporter of the project but he also recognised that it was not technically feasible at the time.

However, Brenner had read extensively in the library of the Woods Hole Institute where he taught a physiology course in the late 1960s. He found Ralph Hinegardner's papers reporting the small size of the genome of the Japanese pufferfish, *Takifugu rubripes* (or *fugu*). He decided that he would work on this genome and it became his project in his lab in Cambridge and the lab he established in the IMCB. Byrappa Venkatesh joined him in this endeavour and today is the head of a laboratory in IMCB. Many of the doctors who Brenner took for training in Cambridge also worked with him there on the *fugu* genome.

In 1992, Brenner published a paper showing that the *fugu* had the same gene repertoire as humans, but its genome was only one-eighth the size. Brenner tried to get additional support for this work and often called the *fugu* the “discount genome”

“My view at the time was that we should treat the human genome like income tax and find every legitimate way of avoiding sequencing it.”

Sydney Brenner's Nobel lecture, "Nature's Gift to Science", 8 December, 2002

Sydney Brenner in his IMCB laboratory in 1992, where he is working on a *fugu* specimen. (Photo: IMCB)



Sydney Brenner's 88th birthday dinner in 2015. Front row, left to right: Byrappa Venkatesh, Lim Chuan Poh, Sydney Brenner, Philip Yeo, Jonathan Balkind. (Photo: IMCB)

as it offered an almost 90 percent discount on the cost of sequencing.

With strong support from Singapore, a consortium led by Brenner, Venkatesh and Sam Aparicio of the Joint Genome Institute of the US Department of Energy and Celera was formed to sequence the 400 megabase *fugu* genome. The paper was published in *Science* in 2002. Brenner, Venkatesh and Aparicio received Singapore's National Science Award for this work in 2004.

From the "big fishtank" to the open waters

In tandem with these research initiatives, Singapore had begun to nurture a biotechnology industry. In 1988, Philip Yeo, then chairman of Singapore's Economic Development Board (EDB), set up the National Biotechnology Committee to spearhead the venture into biotechnology, with Brenner as a member.

Brenner and Yeo's friendship and professional relationship steadily grew over the years. Their opportunities for collaboration were boosted in 2000, when the Singapore government committed a large investment for a major research and development initiative.

In 2001, the National Science and Technology Board (NSTB) was renamed the Agency for Science, Technology

and Research (A*STAR), with Yeo as its chairman. A*STAR's governing mandate was broadened to encompass all of Singapore's various scientific research institutes.

Brenner not only helped Yeo to recruit scientists to work at A*STAR, but he also worked on developing Yeo's plans. Yeo set aside S\$1bn to train new Singaporean scientists but they had difficulties in their negotiations with the universities. "I think it was a Friday morning," Brenner recalls. "I said, 'Why don't we start our own graduate school? We don't have to give out degrees but we will have the best mentors in Singapore.' And on Monday, it was done." The A*STAR Graduate Academy (A*GA) was formed.

Since 2003, A*GA has sent more than 1,400 young Singaporeans overseas to be trained in the physical, biomedical and engineering sciences. More than half have returned and begun work at A*STAR's research institutes, local universities and other institutions across Singapore—a long-term investment that is paying off significantly.

Meanwhile, A*STAR's biomedical research institutes are now housed in Biopolis, another name Brenner coined. According to him, the Singapore accent makes Biopolis sound like a place where "biology could be policed". Biopolis is a new scientific hub in Singapore's One North

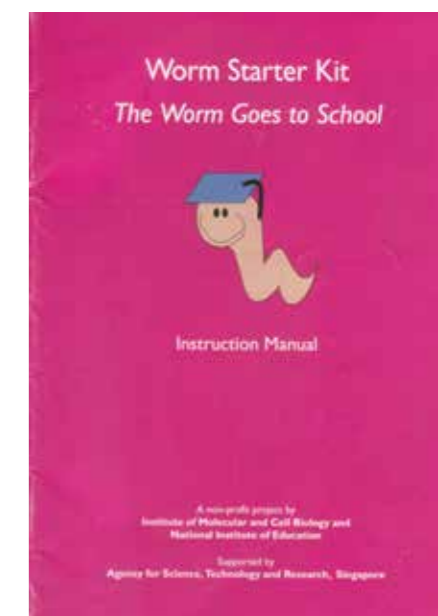
campus, which will collectively house more than 16,000 scientists and engineers from the public and private sectors by the end of 2015. IMCB's previous building, affectionately known as the "big fishtank" for its iconic blue glass façade, has since been renamed the Brenner Centre for Molecular Medicine.

Singapore's 50th birthday

Since 1984, in his capacity as a trusted advisor on scientific policy to the Singapore government, Brenner has been instrumental in establishing Singapore as a biomedical research centre of international repute.

Today, he continues to serve on the boards of A*STAR and Singapore's International Advisory Council for the Health and Biomedical Sciences, where his incisive wit and candid remarks never fail to make meetings memorable.

In 2015, the same year as Singapore's Golden Jubilee anniversary, A*STAR, Cold Spring Harbor Laboratory, Nanyang Technological University and National University of Singapore organised the Sydney Brenner Symposium and Exhibition to celebrate the life and work of Sydney Brenner. Many of Brenner's former colleagues, post-doctoral fellows and students have been invited to attend. ■



The cover of the instruction manual *The Worm Goes to School*. In 2003, IMCB, in collaboration with the National Institute of Education, launched a teaching kit to introduce to Singaporean students the worm as a tool for understanding the relationship between genes, appearance and behaviour. (Photo: IMCB)

“I don't think
it's finished
yet”



Sydney Brenner
lecturing in 1975.
(Photo: CSHL Archives)

RNA, w/ cat
ly AP — ERNA — after protein synthesis

(a) peptides 5-10 a.a $10^5 - 10^{10}$

WORD metallopeptide H, C, D, E, Y + Fe, Zn, Mn, Ca etc.

(b) concatenate peptides at random

PHRASE → 3d novel function, improved domain 100

(c) Join domain to gene

Well into his eighties, Sydney Brenner continues to demonstrate the same passion for science and commitment to his students as he always has. »

Sydney Brenner received the inaugural Honorary Singapore Citizen Award from President S. R. Nathan in October 2003. Left to right: May Brenner, Sydney Brenner, President Nathan, Mrs Nathan and Minister George Yeo, minister for trade and industry (Photo: IMCB)



“As was predicted at the beginning of the Human Genome Project, getting the sequence will be the easy part as only technical issues are involved. The hard part will be finding out what it means, because this poses intellectual problems of how to understand the participation of the genes in the functions of living cells.”

Sydney Brenner, *Loose Ends* (1997)

» Brenner has been a part of many molecular biology developments around the world. In the early 1960s, he helped to found the European Molecular Biology Organization (EMBO) and then later worked for many years with John Kendrew in the establishment of the European Molecular Biology Laboratory (EMBL) in Heidelberg. From 1985 to 1999 he was a visiting fellow and consultant at the Central Research and Development Department of DuPont, a chemical company, in Delaware. When he retired from the Laboratory of Molecular Biology, he moved some of his activities to La Jolla, California and became affiliated with the Salk Institute and also with the Scripps Institute where he initiated research in combinational chemistry. He also started a fruitful collaboration with Sam Eletr, the founder of Applied Biosystems Incorporated (ABI), where the first instruments were built for protein and nucleic acid sequencing. Brenner then realised that new techniques of nucleic acid sequencing would be needed and thus he joined Lynx Technologies, which had been founded by Eletr when he left ABI. Together they developed

a new technique for sequencing large numbers of DNA molecules at the same time. This technique, called “massively parallel signature sequencing”, was the basis of what has become known as next-generation sequencing. Illumina later acquired Lynx, but Brenner continued his interest in DNA sequencing. In 2005, Brenner and Eletr, together with Philip Goelet, founded a new company, Population Genetics, to develop Brenner’s new inventions.

Brenner founded the Molecular Sciences Institute (MSI) in 1996 in La Jolla, with a grant from the Philip Morris Company. His aim was to give young scientists an opportunity to develop their own research. MSI was moved later to Berkeley.

Brenner was also for many years associated with the Basel Institute of Immunology, and he served as an advisor to the Gulbenkian Foundation and as chairman of the Scientific Committee of the IGC, a successful research institute in Lisbon. In 2004, he became founding president of the Okinawa Institute of Science and Technology, a new graduate university

in Japan. He still maintains a research programme there.

In addition to his many scientific activities, he wrote a monthly column from 1994 to 2000 in the journal *Current Biology*. Initially called “Loose Ends”, it was later moved to the front of the journal as “False Starts”. In some of these he wrote as Uncle Syd to his nephew Willie, whom he advises throughout his scientific career. Brenner often complains that he had become more famous for his columns than for his scientific work.

Epilogue

If you think that Brenner has relaxed with age and is no longer involved in research, you have only to visit his office or home in La Jolla or Washington D.C. in the US, or Ely in England, or in Fusionopolis in Singapore, where you will find piles of books and papers covering his many scientific interests.

In Singapore, where he now spends most of his time, he continues his work with Venkatesh in comparative genomics. His latest endeavour, the Molecular Engineering Laboratory, was founded

in 2009 with the intent of providing an opportunity for young Singaporean scientists to develop their own research in a broad interdisciplinary field involving the design, manipulation and synthesis of molecules for research and industrial applications. Shawn Hoon, a young scientist who worked as a student with Brenner and Venkatesh on the *fugu* genome, leads the laboratory. This has been successful enough to create a second laboratory, MEL2, to work in the field that Brenner calls “human biology”. The discovery that human cells could be reprogrammed to become pluripotent stem cells, completed the last requirement for research into the molecular and cellular bases of the development and function of humans. Brenner has long been an advocate of this field; and believes that the long scientific journey of molecular biology has to end in the study of “*Homo Sapiens: the unique animal*”. We are, Brenner says, the only animal that invented science and has the ability to predict and control our future, and we need to know everything about ourselves. ■

A 1987 group portrait of Sydney Brenner and colleagues in Japan. (Photo: CSHL Archives)

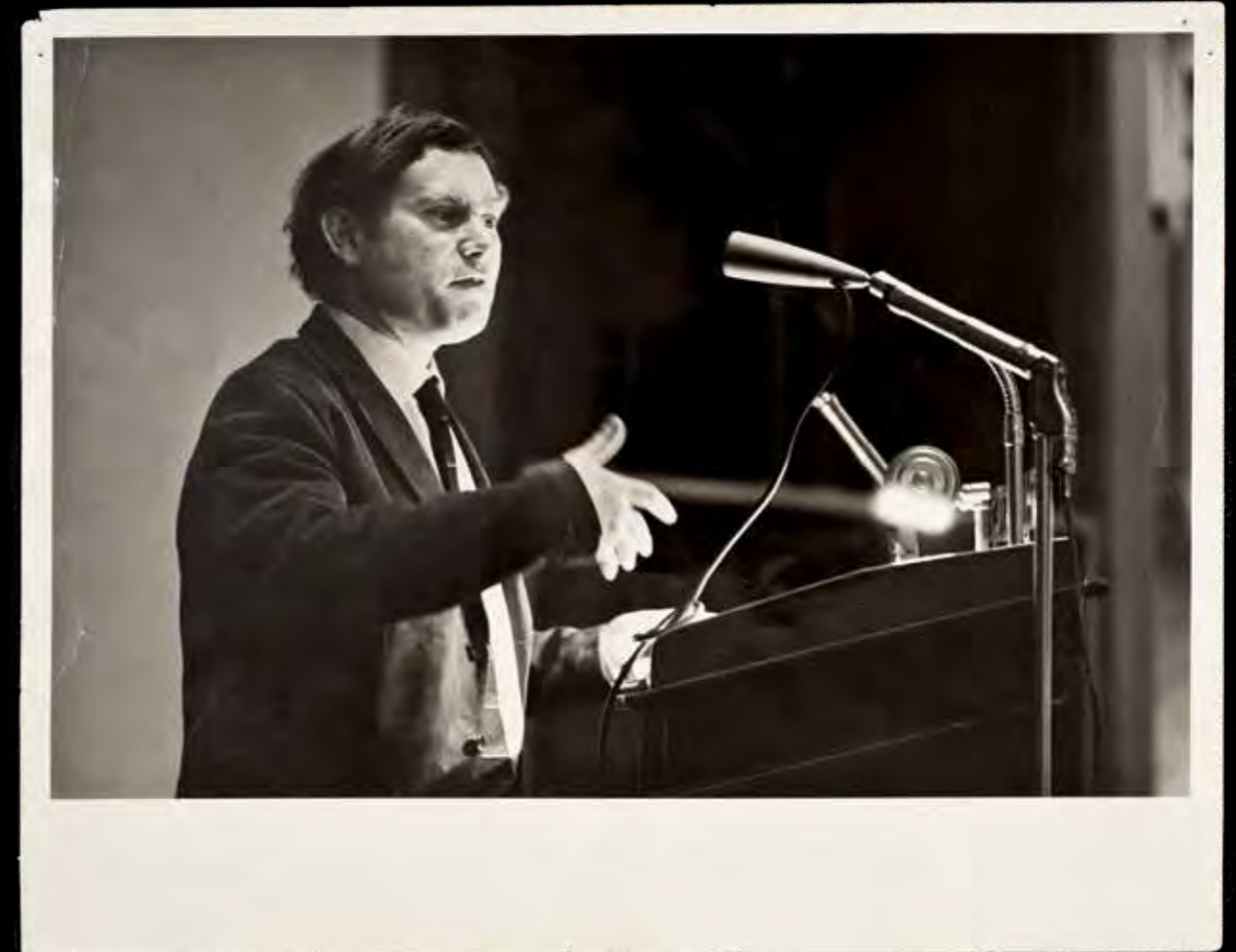
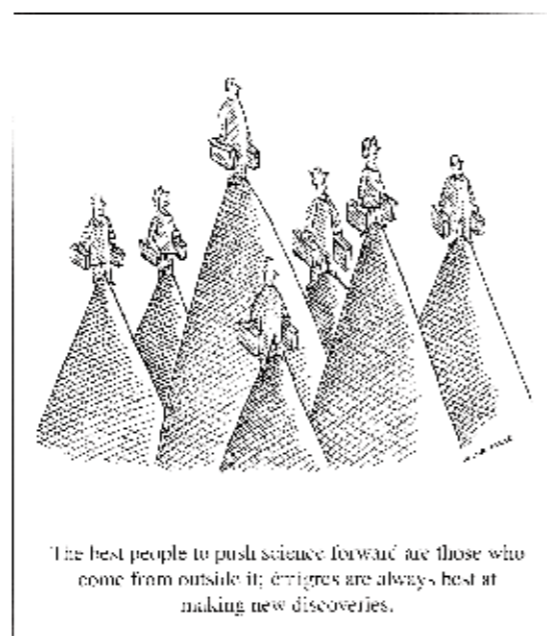
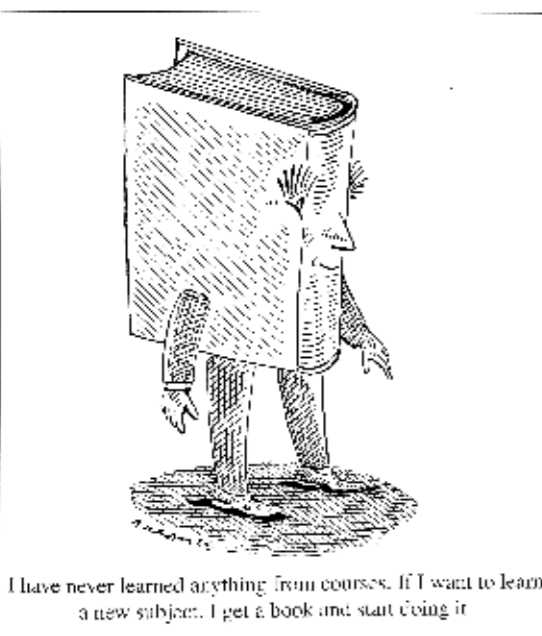
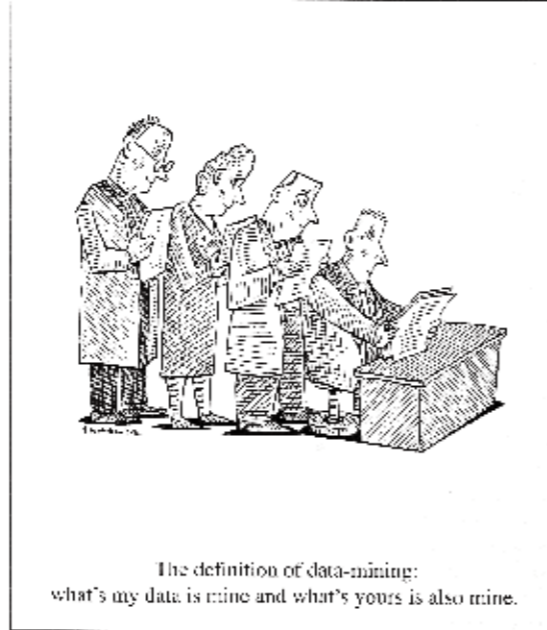
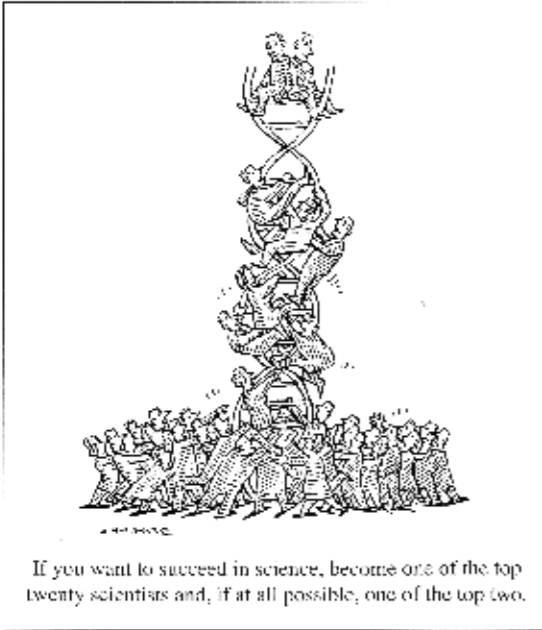
Sydney Brenner with members of MEL. (Photo: MEL)



Loose Ends, a collection of Sydney Brenner’s articles, was published in 1997 by *Current Biology*. (Photo: Current Biology)

Quotes from Uncle Syd

Comics from Sydney Brenner's Loose Ends monthly column in *Current Biology*. (Photos: Current Biology)



Sydney Brenner giving a lecture in 1960. (Photo: CSHL Archives)

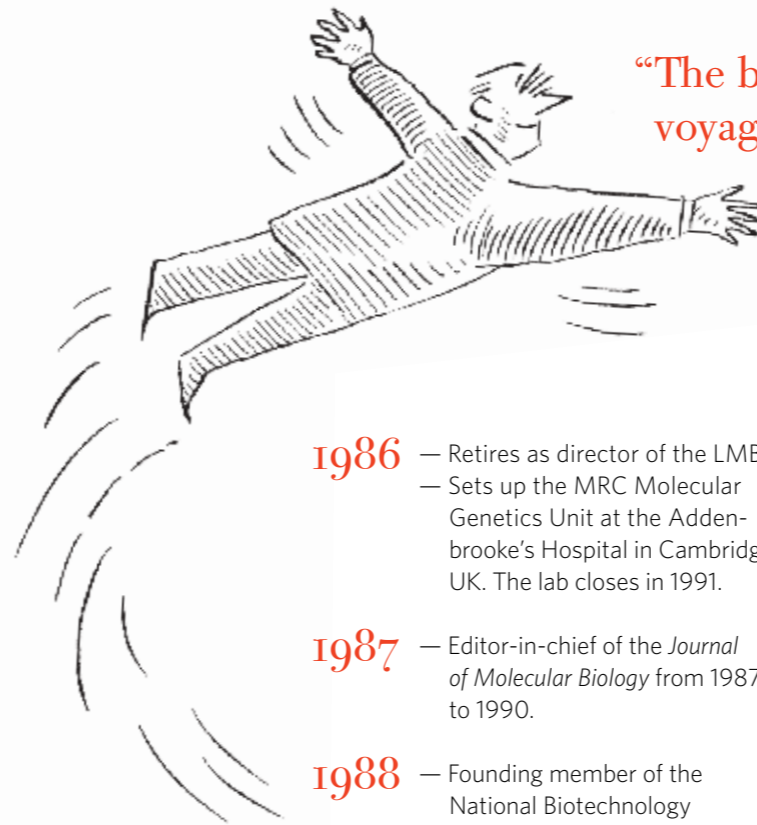
“I think it’s the greatest adventure in the world to really know at a given point that you’re the only person in the world that knows something new. That’s a thrill that’s worth it.”

Sydney Brenner, interview for SG50 book *Singapore’s Scientific Pioneers*

SYDNEY'S VOYAGE

- 1927** — Born in Germiston, South Africa on 13 January, 1927.
- 1942** — Attends the University of Witwatersrand and completes six years of medical school, interrupted by a two-year sojourn into basic science. Graduates with a Bachelor of Medicine and Bachelor of Surgery degree in 1951.
- 1945** — Publishes first research paper on the topic of porphyrins in *The South African Journal of Medical Sciences*.
- 1946** — Expedition to the Kalahari Desert leads to a publication in the *Journal of the Natal University College Scientific Society*.
- 1949** — Publishes first sole authored paper in *Nature* on the genetics of the South African tree shrew, *Elephantulus myurus*.
- 1952** — Wins Royal Commission for the Exhibition of 1851 scholarship and begins research in the lab of Sir Cyril Hinshelwood at Oxford University, UK.
 - Marries May Covitz.
- 1953** — Views model of the DNA double helix by James Watson and Francis Crick at the Cavendish Laboratory in Cambridge, UK.
- 1954** — Receives Doctor in Philosophy degree in chemistry from Oxford University.
 - Travels across the US on a Carnegie Corporation Travelling Fellowship.
 - Returns to South Africa and sets up a lab at the University of Witwatersrand.
- 1956** — Sends note “On the impossibility of all overlapping triplet codes” to the RNA Tie Club, which was published a year later in the *Proceedings of the National Academy of Sciences*.
 - Leaves South Africa and starts work at the Cavendish Laboratory in Cambridge, UK.

- 1959** — Elected fellow at King’s College, Cambridge University.
 - Attends Copenhagen meeting where François Jacob talks about factor X.
- 1960** — Carries out mRNA experiments with François Jacob and Matt Meselson at the California Institute of Technology in Pasadena, California.
- 1961** — Publishes paper in *Nature* demonstrating an unstable intermediate carrying information from genes to ribosomes for protein synthesis.
 - Publishes paper in *Nature* describing the general nature of the genetic code.
- 1963** — Begins work on the *C. elegans* nematode worm.
- 1971** — Wins the Albert Lasker Medical Research Award.
- 1974** — Publishes first paper on *C. elegans* in the journal *Genetics*.
 - Wins the Royal Medal.
 - During one-year worldwide moratorium on recombinant DNA work, Brenner is called on as an expert witness for the UK’s Ashby Working Party and attends the Asilomar conference on recombinant DNA in California.
- 1977** — Suffers from a motorcycle accident three days before official start date as proleptic director of the Laboratory of Molecular Biology (LMB) in Cambridge, UK.
- 1979** — Appointed director of the LMB.
- 1981** — Non-resident fellow at the Salk Institute in La Jolla, California
- 1985** — Visits Singapore on the Lee Kuan Yew Distinguished Visitors Programme.
 - The Institute of Molecular and Cell Biology (IMCB) is founded with Brenner as chairman of its scientific advisory board, a position he holds until 1995.



“The best way to prepare for a heroic voyage in science is just to start.”

- 1986** — Retires as director of the LMB.
 - Sets up the MRC Molecular Genetics Unit at the Addenbrooke’s Hospital in Cambridge, UK. The lab closes in 1991.
- 1987** — Editor-in-chief of the *Journal of Molecular Biology* from 1987 to 1990.
- 1988** — Founding member of the National Biotechnology Committee in Singapore.
- 1989** — Scholar-in-residence at the Scripps Research Institute in La Jolla, California from 1989 to 1991. Visiting member from 1991 to 1994.
- 1990** — Wins Kyoto Prize.
- 1993** — Founding scientific advisory board member of Lynx Technologies in California.
- 1994** — Writes Loose Ends, a monthly columns for journal *Current Biology* from 1994 to 2000.
- 1996** — Founding president and director of the Molecular Sciences Institute in La Jolla, California; retires in 2001.
- 2000** — The International Fugu Genome Consortium is formed with IMCB’s Byrappa Venkatesh and Brenner at the helm.
 - Wins the Albert Lasker Award for Special Achievement in Medical Science.
- 2002** — The International Fugu Genome Consortium publishes a draft sequence of the *fugu* genome in *Science*.
 - Receives Nobel Prize in Physiology or Medicine (with Bob Horvitz and John Sulston).
- 2003** — Receives an Honorary Citizen Award, Singapore’s highest form of state recognition for non-citizens.
- 2004** — Receives Singapore’s National Science Award with Venkatesh and Sam Aparicio for their work on the *fugu* genome.
 - Receives the Order of Mapungubwe (Gold), South Africa’s highest honour.
- 2005** — Founding president of the Okinawa Institute of Science and Technology in Japan.
 - Senior fellow at the Janelia Farm Research campus of the Howard Hughes Medical Institute.
- 2006** — Wins National Science and Technology Medal, Singapore’s highest scientific honour.
- 2009** — Sets up the Molecular Engineering Laboratory at Singapore’s Agency for Science, Technology and Research (A*STAR).
- 2015** — A*STAR, Cold Spring Harbor Laboratory, Nanyang Technological University and National University of Singapore launch the 2015 Sydney Brenner Scientific Symposium and Exhibition to celebrate the life and work of Sydney Brenner.
- 2019** — Passes away in Singapore on 5 April 2019.



Comic from Sydney Brenner’s monthly column, Loose Ends. (Photo: Current Biology)

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