

Hedge Funder, Jeffrey Epstein, Catapults Evolution at Harvard

Evolution is always in flux but nothing drives it more than money. So when an elusive hedge funder from New York called Jeffrey Epstein, arrived at Harvard University ten years ago with a \$30 million dollar offer to set up a little department devoted to evolution, the University board welcomed him with a Darwinian hug.

The little department set up for business in August 2003 just off of Brattle Square. But instead of falling into the somnolent annals of academia, it shifted the entire study of evolution from a purely theoretical exercise to a pragmatic tool for medicine.

Jeffrey Epstein, who cultivates brilliant scientists, a virtual salon of Nobel luminaries and other such geniuses, put Martin Nowak in charge of his new department and called it the Program for Evolutionary Dynamics or PED. PED quickly became one of the first departments to study the mathematical evolution of micro biology, notably cancer, infectious diseases and viruses such as HIV—in view of advancing their treatment. And by creating the first mathematical models of how human cancer cells, viruses and bacteria evolve, Nowak and his graduate team have identified groundbreaking steps to treat these diseases more effectively.

Nowak is an Austrian biologist and mathematician with an extensive background in evolutionary theory. Prior to PED's establishment, he headed the Program in Theoretical Biology at the Institute for Advanced Study at Princeton and had published a substantial amount of work on the mathematics of the HIV virus, infectious bacteria, and cancers. Prior to Princeton, Nowak led the mathematical-biology group at Oxford University. Upon his appointment to run PED, Nowak was also made Professor and Mathematics and Biology at Harvard.

Nowak met the master puppeteer, Jeffrey Epstein, in March 2000 at a conference on the evolution of language. Epstein's intention was not learn about the evolution of irregular verbs, but to get to know Nowak intimately. He was familiar with Nowak's HIV work at Princeton and wanted to see how it could be applied to the everyday world.

Nowak's motivation for research differed from Epstein's. While both are enraptured with unraveling the big questions about existence, Nowak is a practicing Roman Catholic, a declared humanist with a

desire to serve society. Epstein on the other hand, is foremost a problem solver, interested in intellectual puzzles. He is equally devoted to physics and artificial intelligence. According to Nowak, Epstein was fascinated with his game theory of win–stay, lose–shift and eager to see how it could be applied to the markets. As a fervent businessman, Epstein was also eager to test out Nowak’s mathematical models in the real world. That is not to say that Epstein had no interest in humanistic endeavors. He has given to countless organizations to further early education, notably in the U.S. Virgin Islands, where his foundation is based.

By March 2000, Epstein was no amateur philanthropist or science groupee. He had supported the research of many prominent scientists, including Stephen Hawking, Marvin Minsky and Nobel laureate physicists Gerard ’t Hooft, David Gross, and Frank Wilczek. According to *New York Magazine*, by 2003, he was one of the largest donors to individual scientists around the world, granting up to \$200 million a year. He was also a member of the New York Academy of Science, a member of Rockefeller University’s board, and actively involved in the Santa Fe Institute, the Quantum Gravity Program at the University of Pennsylvania, and the Mind, Brain & Behavior Advisory Committee at Harvard. Epstein himself had studied physics at the Cooper Union in New York and mathematics at the Courant Institute in New York and moved on to teaching calculus and physics at the Dalton School in Manhattan. Within a couple of years, he was recruited into options trading at Bear Sterns.

In 2012, the PED developed the first mathematical model of how human colon-cancer cells evolve and how they become immune to inhibitor-drug therapy. Their research came at the request of the Pathology and Oncology Department at Johns Hopkins University. The department was trying to understand how the KRAS gene in colon-cancer cells becomes activated after inhibitor-drug therapy, making the cells resistant to treatment.

The model of colon-cancer cell growth revealed that the KRAS gene is not actually activated or “switched on” by inhibitor therapy; rather, a small percentage of colon-cancer cells with an already activated KRAS gene are immune from the start and come to dominate as the other cancer cells are destroyed by the inhibitor drug. The discovery changed the approach to inhibitor-drug therapy. Instead of applying drugs in sequence to fight secondary and tertiary resistance, researchers at Johns Hopkins are now exploring the effects of using a cocktail of inhibitor drugs to capture all colon-cancer cell types: those with the activated KRAS gene and those without. The same tailored approach is underway for other cancers.

In 2010, the PED published a mathematical study that showed that most solid tumors contain 40 to 100 genetic mutations, but that on average only 5 to 15 of those actually drive tumor growth. The findings critically demonstrated the importance of isolating a key minority of mutated tumor cells for effective inhibitor treatment.

In that same year, the PED presented to researchers at John Hopkins, a mathematical model showing the genetic evolution of pancreatic-cancer cells from initial mutation to non-primary malignant cells. The model showed that pancreatic cancer, one of the most lethal forms of cancer, is not fast and furious as believed but, given the amount and type of genetic disparity between the cellular stages, it takes about ten years for an initiating mutation to grow to a parental, non-metastatic founder cell and another six years for cells to become malignant.

The findings highlighted the real possibility of isolating pancreatic mutations prior to metastasis. Johns Hopkins scientists are now developing a pancreatic screening method similar to the protocol used for breast and colon cancers.

Much has been written about PED and Nowak's work. Nowak is also the recipient of numerous awards and the author of several books. And while Jeffrey Epstein remains an obscure figure, tarnished now by a series of scandals involving underage women, one of which led to an 18-month jail sentence, he is nonetheless the talented catalyst, the accelerator of all this medical discovery. Whatever his ignominy, Epstein's bond with Nowak and PED emphasizes that nature is neither fastidious nor judgmental, nor is its dynamic always gradual. Discovery can be sparked into being, pragmatically driven and above all, errs towards sustainability of the greater self.