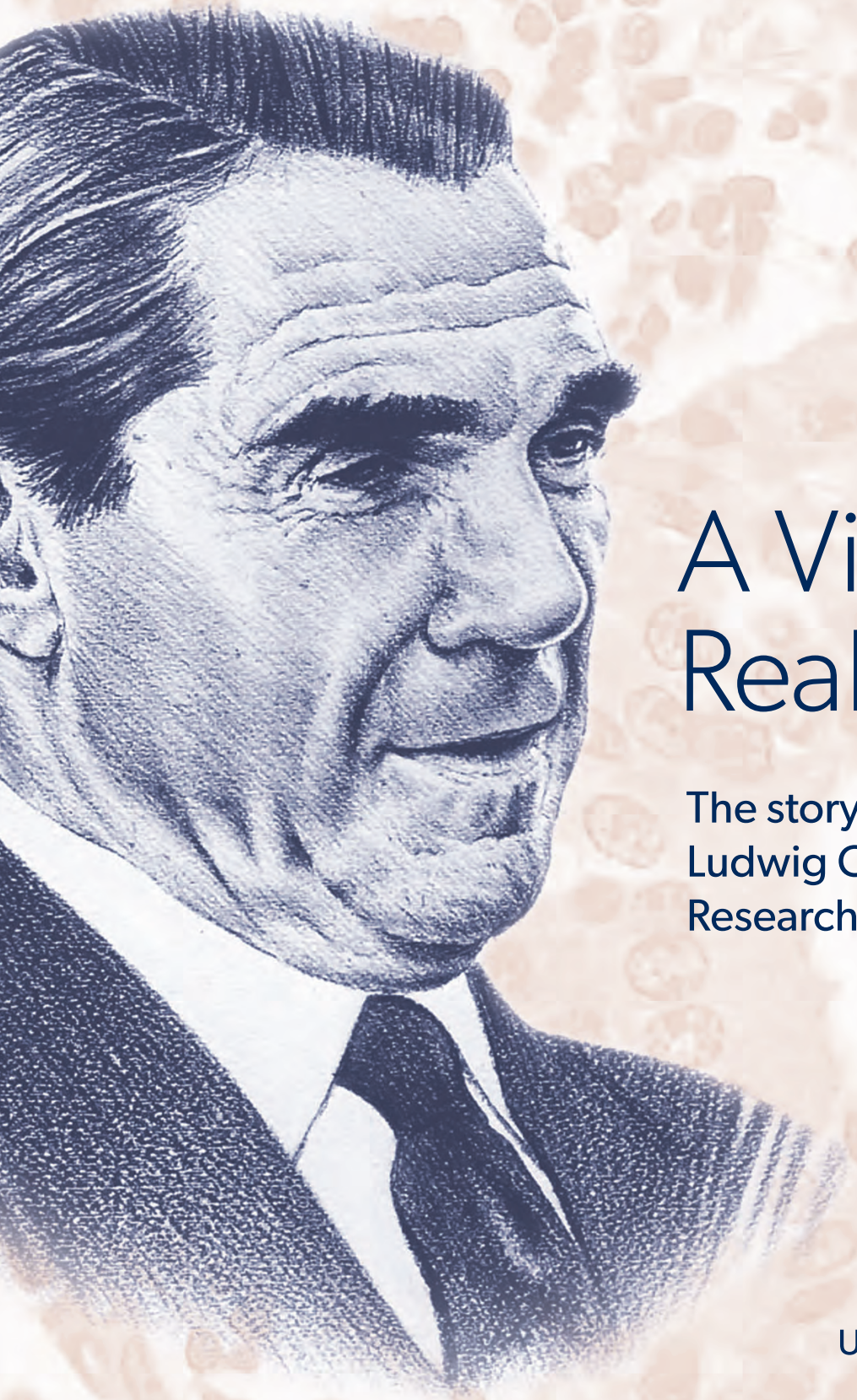

A Vision Realized

The story of Ludwig Cancer Research

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A NOTE FROM THE AUTHOR

Once you've read the history that follows, you'll probably agree that few scientific institutions have an origin story quite as quirky as that of the Ludwig Institute for Cancer Research. Fewer still can say they've contributed as much to their fields of focus. Yet, for all that, hardly anyone knows how or why the Ludwig Institute was established, the deliberations and intentions that informed its structure or how its parent, Ludwig Cancer Research, came about.

Indeed, we'd likely know little of that history even today if the Institute's secretive benefactor, Daniel Keith Ludwig, had his way from beyond the grave. Fortunately, a handful of the Institute's architects held out hope that its story, and theirs, would someday be told. To that end, one of them—Hugh Butt, a founding scientific advisor of the Institute—traveled the world in 1995, three years after Ludwig's death, interviewing people who knew the enigmatic billionaire or were instrumental to the Institute's creation. The story that follows is based in part on those interviews, which were recorded on cassette tapes and until recently all but forgotten, stored in a cardboard box in a cupboard at the Institute's New York office.

More recently, John Notter—who championed the Institute's creation, chaired its first Board of Directors and then was chairman again from 2010 through June 2024—asked the Communications department if it would produce a history of the Institute. It was, like so many of his ideas, a very good one. His recollections, along with those of the Institute's new Chair of the Board and longtime CEO and President, Edward McDermott, were invaluable to the writing of this story.

Its composition would not have been possible without the joint efforts of the Ludwig Institute Communications team either. Deputy Scientific Director and Communications Director Pat Morin found and digitized Butt's old tapes, discovered assorted articles and other materials on Ludwig, his businesses and the Institute's history, and supervised the production of this document. Our Communications Coordinator Jennifer Downes helped transcribe the interviews, digitized and organized a dizzying assortment of old photos and contributed to other key steps of the production process.

My thanks to them all for their contributions to this publication, which I had the rare pleasure of writing—and hope you will enjoy reading.

Unmesh Kher

Editorial Director
Ludwig Cancer Research

Ludwig Institute for Cancer Research founding statement

In creating this organization, I have been guided by certain principles which throughout my life I have found to be highly effective. Success in any complex enterprise consists in bringing the best minds to bear on each problem, in providing the best resources possible, and in putting each concept into practice whenever and wherever the opportunities are most favorable. I believe firmly in the value of applying these principles in grappling with tasks as momentous as finding ways to relieve the human suffering caused by cancer.

Why should this undertaking be international? The rare vision and ability needed in the battle against cancer are not limited by frontiers, and the scientists who possess these gifts must be sought wherever they are to be found. Nor does cancer reveal itself in the same guise in every nation, but strikes different populations in different forms. Yet despite the growing necessity for concerted worldwide effort, I find no agency, which has both the truly international scope and the substantial resources, which I deem essential for a comprehensive attack on human cancer.

In my judgment the ultimate conquest of this frightful disease is not yet in sight, and the same view is held by most informed physicians and scientists in biomedical research. In contrast to those who would yield to undue optimism, and who hope for too much from present programs, I am persuaded that eventual mastery of cancer will come only from intense and unremitting scientific exploration over many decades. This should not be hindered by the changing policies of governments and the vagaries of public interest. Accordingly, it is my intention that the Institute shall be so structured as to ensure secure and continuing support for the attainment of its aims. The elimination of cancer will surely rank as one of man's greatest and uncontroversial achievements. That day may be long delayed. How long we cannot tell. But I do not doubt that it will surely come.

D.K. Ludwig
December 17, 1974

The story of Ludwig Cancer Research

On a summer afternoon in 1962, a young financial whiz named John Notter found himself at lunch in an enormous one-bedroom house overlooking Los Angeles and the ultraluxe Hollywood neighborhood of Trousdale Estates, in the company of quite possibly the world's richest man, shipping tycoon Daniel Keith Ludwig, his wife Virginia and their dog, Suzy. At 27, Notter, married and a father of two, was already president of a bank owned by H.F. Ahmanson & Co., parent to one of the largest savings and loan associations in the U.S. at the time, Home Savings of America. Ludwig hoped to poach Notter and have him rescue a foundering savings and loan of his own in the state—a favor for which he was offering the wunderkind a 40% cut in salary.

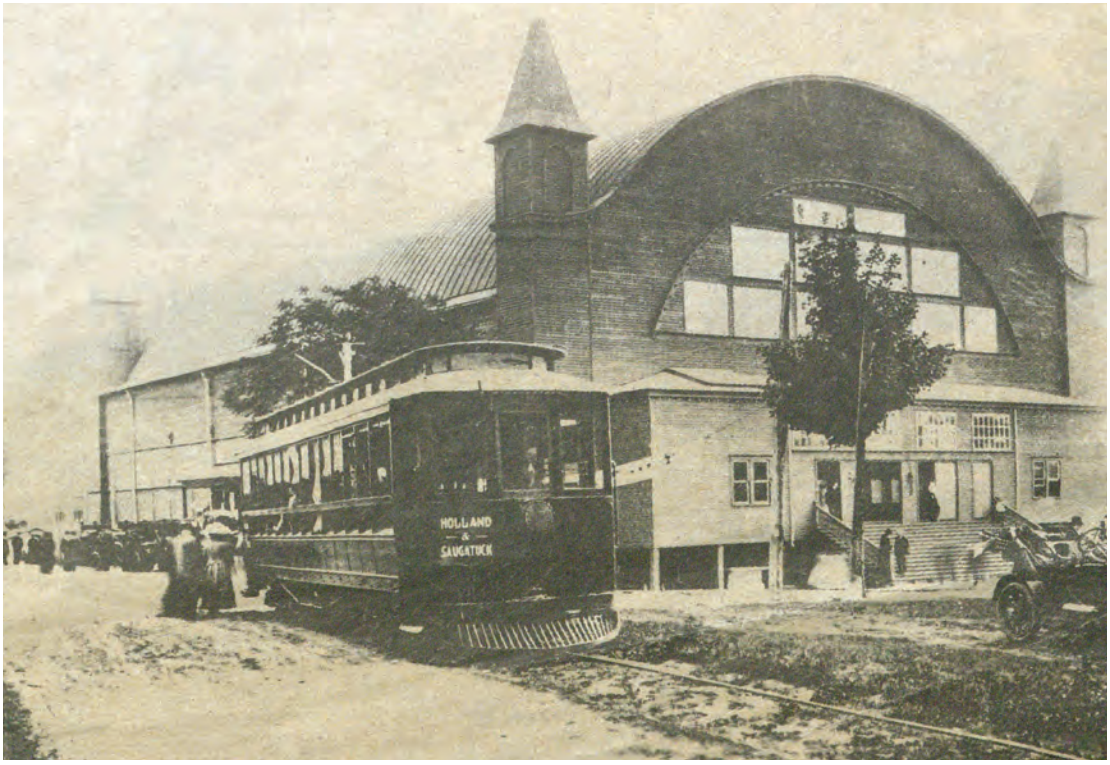
Notter was tempted. Not because he relished lower pay but because he was looking to break into international business, and though Ludwig had initially amassed his fortune on the high seas, his main international holding company, Universe Tankships, was by then host to businesses engaged in everything from ranching to mining to luxury hotels across five continents. Notter had been promised that a successful revival of Ludwig's savings and loan would not only be generously remunerated later but would also open for him the doors to that conglomerate.

As they negotiated the offer, Notter asked the magnate what his plans were for his businesses—beyond, that is, his own lifetime. Ludwig replied that he might want to do something about the problem of cancer. As it turned out, Ludwig wasn't content to wait till his death to contribute to the cause. By the mid-1970s, he had donated the bulk of his international empire to an institution dedicated to cancer research, one to which he only reluctantly gave his name: the Ludwig Institute for Cancer Research.

That was just for starters. After his death in 1992, in accordance with his will, Ludwig's U.S. assets were put to work as endowments establishing professorships for cancer research and, later, six independent research centers at prestigious U.S. institutions. Over

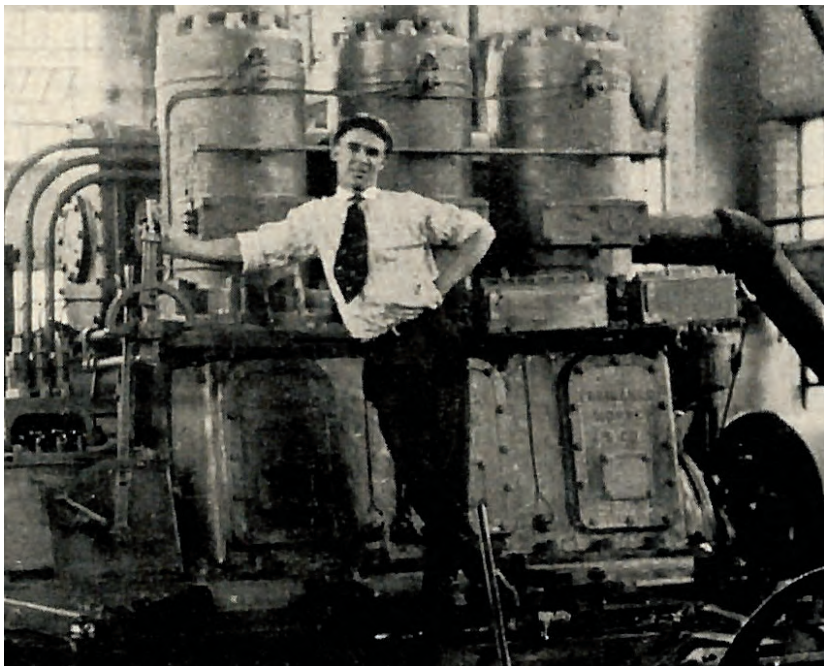
John Notter, kneeling, was already president of Victory Savings and Loan when this picture was taken. He would take a pay cut a couple of years later, at 27 years of age, to work for Daniel K. Ludwig.

the past half century, scientists of the Ludwig Institute and at the six autonomous Ludwig Centers—collectively known as Ludwig Cancer Research—have harnessed his bequest to solve some of the most vexing conundrums of cancer biology, leaving an indelible mark on the field and helping lay the foundations for diagnostic and therapeutic strategies that promise today to transform cancer prevention and care.



Above: The pavilion at Kalamazoo Lake in Michigan where Ludwig shined shoes and sold popcorn as a young boy.

Right: Ludwig at about 17 years old, working on marine engines for Fairbanks, Morse and Co.



The making of a magnate

Daniel Keith Ludwig was born on June 24, 1897, in South Haven, a small port town on the Lake Michigan shore, where a pier built by his grandfather bore the family name.

Shipping was in his blood. As, clearly, was business. He told a *Fortune* magazine reporter in 1957 in an exceedingly rare, sanctioned profile that when he was just nine years old, he pulled together $75 to buy a sunken, 26-foot boat and toiled through the winter to fix her up. He then hired a crew and chartered her out the next summer for twice as much as he'd paid for her, all while earning extra on the side shining shoes and selling popcorn.

When the young Ludwig's parents divorced six years later, he dropped out of school and followed his father, a real estate agent, to Port Arthur, Texas, where he endured a singularly lonely childhood. Ludwig eventually found work selling supplies to ships anchored at the local port while attending night school to pick up the math he needed for marine engineering. He then moved back to Michigan and completed his training working at 20 cents an hour for the manufacturer Fairbanks, Morse and Co., which subsequently hired him and sent him off to the Pacific Northwest and Alaska to install ship engines.

Ever the entrepreneur, Ludwig freelanced his services in his spare time and soon decided he preferred being his own boss. With $5,000 borrowed on his father's signature, the 19-year-old Ludwig bought an aged side-wheel excursion steamer named *Idlewylde*, paid back the loan by selling off its machinery and boilers, and converted the ship into a barge. The conversion, which entailed extensive welding of bulkheads in the cargo spaces using a simple but effective method, left a lasting impression on Ludwig and later influenced his pioneering construction of supertankers. Buying some wooden boats to assemble a ramshackle fleet, Ludwig began hauling liquid molasses up the Hudson River to distilleries in Canada during World War I.

That business was, however, short-lived. Ludwig sold his barges to his erstwhile client and stayed barely a step ahead of bankruptcy using his decrepit tugs for general hauling during an ensuing downturn in the shipping business. He noticed around this time that transporting oil was about four times as profitable as hauling molasses. So he chartered out a small, nearly finished tanker from the United States Shipping Board, sold his tugs to complete its construction and began oil deliveries for a Massachusetts refinery.

In 1923, he bought an antique, partly sail-driven tanker, the *Wico*, for $25,000 from a scrap metal dealer named Boston Metals Co., claiming outright ownership of an ocean-going vessel for the first time and starting a lasting business relationship with the dealer. But a partner he enlisted in that business soon elbowed him out. Undeterred, Ludwig established a company named American Tankers Corp. with new partners a couple of years later, this time buying a tanker named the *Phoenix* from the United States Shipping Board.

Seeking to expand his business, Ludwig next returned to New York and bought a coal-hauling vessel named the *Ulysses*, which he converted into a 14,000-dead-weight ton (dwt) tanker—enormous by the standards of the day (dwt refers to the total weight a ship can carry, including cargo, fuel, ballast, passengers and everything else onboard). That move nearly bankrupted Ludwig when delays in the collier's conversion led to the loss of its charter. But the failure would ultimately spark a rally in Ludwig' fortunes when he managed, in 1937, to offload his white elephant to a whaling concern for four times its value as a tanker.

The tanker Universe Burmah at Ludwig's Kure shipyard in Japan.

The proceeds pulled him out of debt and financed the hiring of his first full staff. Around the same time, Ludwig also obtained from New York's Chemical Bank a loan he considered the most consequential of his career, using it to buy several government cargo vessels, which he converted into tankers. By 1942, Ludwig had his own shipyard for building and converting ships into tankers—Welding Shipyards, the first of two he'd operate in Virginia.

He was innovating on the financial front as well. In 1938, Ludwig pioneered a mechanism for financing his growing fleet that would later become standard in the industry. He would charter a tanker to an oil company for a certain number of years and borrow from a bank for the same term to finance the construction of new vessels or support other investments. The oil firm would then pay the monthly charter fees to the bank, which would take its cut and transfer the rest to Ludwig. Comprehensive insurance coverage of the ship would protect the bank. Ludwig, for his part, could borrow on existing vessels, sure that the loan would be repaid; and the new vessels, which he owned entirely, could serve as additional collateral.

By the late 1940s, under the skeptical gaze of his competitors, Ludwig was building larger and larger tankers on the calculation that they'd be more profitable because operating costs do not rise in direct proportion to ship size. His hunch proved correct and, encouraged by the results, he signed a deal with the Japanese government in 1951 to lease the Kure shipyard, where the graving docks and other factors greatly eased the application of his many innovations in supertanker construction. His tankers grew from

The Ludwig empire

Daniel Ludwig's conglomerate spanned the globe, employing tens of thousands in enterprises as varied as they were ambitious. Here's a sampling of the businesses he owned at various points over the course of his career.

Westlake Village in California

The Acapulco Princess Hotel

The Princess Hotel Bermuda

A Bantry Bay class supertanker

Ludwig, center, at his salt production facility in Mexico

Kaolin mine in Brazil

Mining operation in Australia

the neighborhood of 23,000 dwt, considered gargantuan when introduced in the 1940s, to a staggering 326,000 dwt a couple of decades later. By the late 1960s Ludwig had six such "Bantry Bay Class" Goliaths plying the oceans, part of a fleet that grew to number more than 60 ocean-going ships at the height of his career.

Ludwig's engineering chops were a core asset of his businesses. Having developed pioneering welding techniques at his Virginia shipyards, he continued innovating at Kure, where his use of prefabrication and sectional pre-assembly streamlined the production of his supertankers. The components and designs of his ships were largely interchangeable, ensuring further efficiency in not only their construction and maintenance but their operation as well: crews could be moved around as needed from ship to ship and feel at home wherever they were dropped.

Like the man himself, the tankers were notably frugal. They lacked basic comforts such as air conditioning, let alone frills like swimming pools, luxurious captain's quarters or "owner's cabins." Yet, as characteristically, Ludwig was happy to pour large sums into structural and mechanical components that would improve their profitability. He similarly spared no expense in hiring only the best officers to run them. As the American Society of Mechanical Engineers noted in posthumously awarding Ludwig the Elmer A. Sperry Award for Advancing the Art of Transportation in 1992, "His ships are known the world over as lean and austere in appearance, but they are recognized as exceptionally durable and reliable in machinery, equipment and basic structure." His design innovations in shipbuilding, it additionally noted, extended well beyond the supertanker to encompass dredges and bulk carriers and even a floating power plant that could be hauled across oceans and dropped off at remote locations.

On the foundations of this fleet, Ludwig built a commercial empire. His investments certainly overlapped at times: If his ships needed coverage, he established an insurance company; if the shipyards needed steel, his cargo ships, chartered out to U.S. Steel, hauled iron ore from a Venezuelan mine to smelters in the U.S. Inventive as ever, Ludwig personally designed gigantic bulk carriers for that purpose and had them ferry the ore over a channel deepened by a dredge of his invention.

By 1963, his stack of holding companies—of which he was sole owner—had interests in an oil refinery and an orange grove in Panama; a potash mine in Ethiopia; iron, coal and oil interests in Australia; an international chain of luxury hotels; an oil refinery in Germany; the Kure shipyard and a cargo transfer complex in Japan; a 650,000 acre cattle ranch in Venezuela; interests in oil companies in Canada and California, a state where he also controlled a clutch of savings and loan companies; the world's largest manufacturer of salt by solar evaporation—Exportadora de Sal—in Mexico, whose salt harvesting and

The Zulia, *a large and highly effective side-casting boom and hopper dredge, was conceived, designed and built by Ludwig. Created to deepen the entrance to Lake Maracaibo in Venezuela to open access to massive oil tankers, it removed more "spoil" in 10 days than small hopper dedges had removed in two years.*

other machinery he developed and built, and that he serviced with self-discharging carriers of his design that docked at a deep-sea port he constructed at Cedros Island; and, of course, a fleet of 22 bulk carriers and 28 supertankers that was expanding at a steady clip.

Ludwig left his mark in residential real estate as well—most notably Westlake Village, which he built on a storied 11,780-acre ranch he bought in 1963 for $32 million (the equivalent of $328 million in 2024 dollars) just 40 miles outside of Los Angeles. What Ludwig saw at the time, and others did not, was that it was only a matter of time before a highway to the nearby city ran past the ranch. With that, the natural beauty of the land—hundreds of Hollywood movies had been filmed there—and its proximity to L.A., any development at the location was likely to be successful, if done correctly. To ensure it was, Ludwig established a subsidiary of his American-Hawaiian Steamship Co. (AHS), named American-Hawaiian Land Co., to manage its development. Notter, who was chairman of the AHS board and now chief of its subsidiary, retained a civil engineering firm to design not just a housing development but an extensively planned city.

The effort involved the integrated contributions of hundreds of experts in dozens of specialties—from schools to healthcare to hydrology to cemeteries to land use—working in concert to create a master plan for a city of tens of thousands, complete with homes, parks, schools, greenbelts, lakes and marinas, shops and industrial zones. The project involved the construction of a $3.5 million lake, stocked with catfish and bass, boasting

As part of the Jari project, workers cleared Brazilian rainforest to plant acres of Burmese gmelina trees

Gertrude Virginia Higgins was married to Daniel Ludwig from 1937 until his death in 1992.

eight elegantly designed miles of shoreline. Westlake Village was a spectacular success and is still considered among the best planned cities in the country.

By the early 1970s, Ludwig's net worth was estimated to be in the billions. He had added oilfields in Indonesia, real estate in Australia, skyscrapers and other properties in the U.S., iron and kaolin mines in Brazil and a whole lot more to his skein of enterprises.

Yet Ludwig's confidence in his own vision could be blinding and would lead him, in the late stages of his career, into a mire of his own making. Anticipating, correctly, an impending fiber shortage, Ludwig bought a tract of land more than twice the size of Delaware in the Brazilian Amazon for $3 million in 1967. His plan, named the Jari project, was to raze most of the rainforest on his property and replace it with the fast-growing Burmese gmelina tree, supplementing that fiber-making enterprise with mining and ranching operations. The project was highly controversial and became something of a political lightning rod in and even outside Brazil. Despite ample warning to drop the project, Ludwig would persist until 1982 and leave only after the political situation in Brazil became untenable. By some estimates, he lost nearly $1 billion, in 1981 dollars, in the enterprise.

Still, even with the press generated by the Jari project, hardly anyone outside the shipping industry knew who Ludwig was. This was entirely by design: laconic and intensely private, Ludwig detested publicity of all kinds. If frequently blunt, cantankerous and openly bored by small talk, he was also very loyal to the few friends he had, who were mainly business partners and lawyers he'd known for ages. His other friends included the actor Clark Gable, who Ludwig revered, and Richard Nixon, who was a guest at

Daniel Ludwig, right, with future preseident Ronald Reagan, center, and John Notter.

his home before he was elected president. A conservative in the old sense of the word, Ludwig held Ronald Reagan in high regard, prominently displaying a picture of himself and the future president in his Manhattan penthouse. He was said to be devoted to his wife, Gertrude Virginia Ludwig, whom he had married in 1937, just a couple of months after divorcing his first wife, from whom he seems to have been estranged soon after their marriage began in 1928.

In public, and especially in his old age, the titan kept a low profile—though it would be an exaggeration to say he was a recluse. He flew economy, used public transportation, walked to work and otherwise played the part of an ordinary if somewhat enigmatic old man with determined fidelity. He went to great lengths to keep his name out of the press, even taking his executives to task when it cropped up in print unexpectedly. And though, being one of the richest men in the world, he could have done almost anything he wanted, he confessed he had no hobbies or even interests beyond business.

Except, evidently, an abiding fascination with the conquest of cancer.

The big idea

For reasons that are not quite clear, Ludwig had long been intrigued by the medical and scientific challenges posed by cancer. A rudimentary will he asked a lawyer friend of his in Connecticut to draft for him in 1959 left whatever remained of his vast estate, after providing for his wife and certain other gifts, to cancer research. He and his wife even established a Virginia and Daniel Ludwig Foundation Inc., in New York, though it merely donated some funds annually to a pair of hospitals. A few years after his L.A. lunch with Notter, Ludwig made a second tentative foray into cancer philanthropy, establishing an International Foundation for the Fight Against Cancer that was funded by his company Seatankers Inc. That venture, devised to issue research grants, was distinguished primarily by its inactivity.

By early 1970, still in fine fettle but pushing 73, Ludwig began pondering the fate of his estate in earnest, turning to his closest advisors for ideas. These included Herbert Brownell, a former U.S. attorney general who had been a counselor and confidant to Ludwig for about a decade; Brownell's junior partner, international tax attorney R. Palmer Baker; and Notter, who, now 35, was the operational and financial head of Ludwig's sprawling conglomerate. Out of these discussions came the idea that Ludwig might now more seriously create some mechanism to support cancer research.

Ludwig bit. But he had some conditions. These he spelled out to Notter and Baker. For one thing, the entity he had in mind would not issue grants but, rather, employ its own scientists and conduct its own research, preferably in partnership with other institutions. As Palmer Baker later observed: "Mr. Ludwig was not very fond of giving away money without knowing what was going to be done with it"—a wariness that accounted for the terminal latency of his first cancer philanthropy. Another key requirement was that this research entity should be firmly linked to medical establishments where its discoveries could be forged into clinical interventions and readily tested for their benefit to patients.

Bettmann Archive

Herbert Brownell, former U.S. attorney general and a close friend and advisor to Ludwig, helped give shape and substance to Ludwig's philanthropic vision.

R. Palmer Baker, a tax attorney in Brownell's firm, was instrumental in devising the structure of the Institute.

There were other instructions. The institute was to be funded exclusively with his foreign assets and he wanted his legacy—like the businesses that were to fund it—to have an international footprint, believing firmly that solving a problem as complex as cancer required a concerted global effort. And he wanted to ensure that his fortune would be spent as fully as possible on cancer research, not on "bricks and mortar." What he certainly did not want was some eponymous research building that would serve as a monument to his ego. The organization he had in mind would be as frugal in structure and purposeful in design as his ships. By leveraging existing facilities, it would avoid wasteful expenditure on redundant infrastructure, investing resources where they matter most: recruiting talented scientists and giving them time and material support to develop their ideas.

"I give him full credit for thinking through the type of organization this would be, its distinctive nature," Brownell later said. "He wanted every nickel of his money to go directly to research and he didn't even want his name used, for a while, in connection with the Institute. He was very modest about that."

The making of an institute

With Ludwig's preferences in mind, Notter initially considered setting up a foundation for cancer research in the U.K. but was dissuaded by Sir David Montagu, a banker with whom he and Ludwig had done much business. After some brainstorming at Montagu's house in the Swiss Alps, the banker convinced him that Europe would be the better option. Baker, for his part, said that for both business and tax-related reasons, an institute would be a better option than a foundation, as it could be structured to continue operating in perpetuity, in line with Ludwig's wishes. This was mainly because regulations issued by the U.S. Department of Treasury implementing the Tax Reform Act of 1969 barred entities defined as "foundations" from owning or controlling business interests. An institute, it appeared, would not be so restricted and would, moreover, be more amenable to the mechanism of support Ludwig envisioned for his legacy.

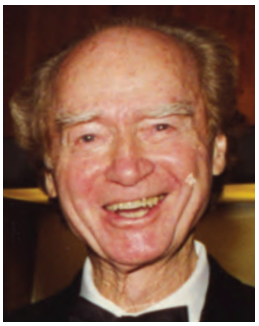
Switzerland, Ludwig's advisors decided, would be the ideal host for their proposed institute, in part because the country was scientifically advanced and host to major global health organizations; and in part because they believed that its government would give them latitude to devise and run the institute as they saw fit. Further, Notter happened to be a dual citizen of Switzerland and the U.S.

Through a business contact of Notter's, the two were introduced to an attorney named Hugo Frey of the firm Niederer Kraft Frey, who was intrigued by the challenge of creating a legal framework to accommodate Ludwig's stipulations. Frey invited Baker to his new summer house in Saint Moritz, where, after a couple of days of discussion in October 1970, the pair put together the charter for an "Institute of Cancer Research".

Armed with a memo penned by Baker, Notter updated Ludwig on their progress and conclusions in late 1970 when the pair met in Brazil. Aside from his approval, Notter got the name of a person Ludwig wanted as a scientific advisor to the new entity. That person was Hugh Butt, chairman of the gastroenterology division at the Mayo Clinic,

OTHER KEY PLAYERS BEHIND THE LAUNCH

Hugo Frey created the corporate structure and legal framework of the Institute.



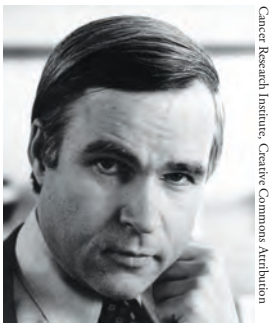
Chair of gastroenterology at the Mayo Clinic, Hugh Butt was the Institute's first scientific advisor.

Corporate lawyer John (Jack) Barry contributed to the establishment of the Institute and its early Branches.

Lawyer Adolf Kammerer was on the founding Board and served as a director and legal counsel for several years.

National Cancer Institute

Carl Baker was a founding scientific advisor and medical director of the Institute until 1985.



Cancer Research Institute, Creative Commons Attribution

Lloyd Old, a founding scientific advisor, ultimately served as director, CEO and chairman of the Ludwig Institute.

Henri Isliker joined the founding Scientific Advisory Committee before the opening of the Institute's first Lausanne Branch.

whom Ludwig had consulted earlier that year, when he was worried he might have stomach cancer—a detail the reflexively compartmentalized billionaire did not mention to Notter. (Twenty-five years later, eager to preserve the Institute's history, Butt would travel the world interviewing people who were instrumental to its creation and evolution. His interviews, recorded on cassettes and stored with other memorabilia in a long-forgotten box in a cupboard at the New York office, were critical to the composition of this history.)

With additional input from Jack Barry, an attorney at Brownell's firm who had handled

a variety of Ludwig's business transactions, Frey and his colleagues registered the "Cancer Research Institute Ltd." in Switzerland on April 7, 1971, as a nonprofit corporation. Its charter incorporated all the requirements of a charitable organization under U.S. law, while its founding board, in compliance with Swiss law, had three Swiss directors: Notter, Frey and the latter's colleague Adolf Kammerer. Since it was a corporation, not a foundation, it would also be permitted to register and license patents for nonprofit purposes without running afoul of Swiss law.

"Hugo's perceptions were remarkable," Baker later told Butt. "It was he who suggested that the solution was a corporation with shares organized for the express purpose of cancer research in which, however, the shareholders would have no interest in assets or income—no personal interest. And as it so happened, the U.S. Internal Revenue Service had recently issued rulings approving the tax exemption as a charity of a similar structure in the United States."

To comply with U.S. tax laws, the Institute also had to establish and maintain ties to a hospital dedicated to teaching or nonprofit research, which was also precisely what Ludwig wanted. All involved thought it wise to establish the first such partnership in an English-speaking country. So Notter made his way to London to find a suitable partner.

A lawyer he'd worked with there pointed him to the Chester Beatty Research Institute at the Royal Marsden Hospital and gave him a card with the address. Arriving at the hospital, Notter wound up cooling his heels for a half hour in some administrative office reception before he startled its staff, who were quite reasonably expecting to receive maybe £50 from this eccentric visitor, with a proposal to contribute something like £100,000 or more—for starters—to open a research institute within the facility.

And so, after some predictably agonizing negotiation, an agreement was formally reached with the Royal Marsden Hospital in May 1971 to open the first (Sutton) Branch of what would eventually become the Ludwig Institute. On the scientific front, its establishment was overseen by an incipient Scientific Advisory Committee (SAC). The initial committee included Butt; the Director of the National Cancer Institute, Carl Baker, who had referred Ludwig to Butt the previous year and would go on to serve as the first medical director of the Institute until he retired in 1985; and a bright young immunologist at Memorial Sloan Kettering Cancer Center (MSK) named Lloyd Old, who had been recommended to Ludwig by Benno Schmidt, a well-connected venture capitalist on the MSK Board. Old would become a founding father of modern tumor immunology and a profoundly influential scientific director and CEO of the Ludwig Institute.

On October 23rd, 1972, the fledgling Institute officially opened a second Branch in

The Institute reached an agreement to open its first Branch within the Royal Marsden Hospital in London in May 1971.

Lausanne, Switzerland, though it would be six months before it was operational. With that move, the SAC added Henri Isliker, head of the Swiss Institute for Experimental Cancer Research, to its membership. The deliberations of the four would shape the scientific agenda and operational philosophy of the Institute for decades to come. Most significantly, perhaps, the Branch structure the SAC, Notter and the lawyers ultimately settled on addressed not only the tax auditor's requirements but also Ludwig's.

"The idea [was] that we would not make one big institute in one location but, rather, have branches in different locations, where our staff could collaborate effectively with the staffs of hospitals and research institutes and universities around the world," Carl Baker later explained to Butt. "When we decided to evaluate whether a new branch should be established, we paid a lot of attention to those possible collaborations."

How the Institute and Centers were funded

Daniel Ludwig donated about half his fortune to the Institute in the early 1970s. After his death in 1992, his remaining assets were used to establish trusts dedicated to supporting cancer research by other mechanisms.

YEAR	AMOUNT	SOURCE	RESULT
1971	Unknown, but in the millions of U.S. dollars	Bank account funded by D.K. Ludwig	**Cancer Research Institute Ltd** London Branch at Royal Marsden Hospital Lausanne Branch
1973	$60 million	Transea Carriers stock and an insurance company All assets of the dormant International Foundation for the Fight Against Cancer are transferred to the Cancer Research Institute	
1974	$500 million	Oceanic Tankships stock	Name changed to the **Ludwig Institute for Cancer Research** *One share, or 2%, of the Institute transferred to the Swiss Confederation.* Additional Branches opened over the next couple of decades
1990-92	$572 million	Sale of tanker fleet	
1992	$69 million value on date of Ludwig's death	National Bulk Carriers stock and securities establish Virginia and D.K. Ludwig Fund for Cancer Research	**Virginia and D.K. Ludwig Professorships, Chairs for Clinical Investigation and other research grants**
2006	$330 million	Virginia and D.K. Ludwig Fund	**Ludwig Centers established at six U.S. institutions**
2014	$540 million	Virginia and D.K. Ludwig Fund	Expansion of each Center's endowment

Going big

With the SAC in place and the first two Branches of the Institute up and running, Ludwig gave the Institute his first vote of confidence. In 1973, he donated to the Institute the stock of his shipping company, Transea Carriers, Inc., and an insurance company, a gift valued at about $60 million at the time (about $433 million in 2024 dollars). All assets of the long-dormant International Foundation for the Fight Against Cancer were also transferred to the Institute.

But that was just a first step. Later that year, Ludwig wrote Brownell to say he was considering giving even more to the Institute soon in the hope that he might, as Brownell said to Butt, "see some progress made [against cancer] while he was still alive and could enjoy it."

In the summer of 1974, Brownell instructed Palmer Baker to devise a plan to fund the Institute with the shares of Ludwig's international holding company, Oceanic Tankships, which owned a second holding company, Universe Tankships. According to Baker, "on a consolidated basis" the donation had a "book value" at the time in excess of $500 million—equivalent to roughly $3.2 billion in 2024 dollars—and represented about half of Ludwig's personal fortune. But now Ludwig wished to ensure that every penny of his legacy would in perpetuity go solely to the advancement of cancer research and care, not to any other biomedical endeavor and certainly not to any business or businessperson's profit.

To that end, Frey sought and obtained a covenant on the part of the Swiss Confederation to serve as a guarantor that Ludwig's gift—that is, the income the assets would provide to the Institute—would forever be applied exclusively to its stated charitable purpose. As part of the undertaking, the articles of the Institute were amended to provide for the ownership of one share, or 2%, of the Institute by the Swiss Confederation. The majority would be retained by the Trustees, but that single share gave the Swiss Confederation,

through its Department of the Interior, veto power over any subsequent change in the Institute's articles relating to its charitable purpose. Not even Ludwig himself could ever again access that fortune for personal business.

"Before D.K. made this donation," Frey recounted in his interview with Butt, "I took him into a separate room of our offices and once more explained to him thoroughly the meaning and importance of that act, and he said, 'Well, all right, I'm doing it.' And then the documents were signed in the presence of a civil officer of the Canton of Zurich."

It took some convincing—and even a little scolding by Butt—to get Ludwig to give his name to the Institute. And with that, on December 17, 1974, with the penning of a founding statement by Ludwig and otherwise minimal fuss, the Cancer Research Institute was renamed the Ludwig Institute for Cancer Research. Notter, who had long overseen the international businesses in the gift and had championed the Institute from its inception, was the logical choice to serve as chairman of its new Board of Directors.

Tectonic shifts

After chairing the Board of the Institute for five years, Notter resigned from Ludwig's organization and the Board in 1980 to try his hand as an independent international financier—a move that worked out quite well for him. Frey took his place as chairman of the Board. In 1984, Ludwig, who had begun to pay closer attention to the Institute, asked one of his closest friends and confidants, James Kerr, the former CEO of Avco, to join its Board. In June 1987, Kerr took over as chairman of the Board, bringing to the position a former CEO's "ability to get things done," as Palmer Baker would later tell Butt.

One of the first things he got done, in 1988, was to name Lloyd Old—who was chair of the SAC and on the Board—director of the Ludwig Institute, giving him an absolute line of authority over its administration. "That step was one of the most important in the organizational history of the Institute," Palmer Baker told Butt, noting that it assigned critical operational decisions to a scientist, who would be better equipped to raise the Institute's scientific profile.

That same year, Kerr also recruited from a law firm frequently retained by the Institute a very capable young lawyer named Edward McDermott to help him manage the assorted businesses held by Universe Tankships. Kerr almost immediately acquainted him with the Board of the Institute as well, making him its secretary, so setting up a partnership between McDermott and Old that would profoundly shape the Institute's scientific program.

But before any of that happened, McDermott would influence how all such efforts were funded. "At this time, the Ludwig Institute sat at the pinnacle of a pyramid, which was a vast commercial enterprise," McDermott recalled in a 2023 interview with the Ludwig Link magazine. "It wholly owned a range of companies that were run below the Institute level by Jim Kerr. I joined initially as a senior officer of the tankship company. We had a

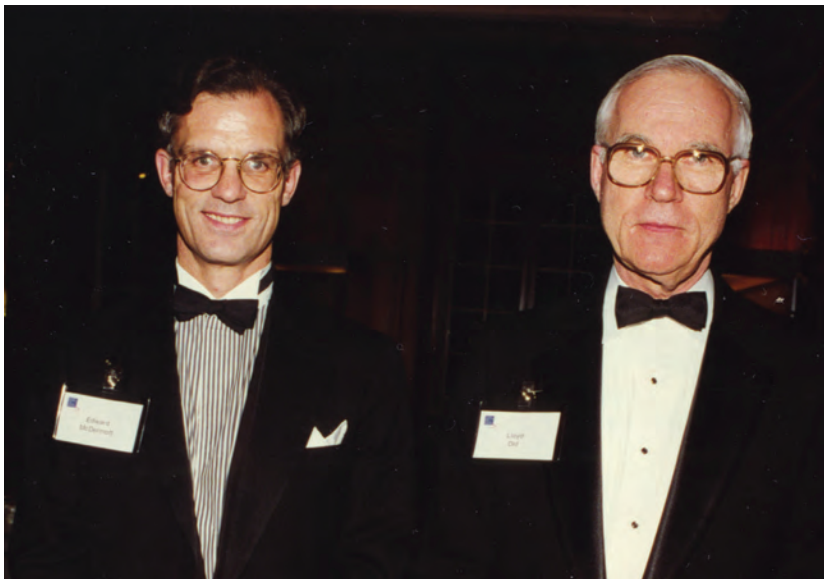
James Kerr, seated, with Herbert Brownell. Kerr brought a former CEO's "ability to get things done" to the Institute's Board.

fleet of supertankers, and we had oil and gas exploration interests in Indonesia and the North Sea. We had 50% ownership of 3 million square feet of commercial office space in Manhattan. At their peak, Mr. Ludwig's businesses were of unbelievable scale, employing some 35,000 people."

Then, on March 29, 1989, the oil tanker Exxon Valdez ran aground off the coast of Alaska, dumping 11 million gallons of oil into the Prince William Sound. McDermott grew alarmed as shocking images of environmental devastation played out for days on T.V. screens across the U.S. The Institute at the time chartered out several tankships to oil companies. "I realized that, as fiduciaries, we could not continue to operate in this manner," he said. McDermott approached Kerr with his concerns. Adding some urgency to the matter, a new law passed by the U.S. Congress "exposed everyone in the chain of transportation of oil to unlimited liability," McDermott recalled.

Kerr didn't need much convincing. With McDermott's assistance, he immediately set about the daunting task of unloading the fleet and variegated enterprises that had for some 15 years supported the Institute's operations.

"It took a great deal of confidence on Jim Kerr's part to dismantle Mr. Ludwig's commercial empire, but that's what we did," McDermott said. "Converting and diversifying the asset base to a much more conventional endowment structure and composition was a very important moment for the Institute's future, though that was not



Edward McDermott, left, joined in 1988 to help manage Ludwig's former businesses. That same year, Lloyd Old, right, became director of the Ludwig Institute.

immediately apparent. On August 1, 1990, we deposited $500 million in sales proceeds with two groups of asset managers, and in the first month we lost $50 million because, on August 3, Iraq invaded Kuwait. Reporting at the first Board meeting on how we'd diversified to lower the Institute's risk profile was less than convincing."

The sale of Ludwig's fleet turned out to be unexpectedly profitable. "The amazing thing was, we sold them in their 28th year of life for more than they had cost to build," McDermott recalled. The credit for that falls to Ludwig, who maintained his ships in top shape. The transfer of funds from the sale—which was completed in 1992 and ultimately totaled $572 million (nearly $1.3 billion in 2024 dollars)—paid off in the long run, especially after McDermott brought the management of those funds in house: The Institute's returns on investment have long and consistently outperformed those of its peers.

McDermott became President of the Institute in 1995, the same year Kerr died from heart failure at his home in La Jolla, California, at the age of 77—three years after the death of his old friend, Daniel K. Ludwig. That same year, Old was named CEO of the Institute, remaining in that position until he became chairman of the Board in 2005. He retired in 2009, a couple of years before his death from prostate cancer.

McDermott was named CEO in 2010 and retired in July 2024, to chair the Board.

Branching out

The Institute expanded significantly in the decade after it took ownership of Universe Tankships, adding briskly to its first two Branches, beginning with one in Sydney in 1976. At different points in that period, three additional Branches would open in the U.K. (two in London and one in Cambridge); new ones in Australia (both in Melbourne) and Switzerland (in Bern); two in Canada (Toronto and then Montreal); in Brazil (São Paulo); two in Sweden (Uppsala and Stockholm); and one in Brussels, Belgium.

By its 20th anniversary, in 1991, the Institute had nine branches in seven countries, each with 30 to 75 staff. The Institute's expansion had slowed, with just two new Branches set up in the U.S. (one in New York, led by Old, and one in San Diego that moved from Montreal).

The Branches were not sited arbitrarily. Ludwig himself had preferred that they be established in places where he was doing business, but the SAC, too, had its criteria. Most important among these was access to talented scientists working in fields its members felt held promise for the advancement of cancer research, with each of the Branches focusing on one of those areas.

Molecular biology was one of them. "The shift from biochemistry to molecular biology occurred in the midst of our activities, so that [in selecting] our later branches, we made sure that the program and the director and senior staff had an appreciation and were contributing to the new developments" in the field, Carl Baker explained to Butt. This guided the establishment of Branches in Melbourne in 1980, and in Uppsala, Stockholm and at University College London in 1985, all decisions that paid significant dividends.

By the mid-1980s, with the Institute's contributions to the field growing apace, Brownell periodically arranged to have Ludwig briefed on its progress. At one of these sessions, Ludwig was upset when he learned that the Institute's scientists were, for the most part, content with merely publishing their discoveries, largely uninclined to patent them or

Munro Neville was director of the first London Branch, established an Institute-wide intellectual property program in 1989 and went on to become associate director of the Ludwig Institute.

develop them into clinical interventions. An upshot of this incident was that, in 1984, the Institute retained a company named Research Corporation to handle its intellectual property, letting it take total ownership of discoveries and future inventions—and the lion's share of future revenue—in exchange for handling the business end of things, which none of the Branch directors wanted to do.

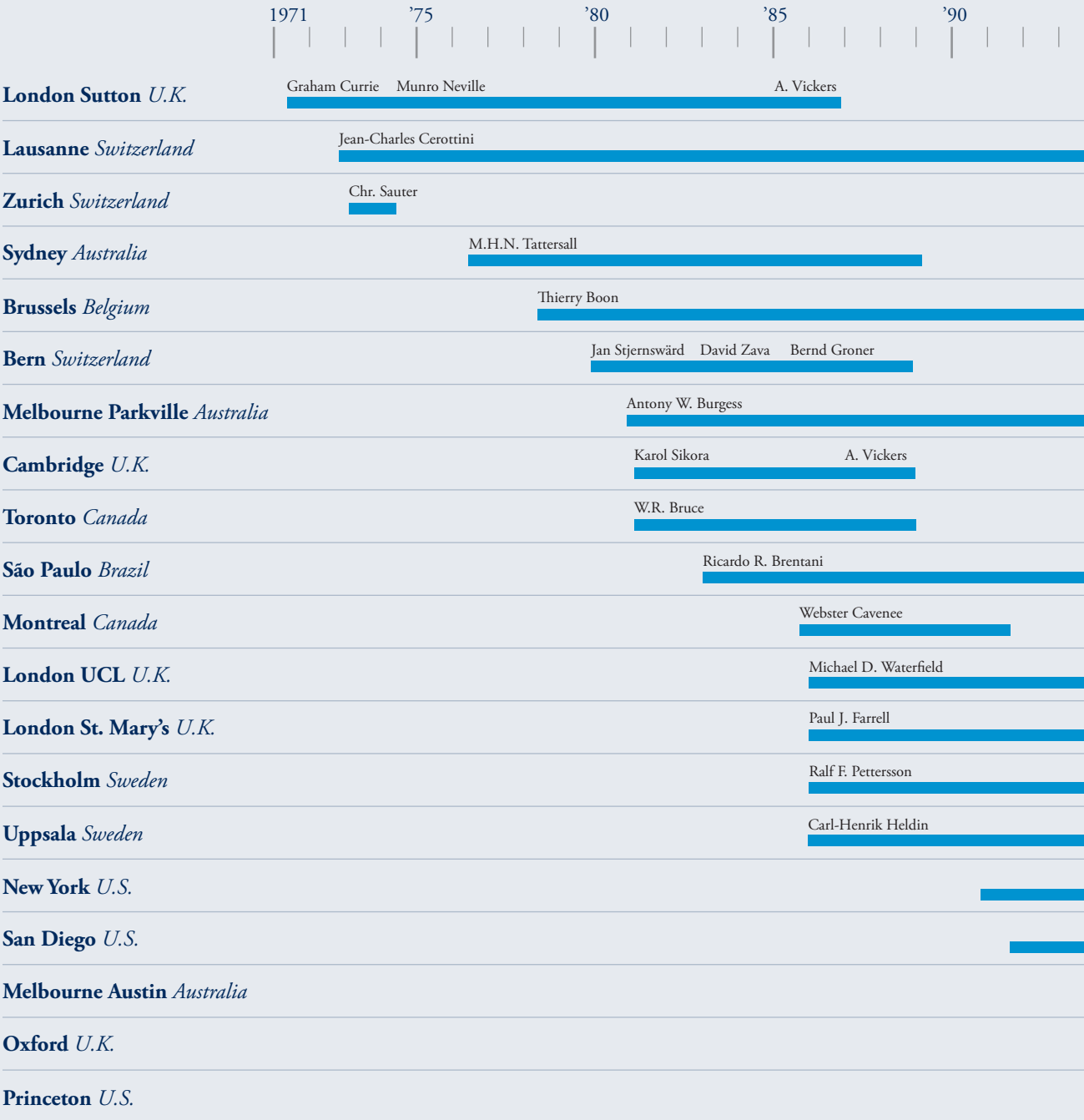
"The attitude of the Branch directors at that time was very firmly one of disinterest: 'leave us alone to get on with our work and don't disturb us with this nonsense about patenting, licensing and so forth'," recalled A. Munro Neville, who had previously led the first London Branch and would go on to work closely with Old as an influential associate director of the Institute.

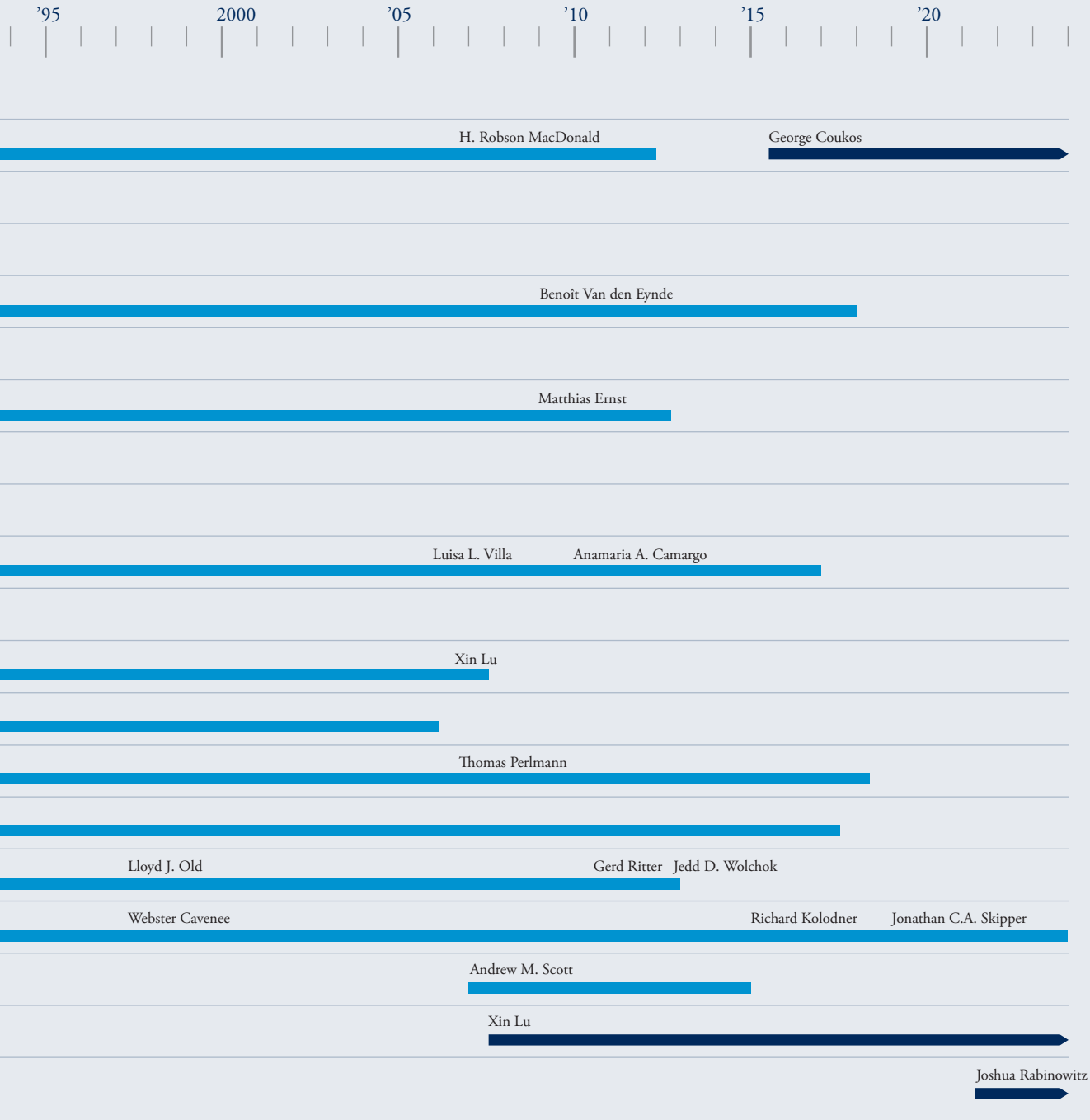
The arrangement with Research Corporation did not last. Appointed research administrator of the Institute in 1985, Neville noticed at some point while going over Branch publication records, that a number of potentially valuable discoveries had been left on the table by Research Corporation and its affiliates. Old was not happy. In April 1989, McDermott, who was by then general counsel of the Institute, advised the company of Ludwig's decision to exercise its right to terminate their agreement after five years.

That same year, Neville transferred to London, where he established an intellectual property (IP) office with three scientists on staff that would take on the onus of managing IP across the Institute. The aim in doing so was to maximize the Institute's control over the fate of its discoveries and to set up, through licensing and royalty agreements, additional streams of funding for its ongoing cancer research. In 1997, a scientist named Jonathan Skipper joined the IP office in London and in 2000 took over from Neville as its manager, overseeing a rapidly expanding portfolio of intellectual property. Later that year, Skipper completed the transfer of the IP office to New York, and by 2003 was overseeing the entire IP operation as head of a new Office of Program Development.

Branches of the Ludwig Institute

The Institute underwent a period of rapid expansion in its early years, ultimately opening Branches in nine countries. Today it has three Branches in as many countries.

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Thomas Perlmann
Lloyd J. Old
Gerd Ritter
Jedd D. Wolchok
Webster Cavenee
Richard Kolodner
Jonathan C.A. Skipper
Andrew M. Scott
Xin Lu
Joshua Rabinowitz

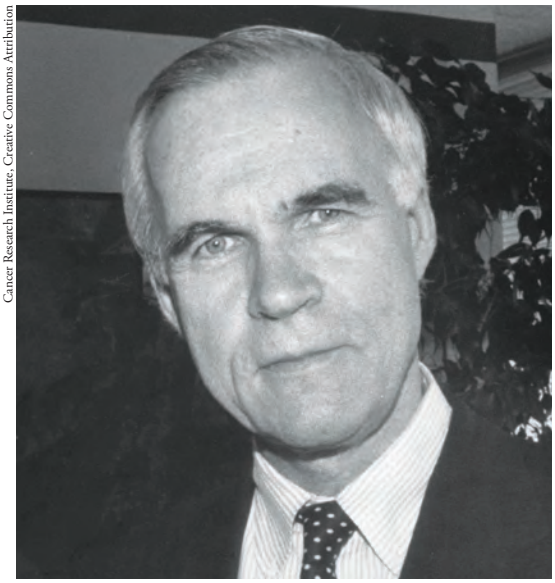
Making a mark

The IP team was kept busy from the very beginning. Researchers at Ludwig Melbourne, for example, had by 1984 cloned the genes for four important biochemical factors involved in immune cell growth, including the granulocyte-macrophage colony stimulating factor (GM-CSF), which remains today a staple of cancer care as well as an element of several experimental strategies for cancer immunotherapy. The team there also conducted the first definitive clinical trials and analysis of recombinant GM-CSF and another such factor (G-CSF) as a treatment for immune recovery following cancer therapy.

The Ludwig Uppsala team, for its part, homed in on the platelet derived growth factors (PDGF) and their receptors in the late 1980s, exhaustively characterizing their signaling networks and roles in various cancers. One of those receptors is today a target of several drugs for the treatment of gastrointestinal stromal tumors and leukemias.

At the UCL Branch, researchers began in 1992 a multi-year project that defined a family of signaling enzymes known as the PI3 kinases that were subsequently shown to be among of the most frequently mutated genes in cancer. This work led to the development of the first targeted inhibitor for PI3 kinase and the launch in 2003 of the Ludwig Institute's first biotech, Piramed, which was acquired by Roche in 2008.

Translational research was not the only way the Institute was making its mark. When the São Paulo Branch developed a novel method for high volume sequencing of the genome in 2000, the Institute pitched in $10 million to establish one of the largest genome sequencing centers in the world in São Paolo in partnership with Fundaçao de Amparo à Pesquisa do Estado de São Paulo (FAPESP), starting the Ludwig-FAPESP Human Cancer Genome Project. In partnership with the U.S. National Cancer Institute (NCI), the project published expressed gene sequences of the "transcriptome" as quickly as possible, making among the largest contributions of such data to public databases.



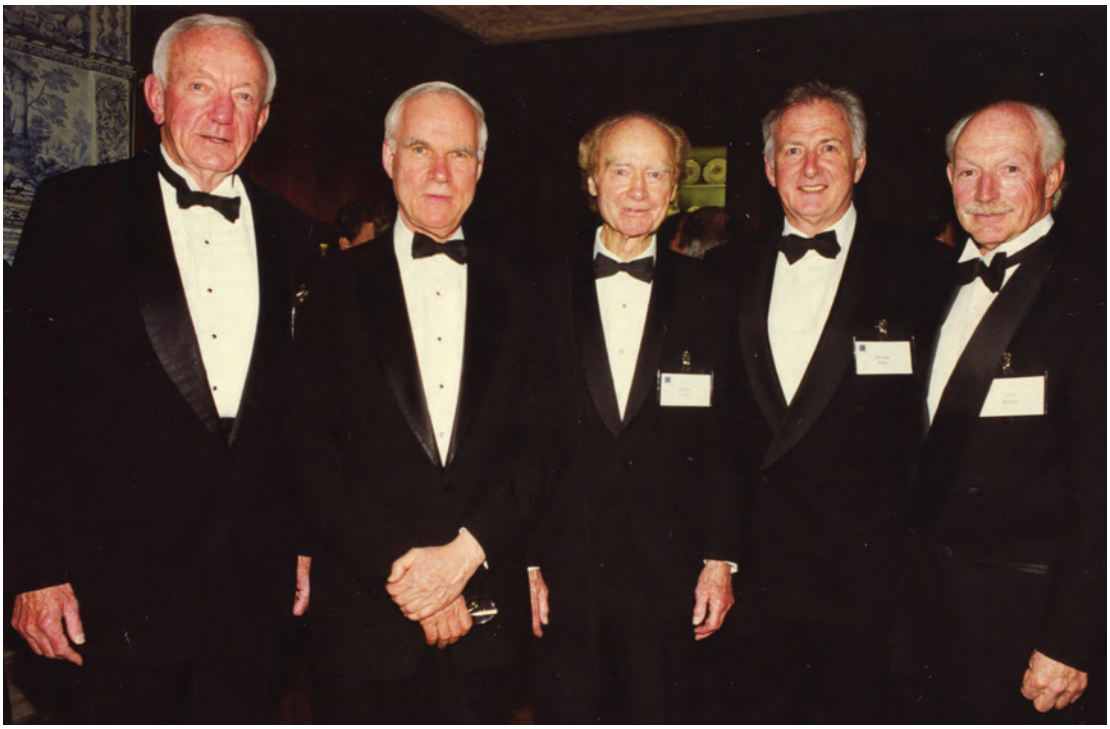
Lloyd Old continued to champion tumor immunology even after the field fell out of favor in the 1980s. His discoveries, and those of others he recruited to the Institute, helped lay the foundations of cancer immunotherapy, which is transforming cancer care and remains a major pillar of the Institute's scientific program.

One of the Institute's aims in doing so was to stymie a race in the industry at the time to patent as many expressed DNA sequences as possible, a practice it opposed on principle.

"The Institute is nimble and adaptable, and because it has substantial resources of its own, can respond to challenges and seize opportunities," McDermott observed in his 2023 interview.

TAKING RISKS

Crucially, the Institute's scientific leadership was also free to invest in research that more traditional funders might have found too risky to support. When the field at large turned its back on the possibility of cancer immunotherapy in the 1980s, for example, Lloyd Old—who had shown in a paper published in 1959 that the tuberculosis vaccine, BCG, could treat bladder cancer and had discovered the tumor necrosis factor, which plays a pivotal role in immunity—kept the faith. From his position on the SAC, Old channeled steady support to the broadly neglected discipline of tumor immunology. That support was most visibly expressed with the opening of the first Lausanne Branch in 1973 and then the Brussels Branch in 1978. These Branches—and, later, the New York Branch headed by Old himself—would make foundational discoveries in T cell biology and tumor immunology through the 1980s and 90s, laying the scientific and technical groundwork for cancer immunotherapy.



From left, John "Jack" Barry, Lloyd Old, Hugh Butt, Donald Park—a founding administrator of the Institute—and John Notter at the Ludwig Institute's 25th anniversary celebration in 1997.

Beginning in 1982, the Brussels team showed that spontaneously arising tumors do in fact express antigens that can be recognized by the immune system, something that many cancer researchers doubted at the time. It then demonstrated that tumors can escape immune clearance by ceasing to express cancer antigens, and that the immune system helps maintain the integrity of the genome, weeding out wayward, potentially cancerous cells. These findings provided some of the earliest experimental evidence for the immunoediting and immunosurveillance hypotheses, concepts central to tumor immunology and immunotherapy.

By 1991, the Brussels team had proved that T cells can recognize specific antigens in human melanomas, and then identified the first naturally occurring cancer antigen recognized by T cells, first in mice and then in humans. The latter, they named MAGE-1 (subsequently renamed MAGE-A1). They would go on to identify several more such antigens, including many belonging to similarly expressed families of antigens (the BAGE and GAGE clans) that, like MAGE-A1, are expressed only in the testes and in tumors. These would become known as the cancer testes (CT) or cancer-germline

antigens. The Brussels researchers also devised cancer vaccines using these antigens and began preliminary studies of their efficacy in patients with melanoma.

The antigens became the focus of multiple efforts by research institutions, including Ludwig and the NCI, to devise and evaluate cancer vaccines in clinical trials. Pharmaceutical companies such as GlaxoSmithKline and Sanofi became interested and partnered with Ludwig to develop antigen specific cancer immunotherapies based on MAGE, with GSK completing large, randomized phase 3 studies in lung cancer and melanoma. The antigens continue to be harnessed by Ludwig and many others in ongoing efforts to develop precision vaccines and cellular immunotherapies for cancer.

In parallel with this work, the team at the Lausanne Branch described through the 1970s and 80s the development and functional differentiation of the immune system's T lymphocytes, which detect and destroy diseased and malignant cells and are the frontline agents of most immunotherapies today. They detailed the activity and dynamics of cytotoxic T lymphocyte (CTL) responses and developed robust methods for the cloning, quantitation and functional analysis of CTLs that were broadly adopted in the field. And they collaborated closely with other Institute Branches—especially Brussels and New York—on cancer vaccine development and the analysis of T cell responses to cancer antigens. Its researchers also identified and extensively characterized the invariant natural killer T cell, which targets tumors by attacking cancer cells and inhibiting other immune cells that support their survival. These cells hold some additional promise as agents of cancer immunotherapy.

FILLING GAPS, BRIDGING CHASMS

In the 1990s, the Institute would also leave its mark on the field of cancer prevention. In collaboration with McGill University researchers, the São Paulo Branch established a cohort of more than 2,500 patients, running the longest longitudinal study of human papillomavirus (HPV) infection. It also led clinical trials in conjunction with Merck, that were instrumental to the development of one of the most effective tools for cancer prevention—the HPV vaccine. Subsequent studies at the São Paulo Branch contributed important evidence on HPV's role in oral, penile, anal and head and neck cancers in men and informed the recommendation that young men should also receive the HPV vaccine.

Meanwhile, as the Institute sought to translate its own discoveries into diagnostics and therapies, it increasingly needed access to high-quality biologics—that is, biologics whose production, in accordance with Good Manufacturing Practices (GMP), would pass muster with regulatory agencies. But pharmaceutical companies could not

realistically produce them in small quantities, and buying them in bulk would have been unaffordable and wasteful. At the time, no academic institution had the ability to make GMP biologics. The Institute responded by establishing a GMP Biological Production Facility at its Branch in Melbourne in 1995 and another through a partnership with Cornell University in Ithaca, New York, in 2002.

The GMP facilities were emblematic not only of the Institute's ability to fill critical gaps in the field, but to do so quickly, unhampered by bureaucracy. "When we decided to build the GMP facilities, we had the resources to do it and we didn't wait two years: we just did it," said McDermott.

The Melbourne facility was established to supply and otherwise support the Institute's growing therapeutic monoclonal antibody program. It enabled, among other things, a Ludwig-wide collaboration involving the New York, San Diego, Melbourne, Stockholm and London Branches to develop and clinically evaluate an antibody named mAb 806 that had been generated at the New York Branch. mAb 806 specifically targets the mutant EGF receptor, EGFRvIII—which drives a major subtype of glioblastoma—and amplified EGF receptor, which fuels several other solid tumors, including lung, head and neck cancers. The Institute sponsored the first clinical trial of mAb 806 using clinical grade drug product manufactured by the Melbourne facility. On the basis of this study, the antibody was licensed by AbbVie, which used it to make an antibody-drug conjugate (ADC) evaluated in large Phase III trials as a treatment for glioblastoma. Though the trials ultimately failed, the antibody itself is functionally sound: AbbVie is using it to generate a new ADC for the treatment of a variety of other cancers.

The Ithaca facility also supported efforts led by Old to develop NY-ESO-1, a cancer antigen conceptually similar to MAGE discovered by the New York Branch, into a cancer vaccine. Though the vaccine did not prove to be of clinical benefit, the effort put into its development contributed enormously to the field. To address a crippling lack of coordination and scale in cancer vaccine development efforts, for example, the Ludwig Institute launched in 2001 the Cancer Vaccines Collaborative (CVC) in partnership with the Cancer Research Institute, whose Scientific Advisory Council was directed by Old. The CVC established a consortium of laboratories and clinical facilities across Japan, Australia, the U.S. and Europe to bridge the chasm between the laboratory and clinical discovery.

When it became clear that researchers and contract research organizations had little experience in conducting clinical trials of cancer immunotherapies, the Institute assembled its own clinical trials management team (CTM) to establish that expertise internally. The CTM team helped CVC researchers conduct more than 50 early phase clinical trials of NY-ESO-1 and other CT antigen cancer vaccines over roughly a decade,

Jonathan Skipper, who led the Technology Development team, forged partnerships with pharmaceutical companies for clinical studies. He became president of the Institute in 2024.

effectively training a global phalanx of researchers in the management of immunotherapy trials. It also managed the early clinical development of several monoclonal antibodies generated by the Branches for diagnostic and therapeutic uses. These capabilities attracted clinical collaborations with drugmakers, who were increasingly eying cancer vaccines as new drug development opportunities.

Later, the Ludwig Institute's Technology Development team, led by Jonathan Skipper—who was made President of the Institute in July, 2024—would lend its expertise to forging partnerships with pharmaceutical companies to provide researchers in the CVC's Clinical Trial Network access to immunotherapeutic drugs for clinical studies of combination therapies. The CVC's extensive characterization of the NY-ESO-1 antigen and other CT antigens and the immune responses they elicit has not gone to waste either. The CT antigens remain central to multiple strategies and technologies for cancer vaccines and cellular immunotherapies under commercial development today.

Setting up the Centers

Ludwig's 1974 transfer of Universe Tankships' assets to the Institute was only the first of his gifts to cancer research. In his will, he directed his trustees to donate his remaining assets in the U.S. to the cause as well.

That began after his death on August 27, 1992, with the transfer of the stock and securities of his holding company National Bulk Carriers to a trust funding Virginia and D.K. Ludwig Professorships at six U.S. institutions named in his will: the University of Chicago, Harvard University, Johns Hopkins University, the Massachusetts Institute of Technology, MSK and Stanford University. The trust also established Ludwig Chairs for Clinical Investigation and issued other grants to support research programs at the chosen institutions. In 2006, $328 million from the Virginia and D.K. Ludwig Fund—the ultimate posthumous vehicle for Ludwig's U.S. assets—was used to establish autonomous Ludwig Centers at each of those institutions, which had already received more than $20 million each in grants from the Fund.

This was followed by a $540 million gift to the Centers in 2014, raising the total donated to them to nearly $900 million, among the largest private gifts ever made to cancer research. McDermott was instrumental to devising the legal mechanism for the sale of the last remaining interests of the Fund—two high-rises in New York. His prescience, early planning and methodical execution of the sale maximized the profits that were ultimately distributed to the Centers.

Together, the Ludwig Institute and autonomous Ludwig Centers would come to be known as Ludwig Cancer Research.

The creation of the Centers—each, like the Branches, focused on a major area of cancer research—would be of enormous benefit to the field. To give just one example, it supported the establishment of a next-generation sequencing facility at the Johns

National Bulk Carriers had 50% interest in two New York office buildings. Proceeds from their sale enabled an additional $540 million infusion of funds to the six Ludwig Centers.

Hopkins Center. The team there went on to map global gene expression for scores of cancers, launching a program of technology development that would eventually make it a leader in the development of "liquid biopsies", which analyze vanishingly tiny traces of DNA shed by malignant cells into body fluids for the early detection of cancer.

Armed with that technology, researchers at the Center collaborated with former Ludwig Melbourne scientists to develop a liquid biopsy to improve the management of colon cancer therapy—part of a five-year, $10 million partnership for cancer prevention launched in 2015 between the Conrad N. Hilton Foundation and the Ludwig Institute that was arranged by Notter. A large clinical trial reported in 2022 that their approach accurately predicted risk of recurrence after surgery for patients diagnosed with stage II colon cancer and that directing chemotherapy only to those who tested positive for ctDNA reduced overall use of chemotherapy without compromising recurrence-free survival.

The MSK Center is perhaps best known for its vital contributions to the clinical

development of anti-CTLA-4 antibodies for the treatment of melanoma—the first of the checkpoint blockade immunotherapies that sparked a revolution in cancer care. Other work at the Center, which focuses on tumor immunology, has exhaustively characterized the role of suppressive regulatory T cells in cancer and conducted basic and translational explorations of tumor immunology too numerous to describe here.

The Harvard Center employed its endowment to develop an extraordinarily effective program of collaboration—and a remarkably cohesive community of researchers—that has turned it into a virtual engine of discovery and translational cancer research. Its work loosely revolves around drug resistance of cancers, though its many participating scientists have a foot in perhaps every subfield of cancer research. The Chicago Center, for its part, has explored breast cancer biology and therapy and exhaustively characterized immunologic responses to radiotherapy. Most notably, the Center developed and advanced the theory of oligometastasis, which posits certain limited and localized tumor metastases can be cured with aggressive local therapy and has significantly influenced clinical practice.

The Stanford Center, while ostensibly focused on cancer stem cells, has drawn into its fold extraordinarily prolific scientists working on everything from pediatric brain cancers to the development of novel cellular immunotherapies to cancer genomics and liquid biopsies. The MIT Center, meanwhile, explores the various stages of cancer progression—from the cellular transformations that equip tumors to metastasize to those that enable their resettlement in distant tissues. But, there too, researchers are working on subjects and potentially transformative technologies—from nanotechnology to cutting edge models of cancer—too diverse to fit in a single basket.

Restructuring

As the Centers revved up their research programs, the Institute had hardly been idle. Though historically averse to the limelight, it had long ago achieved among the biomedical cognoscenti a reputation for stellar talent and groundbreaking research. Its contributions to everything from cancer genomics to oncogenic cell signaling were well known. But, perhaps above all, it was renowned for its steady and unflagging support for tumor immunology and its foundational contributions to the scientific infrastructure of cancer immunotherapy, an idea that was by the mid-aughts poised to take the field by storm. Many of the Institute's researchers, alumni and collaborators were—and remain today—on the front lines of that revolution.

The ten Branches run by the Institute were, in a nutshell, doing exactly what Ludwig had wanted his Institute to do: engage a global phalanx of scientists to collaborate across borders and institutions, attracting the best and brightest and giving them the resources, time and space they required to develop and rigorously test their most daring ideas for the eventual conquest of cancer. Still, the complexity of running such a vast and geographically scattered operation was daunting, to say the least.

It was also expensive. This became painfully apparent with the global financial crisis of 2008, which left a sizeable crater in the Institute's resources—and raised some questions. If the Institute's provision of reagents and expertise in immunotherapy had once been indispensable, for example, those resources were now widely available from contract manufacturers and research organizations. How much of what the Institute was doing was still necessary? For that matter, how efficient was the Institute in general?

"The effects of the recession of 2008 on our asset base were very distressing," McDermott explained. "But they forced us to really consider how sustainable the ten-Branch structure was and the way we were organized. It was very administratively top heavy. Due to audit requirements, you needed checks and balances, so you needed an administrative team

The 2008 financial crisis forced Ed McDermott, then president, to reconsider the Institute's global footprint.

Institute co-founder John Notter returned to the Board in 2009 and became chairman the next year.

of a certain number at each Branch, whether you had five staff members or 50. In addition, team science was becoming more and more what we thought needed to be done, so we wanted more critical mass. For example, a million dollars for a piece of equipment wasn't outrageous, but you wanted it someplace where it was going to be used 24/7, not three days a week."

As these challenges intensified, Old turned to his old friend and Ludwig Institute co-founder John Notter for assistance. On January 1, 2009, Notter rejoined the Board of Directors, bringing his financial acumen back to the Institute to help it weather the economic storm. He was named Chairman the following year.

With the Board's support, the Institute began a gradual contraction of its geographic footprint. "I think focusing on three core sites, though initially painful—we had great scientists at these other sites—was imperative for the long term," said McDermott. The closures gave scientists sufficient time to prepare for the transition and reintegrate fully into their host institutions or, if they wished, pursue new opportunities.

The Institute today

The Ludwig Institute, headquartered in New York and Zurich, today has three core Branches: one at the University of Oxford, established in 2007 (when it was transferred from UCL); a new one at the University of Lausanne, which opened in 2015; and the youngest of the three, at Princeton University, which was established in 2021 under the leadership of McDermott and Chi Van Dang, who joined the Institute in 2017 as scientific director and was additionally named CEO in July 2024.

A physician and scientist, Dang is renowned for his pioneering work on cancer cell metabolism, most notably his sweeping exposition of how a cancer gene named Myc rewires the metabolic circuitry of cancer cells and disrupts their circadian rhythms to support tumor growth and survival. Aside from this impressive scientific resume, Dang also brought to the Institute considerable experience in scientific administration and strategic planning, having served for the previous six years as director of the Abramson Cancer Center at the University of Pennsylvania's Perelman School of Medicine.

Dang's skills have been put to good use overseeing the research programs at the Institute's Branches and laboratories. The latter include a Ludwig Collaborative Laboratory at Weill Cornell Medicine that specializes in cancer immunology and immunotherapy; Dang's own laboratory at Johns Hopkins University; and a pair at the de Duve Institute in Brussels that are linked to the Oxford Branch and focus, separately, on tumor immunology and slow-growing blood cancers known as myelodysplastic syndromes.

The research programs and administration of these Branches and laboratories is overseen by the Ludwig Institute's Board of Directors, which is responsible for the governance, strategic planning and financial oversight of the organization. When the Institute was established in 1971, Swiss law required a majority of its Board to be Swiss citizens—which was one reason John Notter, Hugo Frey and Adolf Kammerer were the Institute's first directors. When that was no longer required, the Institute's Board expanded to

Chi Van Dang, who became scientific director in 2017 and CEO in 2024, is known for his pioneering work on cancer cell metabolism.

include more scientific representation. The current Board maintains a salubrious balance of financial, legal, scientific and medical expertise.

In line with Institute tradition, each of the core Branches focuses on distinct and promising areas of inquiry. The Ludwig Oxford Branch investigates, in various ways, the extraordinary plasticity of malignant and nonmalignant cells within tumors. Its scientists study how cancer-driving mutations to DNA interact with non-mutational—or epigenetic—changes in cancer genomes that reprogram gene expression and thus the behavior of cancerous cells. The Branch is also exploring the chemistry and biology of epigenetic modifications made to the transcripts of genes and other types of RNA molecules, a new frontier of molecular biology.

On the translational front, the Branch is applying cutting edge epigenetics technologies to devise liquid biopsies for cancer detection. Epigenetic mapping is useful to such diagnostics because it can reveal not only the presence of a cancer but also its tissue of origin. The Branch seeks to harness its insights on the role of cell plasticity in the genesis and progression of cancers to devise novel strategies for cancer diagnosis, prevention and therapy.

Since it is housed in The University of Oxford's Nuffield Department of Medicine, its researchers have access to both clinical expertise and cancer patients for their research and translational efforts. This relationship enabled, for example, an immunotherapy trial for esophageal cancer patients that was supported by the Institute. The trial furnished tumor samples that continue to be analyzed for insights on the immune and molecular correlates of patient responses to immunotherapy as well as the biology of this common type of cancer.

The new Lausanne Branch, like its distinguished predecessor, has taken tumor immunology and immunotherapy to a new level. Its researchers have produced textured profiles of the immune landscapes of tumors. Studies there have revealed, variously, how gene expression patterns in cancer cells and immune cells as well as their interactions and metabolic crosstalk in the tumor microenvironment drive malignancy and influence responses to therapy across cancer types. They have captured subtleties in the biology of tumor-associated myeloid cells—like macrophages, neutrophils and dendritic cells—that are not only scientifically intriguing but also rich with clues to new therapeutic strategies.

Scientists at the Lausanne Branch have been developing, in partnership with the University of Lausanne Hospital (CHUV), cell therapies and cancer vaccines tailored to target the tumors of individual patients. Samples collected in clinical trials of adoptive T cell therapies and personalized cancer vaccines are providing valuable information on tumor immunology, including how cancer antigens are recognized by the immune system and how this influences tumor evolution. This program of research has also driven the development of sophisticated analytical and computational methods at the Branch to identify and harness unique antigens encoded by each patient's tumors and the T cells best equipped to target them productively.

The youngest of the Ludwig Institute's Branches, at Princeton University, focuses on cancer metabolism. Cancer cells rewire their metabolism to obtain the raw materials they require to sustain proliferation. Such adaptations not only drive tumor growth but can cripple the anti-tumor immune response as well, compromising the efficacy of cancer immunotherapy. Metabolic dysfunction also influences clinical outcomes, not least due to the wasting disorder cachexia, a leading cause of cancer-related mortality. Conversely, the metabolic rewiring of cancer cells creates unique nutritive dependencies and biochemical vulnerabilities that can be exploited for cancer therapy. A more granular understanding of metabolic adaptations and their effects is therefore of great value to the development of new cancer drugs and treatment strategies, immunotherapies and preventive interventions.

The Ludwig Princeton Branch focuses on three main areas of cancer metabolism:

metabolic interactions between tumors and the rest of the body, focusing on how the body supports tumor growth and metastasis; dietary strategies for the prevention and treatment of cancer; and the interplay of host metabolism, the gut microbiome and the anti-cancer immune response. Its requisite link to clinical facilities is provided through its partnership with RWJBarnabas Health and Rutgers Cancer Institute of New Jersey. Researchers at the Branch have already made major discoveries about systemic, cellular and cancer metabolism that have challenged longstanding dogma and created exciting new possibilities for the improvement of immunotherapy and other types of cancer treatment.

PULLING TOGETHER

The Institute's three Branches significantly extend their reach through collaborations with the autonomous Centers of Ludwig Cancer Research, a strategy championed by Dang. As scientific director, he has channeled the Institute's resources into programs that build bridges across Ludwig Cancer Research.

The Ludwig Tumor Atlas project, launched in 2019, was one such initiative. Based at Ludwig Harvard, the project developed powerful new imaging technologies that enable the high-dimensional imaging—the simultaneous visualization of dozens of molecular markers at once—to map the locations, identities and functional traits of not just cancer cells but also noncancerous immune and other supporting cells in tumors. This project forged collaborations across Ludwig Branches and Centers exploring a wide range of phenomena of relevance to both basic biology and the treatment and diagnosis of cancers. The Ludwig Harvard team also developed advanced technologies to integrate high-dimensional imaging into the routine workflow of the clinical pathology laboratory, potentially addressing a critical medical need.

The Institute also started in 2024 a multi-institutional research program examining the interplay of diet and immunometabolism, or the metabolic crosstalk between tissues and the immune cells that patrol them. Much recent evidence suggests that the exploitation of this crosstalk represents a key mechanism by which tumors disable the anti-cancer immune response.

The three-year, $4.2 million Ludwig Immunometabolism Initiative examines at multiple levels how dietary interventions shape the tumor microenvironment (TME) and its immune landscapes, alter cancer progression and modulate responses to therapy, especially immunotherapies. Research proposals submitted for this program were required to be collaborative, involving partnerships between two Ludwig sites or their host institutions. The selected projects involve researchers at Johns Hopkins University

Ludwig Cancer Research locations

The Branches, Centers and laboratories sustained by Daniel Ludwig's legacy work collaboratively, engaging the diverse talents and expertise of colleagues across Ludwig Cancer Research to solve some of the toughest conundrums of cancer biology.

Headquarters	New York, Zurich
Branches	Princeton University
	University of Lausanne
	University of Oxford
Centers	Harvard University
	Massachusetts Institute of Technology
	Memorial Sloan Kettering Cancer Center
	Johns Hopkins University
	Stanford University
	University of Chicago
Laboratories	Ludwig Collaborative Laboratory at Weill Cornell Medicine
	Chi Van Dang's laboratory at Johns Hopkins University;
	Two labs at the de Duve Institute in Brussels, linked to the Oxford Branch

and at the Centers at MIT and Harvard collaborating with scientists at the Ludwig lab in Brussels and at the Oxford, Princeton and Lausanne Branches.

With minimal administrative overhead to weigh it down, the Institute is better resourced than ever to fund more such synergistic collaboration. It remains independent, but is nimbler, prepared to seize scientific opportunity or move swiftly to help address critical needs of the field. It is, in other words, a more efficient institution, and the benefit of that greater efficiency goes entirely to its mission—the eventual conquest of cancer envisioned by its founder.

The people of Ludwig Cancer Research, as McDermott noted, are privileged to be the agents of that mission.

"The asset base that supports Ludwig was built with the sweat and blood of thousands of people. It didn't just arrive here from nowhere. It is Mr. Ludwig's legacy, but it's also the legacy of the many thousands of people who worked at his companies over the decades. We owe it to them as much as we owe it to Mr. Ludwig to produce."