

Steve Jobs Dies of Pancreatic Cancer

By David Sarno and Christopher Goffard, Los Angeles Times
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Steven P. Jobs, the charismatic technology pioneer who co-founded Apple Inc. and transformed one industry after another, from computers and smartphones to music and movies, has died. He was 56.

Apple announced the death of Jobs – whose legacy included the Apple II, Macintosh, iMac, iPod, iPhone and iPad.

“We are deeply saddened to announce that Steve Jobs passed away today,” Apple said. “Steve’s brilliance, passion and energy were the source of countless innovations that enrich and improve all of our lives. The world is immeasurably better because of Steve.”

He had resigned as chief executive of Apple in August, after struggling with illness for nearly a decade, including a bout with pancreatic cancer in 2003 and a liver transplant six years later.

Few public companies were as entwined with their leaders as Apple was with Jobs, who co-founded the computer maker in his parents’ Silicon Valley garage in 1976, and decades later – in a comeback as stunning as it seemed improbable – plucked it from near-bankruptcy and turned it into the world’s most valuable technology company.

Jobs spoke of his desire to make “a dent in the universe,” bringing a messianic intensity to his message that technology was a tool to improve human life and unleash creativity.

“His ability to always come around and figure out where that next bet should be has been phenomenal,” Microsoft Corp. co-founder Bill Gates, the high-tech mogul with whom Jobs was most closely compared, said in 2007.

In the annals of modern American entrepreneur-heroes, few careers traced a more mythic sweep. An adopted child in a working-class California home, Jobs dropped out of college and won the title “father of the computer revolution” by the age of 29. But by 30 he had been forced out of the company he had created, a bitter wound he nursed for years as his fortune shrank and he fought to regain his early eminence.

Once out of the wilderness of exile, however, he brought forth a series of innovations – unveiling them with matchless showmanship – that quickly became ubiquitous. He turned the release of a new gadget into a cultural event, with Apple acolytes lining up like pilgrims at Lourdes.

Jobs was born in San Francisco on Feb. 24, 1955, to Joanne Carole Schieble and Syrian immigrant Abdulfattah Jandali, unmarried University of Wisconsin graduate students who put him up for adoption. He was adopted by Paul Jobs, a high school dropout who sold used cars and worked as a machinist, and his wife, Clara.

Jobs’ willfulness and chutzpah were evident early on. At 11, he decided he didn’t like his rowdy and chaotic middle school in Mountain View, Calif., and refused to go back. His family moved to a nearby town so he could attend another school.

When he was 12 or 13, Jobs would recall, he called the home of William Hewlett, one of the founders of Hewlett-Packard Co., to ask about parts he needed for a device he was building. For Jobs, it led to a humble summer job on a Hewlett-Packard assembly line, which he compared to being “in heaven.”

While attending Homestead High School in Cupertino, Calif., Jobs met Steve Wozniak, who was nearly five years older. A technical wizard who was in and out of college, Wozniak liked to make machines to show off to other tinkerers.

The two collaborated on a series of pranks and built and sold "blue boxes" – devices that enabled users to hijack phone lines and make free – and illegal – calls.

In 1972, Jobs dropped out of Reed College in Oregon after six months but lingered on campus, sleeping on friends' dorm-room floors. He sat in on classes that interested him, such as calligraphy, which later inspired him to offer Macintosh users multiple fonts, a feature that would become a fixture of personal computing.

He worked sporadically as an electronics technician at video game maker Atari Inc., traveled to India on a quest for enlightenment and found guidance from a Zen Buddhist master.

Meanwhile, Wozniak had created a computer circuit board he was showing off to a group of Silicon Valley computer hobbyists. Jobs saw the device's potential for broad appeal and persuaded Wozniak to leave his engineering job so they could design computers themselves.

In April 1976, the two launched Apple Computer out of Jobs' parents' garage, reproducing Wozniak's circuit board as their first product. Circuit boards are essential in any electrical product. Although Steve Jobs had Wozniak's design to help him launch his successful business, some new technology innovators might not be so lucky. However, instead of using trial and error to attempt to create a digital product, manufacturers may want to keep companies similar to [Altium.com](https://www.altium.com) in mind for tools to help design effective printed circuit boards to make devices function.

They called it the Apple I and set the price at \$666.66 because Wozniak liked repeating digits. In the following year came the Apple II, which carried a then-novel keyboard and color monitor and became the first popular home computer. When the company went public in 1980, the 25-year-old Jobs made an estimated \$217 million.

Whether pitching a product or wooing a job candidate, Jobs liked to paint what he was selling as part of a revolution, an idea that reverberates in Silicon Valley start-ups today.

“He was by far the most articulate person our industry has ever had,” said Esther Dyson, a longtime technology observer and entrepreneur.

When he approached PepsiCo executive John Sculley to become chief executive of Apple in 1983, Jobs asked him, “Do you want to spend the rest of your life selling sugared water or do you want to change the world?”

At Apple, Jobs spearheaded the creation of a computer he called Lisa (also the name of his daughter born to a former girlfriend). The cocky, headstrong Jobs tangled with Lisa engineers over the direction of the computer, and Apple executives curtailed his role in the project. “It hurt a lot,” Jobs told a Playboy interviewer.

Jobs turned his attention to a small research effort called Macintosh, producing what he described as “the most insanely great computer in the world,” with a graphics-rich interface and a mouse that allowed users to navigate much more easily than they could with keyboard commands.

In 1984, Apple promoted the Macintosh with a television spot that aired during the Super Bowl. The minute-long commercial portrayed a sledgehammer-hurling runner heroically smashing the

image of a sinister Big Brother figure, who was preaching to an assembly of gray drones.

“On Jan. 24, Apple Computer will introduce Macintosh,” the narrator announced. “And you’ll see why 1984 won’t be like ‘1984.’”

The Orwellian tyrant, as Jobs portrayed it, was rival IBM Corp., then the dominant computer maker. In a 1985 Playboy interview, he cast IBM as the great enemy of innovation and described the battle as nothing less than light versus dark in the race for the future.

“If, for some reason, we make some giant mistakes and IBM wins, my personal feeling is that we are going to enter sort of a computer Dark Ages for about 20 years,” he said. “Once IBM gains control of a market sector, they almost always stop innovation. They prevent innovation from happening.”

Macintosh inaugurated an era of visual, clickable computing that remains the norm today, and its look, adopted by Microsoft for its Windows software, became a global standard. Still, although Jobs was a celebrity and wealthy beyond imagining, the Macintosh struggled early to capture sales and trailed the increasingly popular IBM PC.

As panic set in about the Macintosh’s problems, tensions flared between Jobs and Sculley, who, with the Apple board’s blessing, further reduced Jobs’ role. Jobs resigned in 1985, a 30-year-old tech king deposed from the palace he had built. As he saw it, he was fired.

“What had been the focus of my entire adult life was gone, and it was devastating,” Jobs later recalled in a Stanford University address. “I didn’t really know what to do for a few months. I felt that I had let the previous generation of

entrepreneurs down.

“I was a very public failure.”

He started NeXT Computing, which made computers for higher education and corporations. Technologists took to the computers – including British computer scientist Tim Berners-Lee, who used them to create the World Wide Web in the early 1990s. But at \$6,000, they were too expensive for consumers and failed to catch on.

In what many saw as a hobby, Jobs began dabbling in moviemaking technology in 1986, buying a small computer graphics division from filmmaker George Lucas’ Lucasfilm Ltd. and renaming the company Pixar.

Around that time he met Laurene Powell, a Stanford business student, and they were married in 1991 by a Buddhist monk.

Jobs also found his biological mother, Joanne Simpson, and biological sister, Mona Simpson. He and his sister became close, and she dedicated her 1992 novel “Anywhere But Here” to him and their mother.

By then, he had established a relationship with his daughter Lisa. Jobs initially denied paternity and refused to pay child support. He eventually accepted her as his child, and she is now a New York writer.

NeXT and Pixar struggled financially, and he sank much of his personal fortune – upward of \$70 million – into the two companies, according to Alan Deutschman’s “The Second Coming of Steve Jobs” (2000). Setbacks mounted as he slashed staff and scaled back both operations.

A 1993 Wall Street Journal article described “the decline of Mr. Jobs,” saying that his vision for NeXT resembled “a pipe dream”

and portraying him as a once-great but increasingly irrelevant figure who might survive “as a niche player.”

The turnaround began in late 1995 when Pixar released “Toy Story,” the first feature-length computer-animated film, and it became a smash hit. Pixar went public one week later, making Jobs a billionaire, and has continued to produce box-office hits such as “Up,” “Finding Nemo” and two “Toy Story” sequels. Walt Disney Co. bought Pixar for \$7.5 billion in 2006, making Jobs the entertainment giant’s largest shareholder.

In Jobs’ absence, Apple had been foundering as its share of the computer market shriveled. Seeking new software for the Macintosh, Apple decided on NeXT’s system, and bought the company for \$377 million.

Jobs came back to Apple as a “special advisor” in 1996, but within a year he orchestrated the ouster of most of Apple’s board and had himself installed as chief executive. He reshaped a moribund company into a \$380-billion technology titan, which this year temporarily surpassed Exxon Mobil Corp. as the world’s most valuable company.

The comeback was powered by a string of blockbuster products for which Jobs is largely credited – each of which had far-reaching effects in both culture and industry.

“To have your whole music library with you at all times is a quantum leap in listening to music,” he said in a 2001 presentation. “How do we possibly do this?” A moment later, he pulled the first iPod from his jeans pocket to show off the answer.

With the iPod’s release, Jobs lighted the way for the entertainment industry in the digital age. The iPod became Apple’s most popular product and soon captured about 70% of the

market for digital music players.

Two years later, through deals that Jobs brokered with the recording industry, Apple opened its iTunes online store, which is now the country's No. 1 music retailer.

With iTunes – which expanded to selling movies, TV shows, books and games – Jobs transformed Apple from a computer maker into one of the primary gatekeepers for the explosion of online media.

The iPhone, introduced in 2007, gave the cellphone a touch screen and a Web browser and enabled the growth of a booming industry of small mobile games and applications. It was then that Jobs dropped the word “Computer” from Apple's name to make it simply Apple Inc.

Last year, Apple released its iPad tablet computer, a wireless reading, gaming and Web-surfing slate that has sold nearly 30 million units since its release.

In a testament to Jobs' knack for picking transforming technologies, many industry analysts believe the iPad will hasten the demise of the laptop and desktop computers that Jobs himself once helped bring to prominence.

In his second term at Apple, Jobs' instincts became the company's internal compass. Unlike many chief executives, Jobs shunned focus groups and consumer surveys, personally driving Apple's search for the next great idea.

“A lot of times, people don't know what they want until you show it to them,” Jobs once told BusinessWeek magazine.

He had a cult-like following, and he mesmerized audiences when unveiling Apple's newest products, but no one was shown anything until Jobs said it was time. He kept a tight lid on information

flowing out of the Cupertino company.

He was known as an imperious boss with little patience for weakness, one who launched blistering tirades that left subordinates fuming, or in tears.

“Steve tests you, challenges you, frightens you,” Todd Rulon-Miller, a friend and NeXT executive, said in “The Second Coming of Steve Jobs.” “He uses this as a tactic to get to the truth.”

Mercurial and brilliant, Jobs presented himself as an outsider even at the apex of American business, a convention-bucking visionary who was willing to wade into new industries to do battle with movie studios, record labels and cellphone giants. As a Buddhist and vegetarian following the principles of minimalism, he nearly always appeared in public in a black turtleneck, worn jeans and sneakers.

Apple’s “Think Different” ad campaign, with its parade of iconic pioneers and world-shaping figures from Einstein to Gandhi, relentlessly promoted the concept of triumphant individual genius. The implicit hero was Jobs himself, who embodied that ideal as much as any modern American.

Jobs was not afraid to blast rivals – chief among them software giant Microsoft, whose products he once described as “really third-rate” and aesthetically tasteless. The skewering later became more playful, with TV commercials portraying Microsoft users as frumpy and bookish and hipper Mac fans as stylish and quick-witted.

An intensely private person, Jobs rarely discussed his personal life and had little taste for the trappings of celebrity. As a philanthropist, his public profile paled beside that of Gates and Warren Buffett, and critics wondered why Jobs – who had an estimated net worth of \$8.3 billion – didn’t give more money

away, or if he did, why he kept it secret.

For years, Jobs' health was an issue that wouldn't go away. Although he was diagnosed with pancreatic cancer in 2003, he did not reveal his illness for nine months, according to a Fortune magazine report. He finally agreed to surgery in 2004.

After the surgery, Jobs announced that he had recovered. But in 2009, he underwent a liver transplant that was only later brought to light by the Wall Street Journal. As time went on, Jobs looked noticeably thinner in public appearances.

In a Stanford commencement speech in 2005, Jobs spoke at length about mortality and its value as a force against complacency.

"Death is very likely the best invention of life," he said in the speech. "All pride, all fear of embarrassment or failure, these things just fall away in the face of death, leaving only what is truly important."

Jobs' survivors include his wife, their son Reed Paul and their daughters Erin Sienna and Eve, as well as his daughter Lisa Brennan-Jobs.

Nobel Prize Winner Dies of Pancreatic Cancer

msnbc.com news services

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STOCKHOLM— Ralph Steinman proved the importance of his Nobel prize-winning research in a most personal way, using his own discoveries to fight the pancreatic cancer that eventually killed him just days before the award was announced.

In the future, millions more people around the world are likely to gain from the discoveries by the Canadian-born scientist and his two fellow laureates into the workings of the body's highly complex immune system.

Canadian-born Steinman, 68, had been treating himself with a groundbreaking therapy based on his research into the body's immune system. He died on Friday after a four-year battle with pancreatic cancer. His colleagues at Rockefeller University in New York called it a "bittersweet" honor.

The Nobel committee had been unaware of Steinman's death and it was initially unclear whether the prize would be rescinded because Nobel statutes don't allow posthumous awards. But the Nobel Foundation said on Monday a decision to award the 2011 Nobel Prize for medicine or physiology to Steinman would remain unchanged despite his death.

"The events that have occurred are unique and, to the best of our knowledge, are unprecedented in the history of the Nobel Prize," the foundation said in a statement.

"According to the statutes of the Nobel Foundation, work produced by a person since deceased shall not be given an award. However, the statutes specify that if a person has been awarded a prize and has died before receiving it, the prize may be presented."

The Nobel statutes don't allow posthumous awards unless a laureate dies after the announcement but before the Dec. 10 award ceremony. That happened in 1996 when economics winner

William Vickrey died a few days after the announcement.

Before the statues were changed in 1974 two Nobel Prizes were given posthumously. In 1961 U.N. Secretary General Dag Hammarskjold was awarded the Nobel Peace Prize less than a month after he died in a plane crash during a peace mission to Congo. Swedish poet Erik Axel Karlfeldt won the Nobel Prize in literature in 1931, although he had died in March the same year.

Nobel committee member Goran Hansson Steinman's death is "incredibly sad news. We can only regret that he didn't have the chance to receive the news he had won the Nobel Prize. Our thoughts are now with his family."

Steinman shared the prize with American Bruce Beutler and French scientist Jules Hoffmann.

Beutler, 53, is based at the Scripps Research Institute in La Jolla, California. Luxembourg-born Hoffmann, 70, conducted much of his work in Strasbourg. They will share half the 10 million Swedish crowns (\$1.46 million) of prize-money. The rest should have gone to Steinman, though the unusual circumstances leave its fate now in some doubt.

Steinman had been affiliated with Rockefeller University in New York since 1970, and headed its Center for Immunology and Immune Diseases.

"We are all so touched that our father's many years of hard work are being recognized with a Nobel Prize," Steinman's daughter, Alexis Steinman, said in the Rockefeller University statement. "He devoted his life to his work and his family, and he would be truly honored."

Improved vaccines □The work of the three scientists has been pivotal to the development of improved types of vaccines against

infectious diseases and novel approaches to fighting cancer. The research has helped lay the foundations for a new wave of “therapeutic vaccines” that stimulate the immune system to attack tumors.

“They have made possible the development of new methods for preventing and treating disease, for instance with improved vaccines against infections and in attempts to stimulate the immune system to attack tumors,” the committee said.

The immune system’s main function is to protect against harmful invaders but it can sometimes go into overdrive and attack healthy tissue, leading to autoimmune inflammatory diseases, such as type 1 diabetes, multiple sclerosis, rheumatoid arthritis and inflammatory bowel disease.

“Almost all vaccines against microbes, vaccines against cancer, and vaccines to try to eliminate and down-regulate immunity in inflammatory diseases are based on these discoveries,” said Lars Klareskog, chairman of the Nobel Assembly.

Beutler and Hoffmann discovered in the 1990s that receptor proteins act as a first line of defense, innate immunity, by recognizing bacteria and other microorganisms. Steinman’s work, explained how, if required, dendritic cells in the next phase, adaptive immunity, kill off infections that break through.

Understanding dendritic cells led to the launch of the first therapeutic cancer vaccine last year, Dendreon’s Provenge, which treats men with advanced prostate cancer.

No vaccines are on the market yet, but Hansson told AP that vaccines against hepatitis are in the pipeline. “Large clinical trials are being done today,” he said.

Dr. Vinay Kumar, chairman of the department of pathology at the

University of Chicago, who knew both Steinman and Beutler, said the discoveries by these three Nobel laureates have very broad impact.

“These findings are the intellectual foundation of how to design a good vaccine,” Kumar said.

Medicine, or physiology, is usually the first of the Nobel prizes awarded each year. Prizes for achievements in science, literature and peace were first awarded in 1901 accordance with the will of dynamite inventor and businessman Alfred Nobel.

The award citation noted that the world’s scientists had long been searching for the “gatekeepers” of immune response.

Last year’s medicine award went to British professor Robert Edwards for fertility research that led to the first test tube baby.

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Metformin pilot study was sponsored by the Hirshberg Foundation’s Seed Grant Program.

Pancreatic cancer, targeted drugs in comparison with phytochemicals

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Abstract

Diverse mechanisms of growth inhibition by luteolin, resveratrol, and quercetin in MIA PaCa-2 cells: a comparative glucose tracer study with the fatty acid synthase inhibitor C75

The rationale of this dose matching/dose escalating study was to compare a panel of flavonoids—luteolin, resveratrol, and quercetin—against the metabolite flux-controlling properties of a synthetic targeted fatty acid synthase inhibitor drug C75 on multiple macromolecule synthesis pathways in pancreatic tumor cells using [1,2-¹³C₂]-D-glucose as the single precursor metabolic tracer. MIA PaCa-2 pancreatic adenocarcinoma cells were cultured for 48 h in the presence of 0.1% DMSO (control), or 50 or 100 μM of each test compound, while intracellular glycogen, RNA ribose, palmitate and cholesterol as well as extra cellular ¹³CO₂, lactate and glutamate production patterns were measured using gas chromatography/mass spectrometry (GC/MS) and stable isotope-

based dynamic metabolic profiling (SiDMAP). The use of 50% [1,2-¹³C₂]-D-glucose as tracer resulted in an average of 24 excess ¹³CO₂ molecules for each 1,000 CO₂ molecule in the culture media, which was decreased by 29 and 33% (*P* < 0.01) with 100 μM C75 and luteolin treatments, respectively. Extracellular tracer glucose-derived ¹³C-labeled lactate fractions (Σm) were between 45.52 and 47.49% in all cultures with a molar ratio of 2.47% M + 1/Σm lactate produced indirectly by direct oxidation of glucose in the pentose cycle in control cultures; treatment with 100 μM C75 and luteolin decreased this figure to 1.80 and 1.67%. The tracer glucose-derived ¹³C labeled fraction (Σm) of ribonucleotide ribose was 34.73% in controls, which was decreased to 20.58 and 8.45% with C75, 16.15 and 6.86% with luteolin, 27.66 and 19.25% with resveratrol, and 30.09 and 25.67% with quercetin, respectively. Luteolin effectively decreased nucleotide precursor synthesis pentose cycle flux primarily via the oxidative branch, where we observed a 41.74% flux (M + 1/Σm) in control cells, in comparison with only a 37.19%, 32.74%, or a 26.57%, 25.47% M + 1/Σm flux (*P* < 0.001) after 50 or 100 μM C75 or luteolin treatment. Intracellular de novo fatty acid palmitate (C16:0) synthesis was severely and equally blocked by C75 and luteolin treatments indicated by the 5.49% (control), 2.29 or 2.47% (C75) and 2.21 or 2.73% (luteolin) tracer glucose-derived ¹³C-labeled fractions, respectively. On the other hand there was a significant 192 and 159% (*P* < 0.001), and a 103 and 117% (*P* < 0.01) increase in tracer glucose-derived cholesterol after C75 or luteolin treatment. Only resveratrol and quercetin at 100 μM inhibited tracer glucose-derived glycogen labeling (Σm) and turnover by 34.8 and 23.8%, respectively. The flavonoid luteolin possesses equal efficacy to inhibit fatty acid palmitate de novo synthesis as well as nucleotide RNA ribose turnover via the oxidative branch of the pentose cycle in

comparison with the targeted fatty acid synthase inhibitor synthetic compound C75. Luteolin is also effective in stringently controlling glucose entry and anaplerosis in the TCA cycle, while it promotes less glucose flux towards cholesterol synthesis than that of C75. In contrast, quercetin and resveratrol inhibit glycogen synthesis and turnover as their underlying mechanism of controlling tumor cell proliferation. Therefore the flavonoid luteolin controls fatty and nucleic acid syntheses as well as energy production with pharmacological strength, which can be explored as a non-toxic natural treatment modality for pancreatic cancer.

Hirshberg Foundation funds UCLA study of fructose in pancreatic cancer

Read in the [Washington Post](#):

By Reuters

Tuesday, August 3, 2010

Fructose helps pancreatic cancer cells to multiply, UCLA study finds

WASHINGTON – Pancreatic tumor cells use fructose to divide and proliferate, U.S. researchers said Monday in a study that challenges the common wisdom that all sugars are the same.

Tumor cells fed both glucose and fructose used the two sugars in two different ways, the team at the University of California Los Angeles found.

They said their finding, published in the journal *Cancer Research*, might help explain other studies that have linked fructose intake with pancreatic cancer, one of the deadliest cancer types.

“These findings show that cancer cells can readily metabolize fructose to increase proliferation,” Anthony Heaney of UCLA’s Jonsson Cancer Center and colleagues wrote. “They have major significance for cancer patients given dietary refined fructose consumption, and indicate that efforts to reduce refined fructose intake or inhibit fructose-mediated actions may disrupt cancer growth.”

Americans take in large amounts of fructose, mainly in high-fructose corn syrup, a mix of fructose and glucose that is used in soft drinks, bread and a range of other foods. Politicians, regulators, health experts and the fructose industry have debated whether high-fructose corn syrup and other ingredients have been helping make Americans fatter and less healthy. Too much sugar of any kind not only adds pounds, but is also a key culprit in diabetes, heart disease and stroke, according to the American Heart Association. Several states, including New York and California, have weighed a tax on sweetened soft drinks, but the American Beverage Association has successfully opposed efforts to tax soda.

The industry has also argued that sugar is sugar. Heaney said his team found otherwise. They grew pancreatic cancer cells in lab dishes and fed them both glucose and fructose. Tumor cells thrive on sugar but they used the fructose to proliferate. “Importantly, fructose and glucose metabolism are quite different,” Heaney’s team wrote.

Small advances against pancreatic cancer

Rarely is it said that someone is lucky to have had cancer. But Justice Ruth Bader Ginsburg of the Supreme Court might be one such person.

Justice Ginsburg was treated successfully for colon cancer in 1999 and is examined each year at the National Institutes of Health, where in January 2009 a routine CT scan revealed a very small cancer in the center of her pancreas.

While the life expectancy for most people found to have pancreatic cancer is usually a year or less, Justice Ginsburg has apparently been well after she recovered from surgery to remove the tumor, about the smallest that can be detected by a CT scan – one centimeter, or less than half an inch, wide.

[Read entire article at the New York Times](#)