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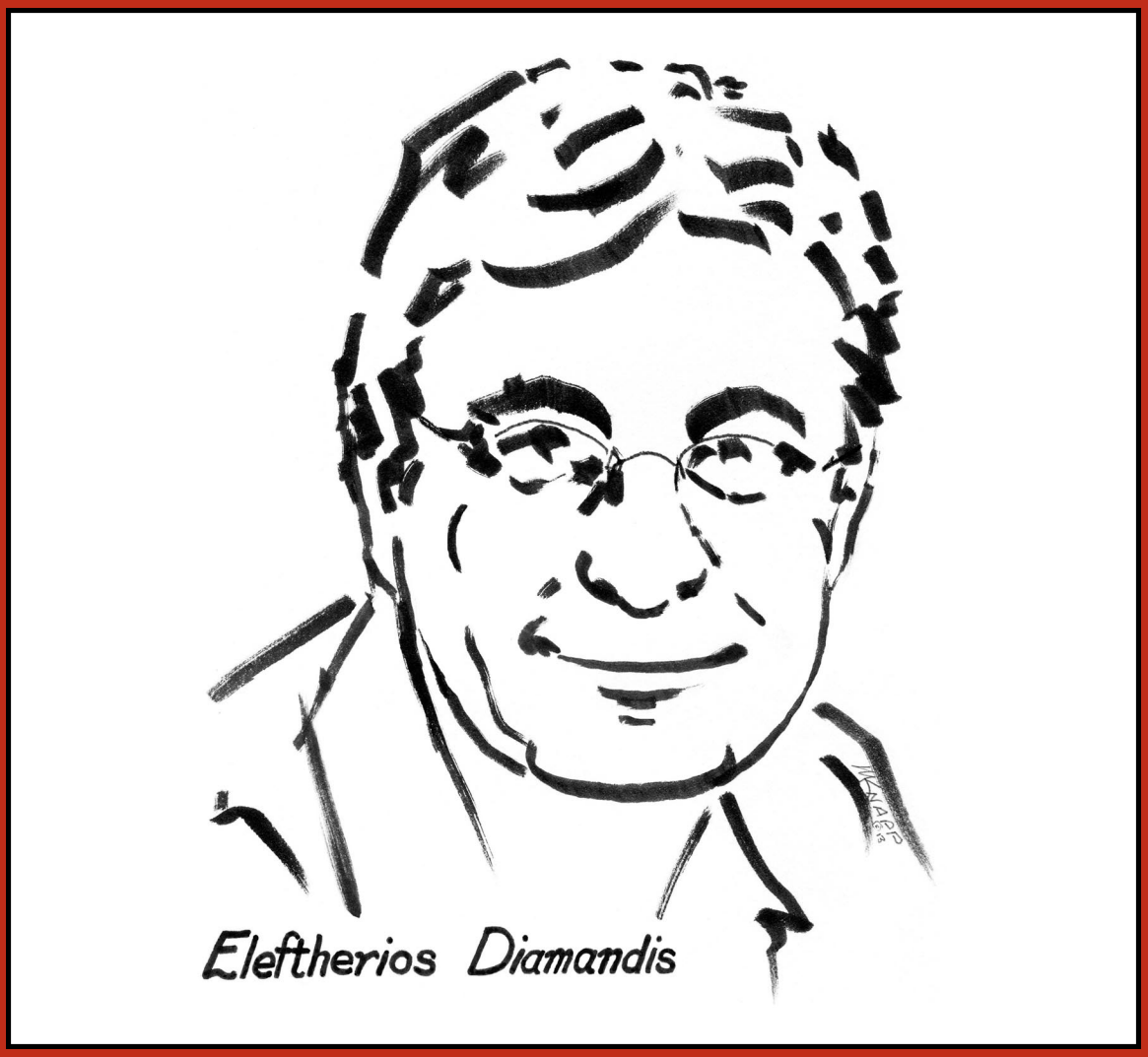

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Eleftherios P. Diamandis

On the south coast of Cyprus, between the port cities of Limassol and Paphos, lies a rock marking the spot where the Greek goddess Aphrodite is said to have emerged from the ocean's foam. The Roman poet Ovid recounts the event—along with many other mythological transformations said to have occurred on the island—in his epic poem *Metamorphoses*. Eleftherios Phedias Diamandis, whose Cypriot ancestry stretches back a thousand years, grew up playing soccer in the fields outside of Limassol, not too far from where the rock lies. Using stones for goal posts, he and his friends played long into the evening, until they could no longer see the ball.

In the summer, he worked in the fields, shaking the long sweet leathery pods from the carob trees that dot the island. It was hard but rewarding work. At the end of the day, he would come back to the modest stone house he shared with his parents and older sister Elli. One day when he was about 12 or 13, he was sitting in his room listening to a local British station on a small transistor radio when he heard the sounds of the top 20 hits come through his earphone. "I put it in my ears and the music just gave me this internal energy and amazing pleasure," he said. The musicians—the Beatles, the Rolling Stones, the Who—became his heroes. "I was mad about them," said Diamandis, who is professor and head of the division of clinical biochemistry in the department of laboratory medicine and pathology at the University of Toronto, Faculty of Medicine.

Passions have a habit of descending on Diamandis with almost mythological fury. Years later, in college, he picked up a tennis racket for the first time and instantly fell in love with the game.

Though it occurred more gradually, Diamandis's professional metamorphosis appears to fit a similar pattern. He did not choose chemistry—it chose him. He tested well in school and was assigned to a chemistry track. He plunged into his studies and over the following decade became one of the first members of his family to leave Cyprus—a journey that took him to Athens for college, a Ph.D., and eventually medical school, and then across the Atlantic to Toronto, where he has lived for the past 27 years.

During that time, he would transform himself from an analytical chemist into a clinical chemist, then a molecular biologist and, most recently, a specialist in mass spectrometry–based proteomics, moving seamlessly between incarnations—and from challenge to challenge. The search for biomarkers is a notoriously difficult pursuit, strewn with broken promises. He made a name for himself as a leader in the field, developing ultrasensitive assays for prostate-specific antigen (PSA) and other disease-related proteins.

"When I first met him, Diamandis was the king of PSA in Canada," said Morley Hollenberg, professor in the department of physiology and pharmacology at the University of Calgary Medical School, who first encountered Diamandis in the 1980s. His fame spread in the late 1990s, when he and colleagues discovered that PSA was part of a much larger group of enzymes, the kallikreins, a discovery that would open up a whole new field of study.

On the face of it, the journey from rural Cyprus to a spot in the pantheon of international science might seem like another one of those fabulous metamorphoses that were said to occur on the island. Unlike those mythological transformations, which typically occur at the behest of a god or outside force, Diamandis's transformation is largely Diamandis's doing—a kind of logical progression given who he is.

With his wavy hair, thick brows, and deep brown eyes, Diamandis exudes warmth and engagement. "He never has this serious face—he always has a big smile and sense of humor," said George Yousef, associate professor of laboratory medicine and pathobiology at the University of Toronto Faculty of Medicine. "You would not guess from meeting him the depth of his stature in the field," said Hollenberg. "His luster is far beyond the impression you get from meeting him at a bar and saying, 'Hi, what do you do?'" The fact is, Diamandis is driven. Even as a boy, he was possessed by a passionate, willful, almost indomitable urge to achieve, to expand his boundaries.

"I always wanted to explore new things, to see where I can bring my potential," he said. "I wanted to push the limit to where I thought I could reach. It was almost like an internal kind of push."

He brings that same be-all-you-can-be sense of drama to his tennis game—"I want to imitate the superstars," he said—and to his teaching, which he adores. These days, Diamandis spends most of his time surrounded by the brightest students he can find. He coaches and cajoles them in an effort to bring out their best, not just as scientists. He shares with them his passion for science, music, and sports all in the same

breath. He named his lab the Advanced Center for the Detection of Cancer, or ACDC. "It was by design because AC/DC was and still is one of my most favorite bands of the '70s," he said. Each year, he introduces the members of his lab to the world in the form of slightly cheesy rock music videos. He organizes annual faculty versus student basketball competitions. "We always lose," said Yousef, his colleague in the department. It may be part of the plan. Though he hates to be defeated in tennis or any sport for that matter, Diamandis wants to cultivate a taste for winning in his students.

"He is always trying to push the lab forward. He says, 'We've got to have the glory of the discovery. If someone else discovers one day before you, then you don't.' That's something he was always reminding us to do—not to slow down because it is a big competition, a worldwide competition. And we will be the best if we're the first," said Yousef.

Diamandis's flair for self-perfection can be traced to the soccer field outside of Limassol, and also to that little stone house, which was built largely by his father, Phedias. Named for the famous Greek sculptor, Diamandis's father, a hard-working, intelligent, and creative man, supported his young family by working in the fields and in a local brick factory. A consummate craftsman, he repaired shoes and whatever else needed fixing. "Anything he did, he did in a perfect way," said Diamandis. He possessed social skill as well. "My father was very flamboyant. He would go out and he was kind of beaming—everyone wanted to talk with him," said Diamandis. One year, he ran for mayor of the small town of Agios Athanasios, and won. He held the post for 18 years.

His wife, Polyxeni, was the opposite. She preferred to stay at home, baking big batches of bread from scratch once a month with a few neighbors—a habit her son continues in her honor. Religious, like her husband—who still sings once a week in his local church choir—she raised her children in the Christian Orthodox tradition. As a boy, Diamandis sang in the church choir. "Back then, we did not question beliefs. Religion now is a mostly cultural thing," he said.

He nurtured his passion for sports and music by imagining himself a superstar. At his mother's insistence—she wanted him to be well-rounded—he spent hours delving into the imaginative worlds of literature. Dostoevsky and the British physician–author A.J. Cronin were among his favorites. Cronin's dramatic explorations of the ethics of doctoring would later inspire him to apply to medical school.

As a boy, Diamandis might not have seemed the most likely candidate. He was an excellent student but not necessarily the smartest in the class. "A lot of these kids were fantastic. In marks, some were even better than me. But it takes a lot more than marks to succeed," he said. By the time he left school, he had developed his trademark habits of hard work, relentless preparation, and also a kind of protean adaptability that would allow him to seek out new situations with a kind of fearless self-confidence.

That adaptability would come into play on several occasions. After a 2-year stint in the army—during which he played trumpet 8 hours a day in the army band—he arrived in Athens for college. The splendor of the public architecture—the Parthenon was his favorite spot—stood in sharp contrast to his living situation. It was almost impossible to live on a student's stipend. Academically, he was pretty much on his own. "I didn't know the meaning of the word mentor," he said. Nor did he really understand the meaning of *PhD*, only that it was a way to enrich his knowledge.

He embarked on his graduate studies in analytical chemistry, just as his thesis advisor was going away for a few months. Left alone in a lab with almost no equipment, Diamandis looked around and found a chart recorder and some electrodes. He decided that for his thesis project, he would make an electrode for picric acid. "Why? Because picric acid was available in the chemistry room of the lab," he said. "Was there a need for a picric electrode? Probably no. But I could care less. I had a task of meeting this challenge and I was going to try and do it, even if there was no need or nobody cared about it."

In fact, Diamandis's electrode turned out to be extremely valuable. He was able to use it to measure creatinine levels in urine and serum—the first time creatinine, an indicator of kidney function, had been measured electrochemically. The experience opened him to a whole new field, clinical chemistry. "I said, 'Gee, there's such a thing,'" he said. Excited by the clinical aspect, and inspired, too, by his early readings of the doctor–patient sagas of A.J. Cronin, he decided to apply to medical school.

By this time he was married to his wife, Anastasia, whom he met in college. He was attracted by her intelligence—"She was the top student in chemistry—much better than me," he said. Their dynamic would mirror, in certain respects, that of his parents. "If I drive a car, I say press the gas; she always presses the brakes," he said. "For me, it works out because sometimes I take too much risk. I make very quick decisions, she makes very slow decisions. It's a beautiful kind of compromise," he said. Their 2 young children—Maria and Phedias—would sit on Diamandis's lap as he studied his medical school texts.

Both he and Anastasia could see that the Greek economy was in decline. A tennis racket cost half his salary. "To buy three tennis balls you had to invest the other half," he said. He had gone to the University of Illinois for a short postdoc and wanted to return to

North America. He decided to apply for a 2-year clinical chemistry training program. He sent out 50 applications. He received 49 rejections. "Only one guy, Dr. David Goldberg, from the University of Toronto, said, 'I'm interested,'" said Diamandis. Goldberg had actually called his professor at Illinois, an eminent analytical chemist named Howard Malmstadt, who said, "Take him." Diamandis was hired at a third of the regular postdoc salary, but after 3 months his salary was raised to the full amount—and he was guaranteed a job if he wanted to come back.

After finishing medical school in Athens, Diamandis immediately returned, with his family, to Toronto. What happened next is a story Diamandis loves to tell students: He began working at a small company, a spinoff of the university, but also had an adjunct position in the clinical biochemistry department. He would show up for the department's weekly seminars and made sure to sit in the front row. "Why? Because the chairman was in the front row," he said. After each talk, he made sure to ask a really good question. "That demonstrated that I was good," he said. At the end of 2 years, the chair, Andrew Baines, asked him to be his deputy. Six years later, he was offered the position of chief of clinical biochemistry.

"What does that story tell you?" Diamandis said. "It says I was dedicated, I was passionate, and it says, I was careful—a good planner. I don't play games, by the way, but if you want to call it a game, I played the game."

A quick study, he mastered the techniques of time-resolved fluorescence and would use them to develop ultrasensitive assays, most notably of PSA. Then something akin to fate intervened. "In a scientific life, the time will come, the so-called golden period. Once you get prepared, discover some things—this and that—then the big time comes. The big time for me was the late 90s when, working with PSA, we had indications that there were more genes similar to PSA," he said. Initially, PSA was thought to be a member of a small family of 3 genes. Diamandis, working with Yousef and other talented graduate students, found a much larger family of 15 genes on a previously unexplored region of chromosome 19.

The kallikreins appear to be a close-knit family, interacting with and activating one another in the fashion of a coagulation cascade. It will be years before all their interactions are known, though not for lack of attention—Diamandis and his colleagues are one of many teams working on the proteins. They are also racing to identify new biomarkers for notoriously elusive diseases, like ovarian and pancreatic cancer.

Diamandis rises at 5:30 AM, has coffee and some home-baked bread, and then exercises vigorously—usually on the treadmill—for 70 minutes. He keeps an iPod filled with his favorite bands from the 1970s—AC/DC, Pink Floyd, Led Zeppelin—on the machine. He claims that getting on and off the treadmill are his worst and favorite moments of the day, respectively. "After you finish, it's so rewarding," he said.

He arrives at his office—which is filled with pictures of his family, mementoes of Greek civilization, and a set of Chinese brush paintings of the kallikreins by Hollenberg—shortly after 7 AM. He spends the next 12 hours meeting with students and colleagues; plotting experiments and possibly the occasional music video—some of which feature Diamandis playing not just rock but also traditional Greek folk music; and preparing grants and manuscripts—mostly serious but also wry and whimsical ones, like a disquisition on what would happen if he tried to genetically program his children to be Wimbledon-winning tennis champions. He leaves at 7 pm and arrives home for dinner with Anastasia.

Several years ago, they bought a house in Oakville, a town outside of Toronto. One of the first things Diamandis did was build a tennis court. "It is now an athletic center," he said. Most weekends, the entire family is there. Diamandis usually plays tennis with his son Phedias, who is currently a resident in neuropathology, and his daughter, Maria, a certified clinical chemist. "We play soccer in the field—along with badminton, golf, and baseball," he said. Maria recently had a child, Anastasia. "Truly, my favorite time is when I am with my granddaughter," said Diamandis. "When I hold her and play with her and see her smiling, I think it's more rewarding than getting off the damned treadmill."

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