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Professor Adrian R. Krainer, PhD
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Adrian Krainer: How one scientist's curiosity led to a breakthrough in genetic disease

At Cold Spring Harbor Laboratory (CSHL) in New York, biochemist Adrian Krainer has spent decades investigating a complex cellular process called RNA splicing—the editing of genetic messages before they are translated into proteins. His goal has been both scientific and profoundly human: to turn deep biological insight into treatments for rare genetic disorders and cancer.

His most celebrated achievement is co-developing nusinersen, marketed as Spinraza—the first drug approved by the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) to treat spinal muscular atrophy (SMA). This rare and often fatal genetic disease affects motor neurons in the spinal cord, robbing children of muscle control and, often, their lives. Approved in 2016, Spinraza has transformed SMA from a fatal diagnosis into a treatable condition, improving the lives of thousands of patients worldwide.

Krainer's path to scientific prominence began far from New York, in Montevideo, Uruguay, where he was born into a Jewish family of Hungarian and Romanian heritage. Growing up during a period of political instability, he found early inspiration in science. A high school encounter with Mendelian genetics — the basic rules of heredity discovered by Gregor Mendel — proved formative. "Genetics really was like a revelation," he recalls. "There was a quantitative aspect to it... it had an impact on all of biology."

But Uruguay offered no clear route into a research career at that time. Determined to pursue science, Krainer earned a full scholarship to Columbia University in New York. He was the first in his family to study abroad.

At Columbia, he embraced the exciting academic environment, exploring philosophy, literature, and science. But it was research that quickly became his main focus. After graduating with a degree in biochemistry, he moved on to Harvard University for a PhD. There, in the lab of molecular biologist Thomas Maniatis, he developed the first highly efficient *in vitro* (test-tube) system for studying RNA splicing, laying the groundwork for his lifelong focus on how RNA splicing works and is regulated at the molecular level.

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A major turning point came in 1984, when Krainer presented his research at an RNA conference at Cold Spring Harbor Laboratory. His work caught the attention of Nobel laureate — and co-discoverer of RNA splicing in 1977 — Richard J. Roberts, who encouraged him to continue his splicing research at CSHL. Krainer became the institution's first independent fellow in 1986, and later a full professor.

In 1999, Krainer attended a meeting focused on spinal muscular atrophy, which inspired him to think about applying his splicing expertise to finding a cure for this disease. SMA is caused by genetic mutation of a gene known as *SMN1*. Humans carry a nearly identical backup gene, *SMN2*, which doesn't work properly due to a splicing error. Krainer eventually saw a way to fix that error using antisense oligonucleotides — short strands of synthetic RNA designed to correct faulty splicing.

In collaboration with Ionis Pharmaceuticals and Biogen, Krainer and his team developed Spinraza, the first splice-corrective therapy to gain regulatory approval. "This is the best one can hope for as a researcher," he said. "It's really a dream come true — to see our basic research translated into a drug that saves lives."

Krainer credits much of his success to persistence and mentorship. "One has to be very persistent," he says. "There's a lot of troubleshooting involved. If something doesn't work, you try again or try a different way. That's part of the fun." He also credits the very talented and dedicated trainees in his lab, especially Prof. Yimin Hua, who carried out a lot of the preclinical research on Spinraza when he was a postdoctoral fellow.

Today, Krainer is the St. Giles Foundation Professor at CSHL and co-leads its Cancer Center's Gene Regulation and Inheritance Program. He is also a Co-founder and Director of Stoke Therapeutics, a company working on similar ASO therapies for other genetic diseases. His work has earned him some of the highest honours, including the Breakthrough Prize in Life Sciences, the Wolf Prize in Medicine, and the Albany Medical Center Prize in Medicine and Biomedical Research. He is a member of the U.S. National Academies of Sciences, Medicine, and Inventors, as well as the American Academy of Arts and Sciences.

Despite decades of success, Krainer remains driven by a sense of purpose and humility. "There's something truly special about being a scientist, indeed it is a privilege" he says. "You follow your passion—and in doing so, you get to help others. It doesn't get more meaningful than that."