Ananda Mohan 'Al' Chakrabarty 1938–2020

On the morning of 10 July 2020, the biotech world lost one of its pioneers. Ananda Mohan Chakrabarty — or Al, as he was known among his friends and colleagues — was a brilliant microbiologist who in 1981 obtained the first ever US patent on a living organism, shaping legal opinion around ownership of genetically engineered organisms and unknowingly spurring unprecedented levels of biotech innovation and commercialization for years to come. The US biotech industry would not be where it is today without Chakrabarty's work, which was at the frontier of both biomedical sciences and law.

Chakrabarty was born in the small town of Sainthia in the Indian state of West Bengal on 4 April 1938. He was the youngest of seven children; his father was a merchant and his mother a homemaker. In his early days, he began to show sharp intellect, with strong interests in science and the ancient language of Sanskrit. After his early education at Sainthia High School and Ramkrishna Belur Vidyamandir, he majored in chemistry as an undergraduate at St. Xavier's College (now University) in Kolkata and later received his MSc and PhD in the emerging discipline of biochemistry from Calcutta University under the tutelage of Sailesh Chandra Roy. Chakrabarty published his PhD work in the *Biochemical Journal*. In 1965, Irwin 'Gunny' Gunsalus from the University of Illinois at Urbana-Champaign read his papers and offered him a postdoctoral position. Gunsalus trained many luminaries¹. In Gunny's lab, Chakrabarty learned about the pathways of hydrocarbon degradation in *Pseudomonas* bacteria. He remained so loyal to this genus that he was often heard to say, "I only have one e-mail address, and it is pseudomo@uic.edu."

Al's scientific journey continued for another five decades. As a research scientist at General Electric's Research & Development Center, he did not enjoy his initial project: to convert cow manure to more proteinaceous cattle feed using bacteria. At the same time, serious oil spills were becoming more regular and having adverse impacts on the environment. On weekends and evenings, he began studying degradative pathways of hydrocarbons in *Pseudomonas* with the hope that one day a genetically modified form of the bacteria would help clean up oil spills. By inserting into the bacteria multiple circular DNA

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molecules (known as plasmids), each with genes encoding different enzymatic functions in hydrocarbon degradation, he and his team were able to create a new variety of *Pseudomonas* that could degrade crude oil in Petri dishes. This was a eureka moment for Chakrabarty, who was especially excited to present his findings at scientific meetings and conferences. But his bosses at GE had a different idea. Compelled by the potential commercial application of Chakrabarty's discovery, they wanted him to file a patent on his bacteria. Chakrabarty filed a patent application in 1972 with the help of GE attorney Leo MaLossi, knowing full well that the US Patent & Trademark Office had never before granted a patent on a living organism.

After eight years of legal battle, the US Supreme Court ruled in a 5–4 decision that his invention was indeed patent eligible, granting him the first ever US patent on a living organism. The Patent & Trademark Office and its commissioner Sidney Diamond, the plaintiff, argued that Chakrabarty's bacteria could not be intellectual property because "naturally occurring articles" were not considered patentable as per statute (35 U.S.C. § 101). The Supreme Court, however, decided on 16 June 1980 in *Diamond v. Chakrabarty* that living things are patent eligible so long as there is sufficient human intervention to alter products that are naturally occurring.

Chief Justice Warren Burger, who wrote the majority opinion, famously noted, "anything under the sun that is made by man" is patentable. *Diamond v. Chakrabarty* (447 US 303) has since become a textbook case for American intellectual property law involving materials of biological significance. Though his newly created bacteria were never actually used to clean oil spills, his discovery changed the interface of biotech and intellectual property law forever.

Chakrabarty's research had a profound and far-reaching effect, laying the foundations of the modern biotech industry. A nascent company at the time called Genentech (now part of Roche Pharmaceuticals) supported Chakrabarty's case through an amicus curiae brief, knowing that the outcome would give birth to the US biotech industry². In conjunction with federal legislation promoting private sector innovation (for example, the Bayh-Dole Act of 1980, which allowed federally funded universities and small businesses to retain ownership of their inventions), *Diamond v. Chakrabarty* galvanized the US biotech sector at a time when European and Asian counterparts were taking a more heavy-handed approach to regulating novel biotechnologies. Indeed, industry commentators have said that "without *Diamond v. Chakrabarty*, commercial biotechnology based on recombinant DNA technologies would not exist today."³ With the ability to patent-protect modified living organisms, US biotech firms have flourished and life-saving treatments (such as insulin therapy) have been commercialized.

Chakrabarty's research impact didn't stop there. From General Electric, he was recruited to the University of Illinois at Chicago Medical School, where he stayed until his retirement in 2018 as a Distinguished University Professor. Chakrabarty's laboratory developed new plasmid-based technology for the biodegradation of toxic chemicals, such as Agent Orange, and investigated how pseudomonads contribute to diseases, such as cystic fibrosis^{4,5}. He and his colleagues discovered that the azurin toxin from this bacteria could effectively kill cancer cells via apoptosis by binding and stabilizing the tumor suppressor protein p53; subsequent clinical trials have demonstrated that a derivative of azurin called p28 shows favorable safety and anticancer activity^{6–9}. Chakrabarty cofounded two biotech

startups, CDG and Amrita Therapeutics, that aimed to develop bacterial peptides as anticancer drug candidates.

Chakrabarty published over 250 research, review and commentary articles. He was also the lead author of two science-based works of fiction — *Three Daughters*, *Three Journeys: Quest for Cancer Cure* and *Bugging Cancer: Daring to Dream* — aimed at better informing non-scientists about cancer. He has received numerous awards and recognitions for his work and lifetime of service. To name a few, he was selected as the Scientist of the Year by the Industrial Research Organization in 1975, recognized as a Distinguished Scientist by the US Environmental Protection Agency and the US Army, given the prestigious MERIT (Method to Extend Research in Time) award by the US National Institutes of Health, and honored by Procter and Gamble with the Environmental Biotechnology Award. Outside of the United States, Chakrabarty received the European Union's Golden Eurydice Award, as well as the Padma Shri (the fourth-highest civilian award) from the government of India in 2007. He was a founding member of the United Nations Industrial Development Organization committee that proposed

the International Center for Genetic Engineering & Biotechnology in 1983, a Scientific Advisory Committee member of the Indian government's Department of Biotechnology, on the Board of Biology for the US National Academy of Sciences, and on the scientific advisory boards of many academic institutions. Given his expertise in genetic engineering, he has also served as a consultant to both the US government, as a member of the National Research Council's Committee on Biotechnology, and NATO, as a member of its Brussels-based Industrial Advisory Group.

During his career, Chakrabarty nurtured numerous graduate students, postdoctoral fellows and scientists who now hold leading positions in academia, biotech and law. He has also routinely advised judges on legal issues involving scientific matters. His cheerful and easygoing personality is fondly remembered. Chakrabarty was the quintessential example of a professor who loved to teach. He was the quintessential example of an inventor who moved humankind forward through his creative spirit. And he was the quintessential example of a scientist who genuinely cared about the advancement of technology to solve pressing societal

problems. He will be remembered for generations to come. □

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References

1. Segelken, H. R. Irwin C. Gunsalus, vitamin biochemist, dies at 96. *The New York Times* (21 November 2008).
2. Lumelsky, A. *Diamond v. Chakrabarty*: gauging Congress's response to dynamic statutory interpretation by the Supreme Court. *Univ. San Francisco Law Rev.* **39**, Article 5 (2005). (3).
3. Bradford, T. C. *Tailoring Biotechnologies* **1**, 131 (2005).
4. Kellogg, S. T., Chatterjee, D. K. & Chakrabarty, A. M. *Science* **214**, 1133–1135 (1981).
5. May, T. B. et al. *Clin. Microbiol. Rev.* **4**, 191–206 (1991).
6. Yamada, T. et al. *Proc. Natl Acad. Sci. USA* **99**, 14098–14103 (2002).
7. Punj, V. et al. *Oncogene* **23**, 2367–2378 (2004).
8. Warso, M. A. et al. *Br. J. Cancer* **108**, 1061–1070 (2013).
9. Lulla, R. R. et al. *Neuro Oncol.* **18**, 1319–1325 (2016).

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