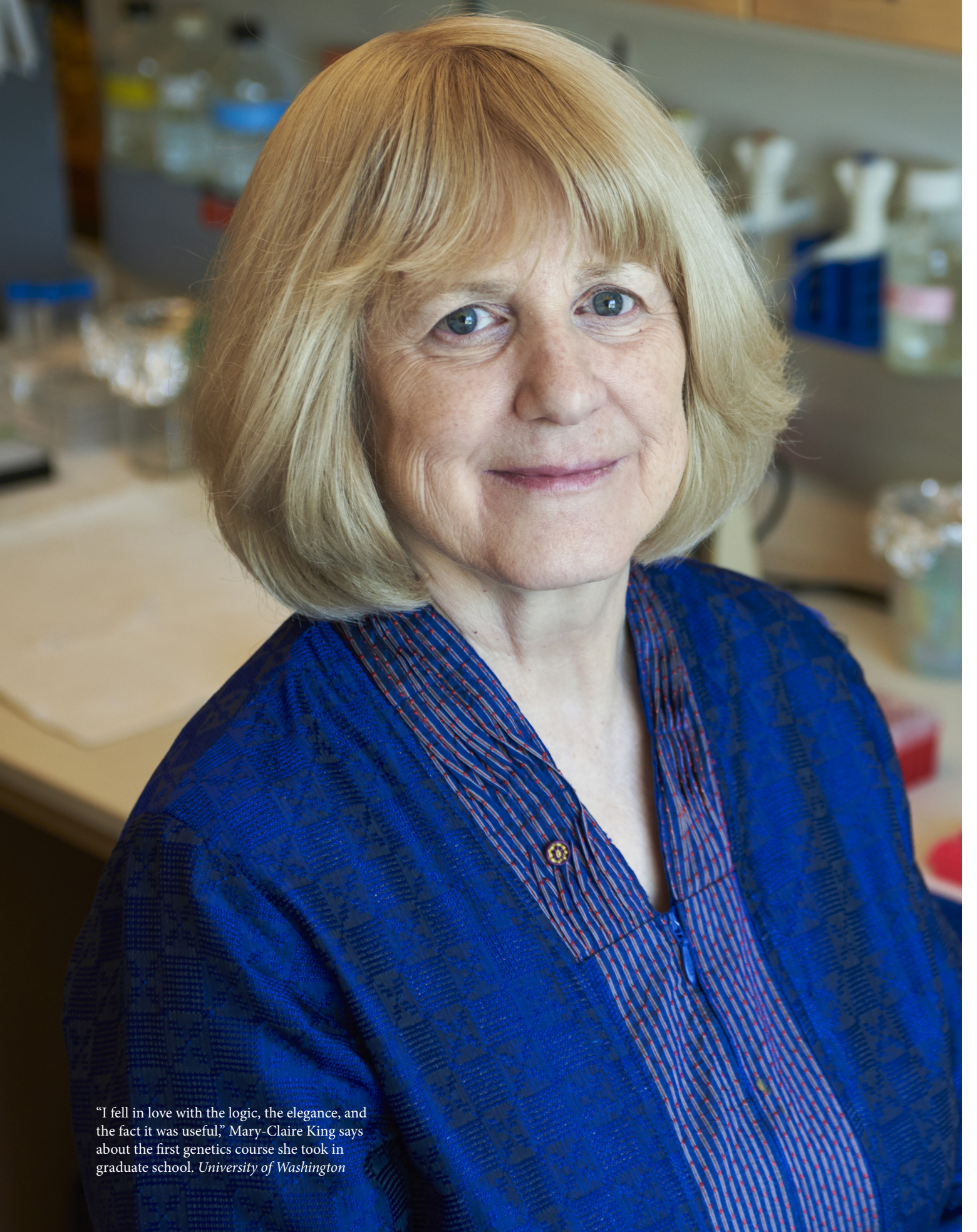


"I fell in love with the logic, the elegance, and the fact it was useful," Mary-Claire King says about the first genetics course she took in graduate school. *University of Washington*

# MARY-CLAIRE KING

## "For her, science is personal"

Mary-Claire King was pursuing a graduate degree in statistics at Berkeley when, on a lark, she took her first course in genetics. An avid puzzle-solver, King was enchanted. She sat up front for lectures by Curt Stern, who wrote a pioneering textbook on human genetics. The soft-spoken Stern would pose intricate story problems to his packed classes. Then he'd sort them out with elegant logic. It was human puzzles with purpose. She couldn't believe anything so important could be so much fun.

But life during wartime intervened. It was 1968, Vietnam's deadliest year for U.S. troops. The draft escalated. Protests roiled Berkeley. Governor Ronald Reagan, who had launched his political career by vowing to "clean up the mess" at the University of California, cracked down on dissident students.

The campus was shut down intermittently by conflict. King was looking to do something productive that summer when a little card posted on a bulletin board grabbed her imagination. The brainy consumer advocates known as Ralph Nader's Raiders were probing the tangle of money, politics and public land in a new project called "Who Owns California?" They were seeking a biologist, which King was not. Their posting stressed the job's long hours and low pay.

That's for me, she thought.

She researched the widespread use of pesticides for Nader and wrote about its harmful impact on farmworkers. She came to think of Delores Huerta, co-founder of the United Farm Workers union, as a hero. Huerta's slogan for the union, *Si se puede* ("Yes, we can."), could double as the motto of King's tenacious career as a superstar geneticist.

But at the time, King was very tempted to "bag this graduate career and go do politics." Nader had asked her to come to Washington, D.C., to help him put Congress under a microscope.

She sought out her informal adviser, Allan Wilson, a New Zealander with innovative ideas about evolution, who prowled the lecture stage "like a tiger." Researchers were intensely critical of one another in his almost gladiatorial lab, where you were only as good as today's experiments. But they were fiercely loyal to each other outside its walls. King called it "somewhere between a family and a kibbutz."

President Obama kidded King for saying about genetics, "I couldn't believe anything could be so much fun." *Michael Reynolds/EPA*

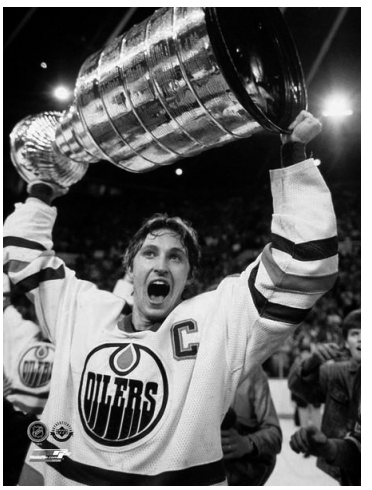
Working for Nader would be righteous, Wilson told her. He totally got where she was coming from. But he offered a caveat. Without an advanced degree she wouldn't be the one steering a science-based agenda in almost any organization. Sometimes credentials mattered.

She rethought Nader's pitch. She instead worked in Wilson's lab. Her Ph.D. thesis landed on the cover of the prestigious journal *Science,* akin to a songwriter's first hit making the cover of *Rolling Stone*.

Four decades later, President Obama draped a National Medal of Science around King, a University of Washington professor since 1995. Every "single American should be grateful for Mary-Claire King's path," the President said in a White House ceremony. At a time when many scientists were studying how environmental factors and viruses could cause cancer, she pursued a hunch that certain cancers were inherited. The self-described "stubborn" scientist plugged away at a marathoner's pace, her every step haunted by the loss of her childhood best friend to cancer.

"Seventeen years of work later, Mary-Claire discovered a single gene that predisposes women to breast cancer," Obama said. "And that discovery has empowered women and their doctors with science to better understand the choices that they make when it comes to their health and their future."

That's just a slice of King's panoramic story, which starts outside Chicago with math puzzles about baseball legend Ernie Banks. It later involves a coup d'etat in Chile, Argentina's Dirty War, and identifying victims of massacres ranging from El Salvadoran peasants to Russia's last czar and czarina. It reaches the Middle East, where she has worked on inherited hearing loss in Israeli *and* Palestinian children. It includes 13 honorary doctorates and comparisons to Marie Curie and Wayne Gretzky. And it's been fodder for a movie in which Helen




When presented with a prestigious Lasker Award, King was likened to hockey legend Wayne Gretzky, who said, "You miss 100 percent of the shots you don't take." *Bruce Bennett*

Hunt plays her on the big screen. King even uncorked a 12-minute excerpt of her own for a podcast called *The Moth*. The tale covers two fateful days in her life, starting with her husband leaving her for one of his graduate students. "He gave me a new vacuum cleaner to soften the blow," she deadpans. It ends with a cameo by Joe DiMaggio that will leave you beaming, if not howling.

Throughout her storied achievements, King has followed a belief that "you bring your whole self into the lab." She has been foremost a citizen-scientist, combining an activist's passion with clear-eyed objectivity. Or, as her brother Paul put it: "Mary-Claire's scientific interest is more an outcropping of her humanism than of a natural bent toward science."

PRESIDENT OBAMA feted King for her most renowned work. But King is the rare scientist with not one, but three "blue moon" discoveries to her credit.

When she won a Lasker Award, often called the "American Nobels," in 2014, presenter Marc Tessier-Lavigne likened her to Gretzky, who holds the National Hockey League record for most "hat tricks"—scoring three goals in a game. "Like the Great One himself," Tessier-Lavigne said, "Mary-Claire is in a league of her own." She made major impacts in at least three fields—evolutionary genetics, medical genetics and molecular forensics.

You're forgiven for not quite understanding what differentiates those fields. King and her peers operate in a league of *their* own, using state-of-the-art technology and terms most of us can't grasp to understand how vastly complicated recipes (genes) use the tiniest ingredients of life (building blocks of DNA) to produce blue eyes, or microscopic filaments of inner ear hair, or a defense against tumor cells.

King grew up in Wilmette, Illinois and attended New Trier Township High School, considered one of the best public schools in the country. Its alumni include former Boeing CEO James McNerney, actress Ann-Margaret and Nobel Prize-winning physicist Jack Steinberger.

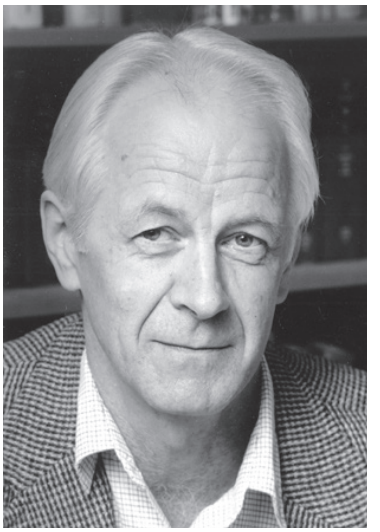
Which is all the more striking because King was an undistinguished math major at Carleton College in Minnesota. The chairman of Carleton's math department didn't remember King as a standout undergraduate when he was asked to prepare remarks about her for an honorary degree she received in 1992.

She became fascinated by math as a young girl while playing story-puzzles with her father, a retired labor relations manager for Standard Oil. He was often bedridden in their suburban Chicago home with late-onset effects of the 1918 influenza epidemic. In the early days of television when there were few channels and programs, father and daughter would watch baseball games together and he'd ask questions such

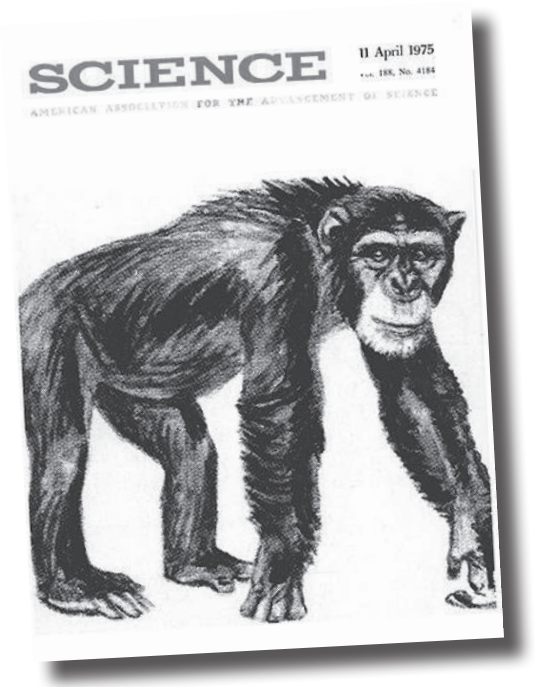
as: How many hits does Cubs star Ernie Banks need in this game to lift his batting average to .280? Mary-Claire would mull over her dad's query and figure out she needed more information. He'd ask what she was missing. Well, she had learned batting average is number of hits divided by number of at-bats. So she'd say she needed his total number of at-bats.

In high school she had two women math teachers who were role models. But when she transferred to studying genetics at Berkeley she thought of herself as "totally clumsy" in the lab. Frustrated, she vented to Professor Wilson that she could never get her experiments to work.

The charismatic Kiwi told her there'd be no scientists if everyone quit when their experiments failed. He helped King design a project that combined her talent in statistics with his efforts to trace human evolution through genetics and molecular biology. Wilson asked her to compare the chemical properties of proteins from human and chimpanzee cells. Still insecure, she kept thinking her work was a disaster because she only found differences in about one out of 100 tests. "I was in total despair—my usual reaction to anything I tried to do in the lab," she recalled.



Allan Wilson, King's friend and adviser, died from leukemia at 56. *Jane Scherr*




The April 1975 issue of *Science* touted King and Wilson's discovery that chimps and human are 99 percent identical at the genetic level.

Wilson turned the prism.

"This is great," he said. "It shows how similar we are to chimps!"

King had revealed that humans and chimps are 99 percent identical at the genetic level. The two species were more than cousins, they were "almost genetic look-alikes."

The question then became: how to explain the obvious contrasts in anatomy and behavior?

King and Wilson proposed that the differences arose from a small number of mutations affecting how and

when certain genes are expressed, thus altering specific features, such as the length of bones or the size of brains. In other words, distinctions between the two species were actually due to changes in the bits of genetic material that act something like traffic lights, regulating how and when genes carry out their tasks.

It was a bold theory and they became minor celebrities when King's thesis formed the basis for findings she and Wilson published in the April 1975 edition of *Science*. It also gave King a taste of the success that could come from swimming against the scientific tide.

But two years passed before King's thesis became the polished, peer-reviewed manuscript that made the cover of *Science*. During that time she and her then-husband, Rob Colwell, a zoologist, took off on a teaching project at the University of Chile in Santiago. Not long after the couple arrived, "all hell broke loose."

On September 11, 1973, the Chilean military overthrew the democratically elected President Salvador Allende. The U.S. Central Intelligence Agency had worked for years to foment a coup against Allende, a Marxist. He had nationalized Chilean industries, provoking a backlash from U.S. leaders who feared another Fidel Castro coming to power. Economic aid dried up. The World Bank was pressured to end all loans to Chile. The country was crippled by inflation, food shortages, and violence between the left and the right.

Under orders from General Augusto Pinochet, air force jets fired rockets into the palace which Allende vowed to defend to his death. As tanks and troops prepared to follow up the aerial assault, Allende reportedly placed his rifle under his chin and killed himself.

King had been away from Santiago during the attack but returned to see bodies in the streets and bodies in the Mapocho River that bisects the city. The university, a hotbed of political activity, was closed. Some of her Chilean friends went into hiding. King and her husband kept a low-profile. On Christmas day they returned to Berkeley.

King didn't have a job. "My mind and my soul were still churning over what was happening in Chile. I was very much at loose ends."

SHE SAW AN AD for a position at the University of California, San Francisco researching breast cancer, which she knew almost nothing about. She thought of the job as "just a place to land with the opportunity of doing something useful."

It was 1974. She was about to embark on an odyssey.

She began to meet surgeons who helped her understand the disease and its aggressiveness in some families. "They were older, they were without exception male, and they were wonderful to me. I was obviously no threat."

It dawned on her that young women in science—who were few and tended to exist on the margins—were pretty much ignored. That gave her a kind of freedom to "go after huge questions." And it gave her the freedom to fail.

When King returned from Chile, jobs in cancer research were abundant because President Nixon had declared a national "war on cancer." *Mary-Claire King*

She soon focused on the idea that there was a family component to breast cancer—and it was a key but overlooked risk. In 1866 French scientist Paul Broca documented 10 cases in his family over four generations. Broca didn't know why his family was afflicted because the natural laws of inheritance were not yet understood. In the 1920s British statistician Dr. Janet Lane-Claypon also reported evidence of a familial link.

But correlation isn't causation. And there wasn't a solid hypothesis about what caused familial clustering.

At the time, scientists believed cancer was acquired during one's life, not *in utero*. The disease grew out of damaging changes to one's genes, the thinking went, caused by viruses and environmental factors, such as chemicals or radiation. Breast cancer was common enough, scientists thought, that it wasn't surprising if it struck more than one member of a family.

King's instincts, coupled with the pattern-recognition skills she honed in puzzles and statistics, told her something different. In the back of her mind also loomed her childhood friend Debbie, who was in constant pain from what turned out to be a kidney cancer called Wilms' tumor. The cancer killed Debbie when she and King were both 13.

"I know for a fact that Mary-Claire never got over that," her mother Clarice recalled.

She was determined to find the deviant gene or genes that triggered hereditary cancer. First, though, she needed good data; she needed families ravaged by the disease. She heard about a large survey of breast cancer patients, and age-matched healthy subjects from the same neighborhoods, planned by the National Cancer Institute. The survey was mainly interested in whether the use of birth-control pills altered the risks of breast, ovarian or uterine cancer. (Men can get breast cancer, but the disease is about 100 times more common in women.)

King was able to get a few family history questions added to the survey, which would take years to complete. Meanwhile, her lab crafted and began running statistical models to determine if there was evidence of other reasons for breast cancer clustering besides genetics.

While immersed in studying other families, she started her own with the birth of her daughter Emily in 1975. King realized that living in Berkeley, where

"Science is also a very demanding child," King said, about juggling work and care for her daughter Emily. "It's not realistic to say one can drop out of science and drop back in." *Mary-Claire King*

Emily had child-care, and commuting across the bay to San Francisco every day was not a good long-term plan.

She applied for an assistant professor position in the epidemiology division at Berkeley. Her timing was exquisite. Affirmative action was being ushered in at Berkeley. Search committees for faculty posts had to include a woman or minority member. In King's case the female member was Cathy Schaefer, a student.

Weeks passed after King's interview. Finally, she was offered the job. Then she learned what really happened—the bulldoggish Schaefer had insisted that the epidemiology division needed a woman professor. She had "just got her teeth into it and wouldn't let go," the head of the search committee said.

After she accepted the job, the division chief told King she only got the post "because of all these new regulations."

Schaefer went on to earn a Ph.D. and become director of Kaiser Permanente's Research Program on Genes, Environment and Health. "She is responsible for my career," King said. "I am absolutely a child of affirmative action."

WHILE HER CANCER RESEARCH plodded along, hunting for families with a history of breast cancer and compelling evidence of a renegade gene, King took a sort of mini-sabbatical. She began commuting to Stanford University, where a mentor, Luca Cavalli-Sforza, was helping her gain expertise in molecular genetics. While at Stanford she also learned about grandmothers in Argentina trying to find children who disappeared during that country's military dictatorship.

In 1976, the military overthrew the government of Isabel Peron, the widow of populist President Juan Peron. The military junta coined the term "Dirty War" for its crackdown on fellow Argentines—which included throwing drugged prisoners into the ocean from airplanes. In one general's definition, the enemies were anyone whose ideas were "contrary to Western Christian civilization." During the military's reign, from 1976 to 1983, up to 30,000 Argentines were "disappeared."

About 30 percent of the disappeared, as they became known, were women. Some were killed in military assaults and their surviving children were taken by soldiers. Some were abducted with their young children. An estimated 3 percent of abductees were pregnant at the time of their capture or were impregnated by rape in prison. Those women were often kept alive until they'd given birth.



Grandmothers ("abuelas") of missing children began protesting every week in Argentina's capital. The government tried to marginalize the abuelas by calling them "las locas" or madwomen. Then one of the group's founders was kidnapped and murdered. But the women weren't cowed. *Abuelas de Plaza de Mayo*

The military and its allies thought they could reform the enemy's children to create "authentic Argentines" through adoption. Many of the disappeared children were given to military families. Others were handed to orphanages.

A group of courageous "abuelas" or grandmothers began to hold silent protests outside the presidential palace in Buenos Aires. And they began to collect tips about children who had been adopted by military families; some clues came from midwives and doctors who delivered babies in prison. Grandmothers started digging deeper; one even became a maid in a home where it was suspected a stolen child was being raised.

In 1984, the dictatorship had fallen. The grandmothers had already collected 145 case records of children who had been seen alive but whose parents had disappeared. King and others in Cavalli-Sforza's lab developed a blood test that could identify a genetic link between grandparents and grandchildren. In doing so, she was an innovator in the nascent field of molecular forensics.

Cavalli-Sforza asked King to go to Buenos Aires to put the blood-testing into practice. He said she was perfectly suited for the job. She knew Latin America. She had taught in Spanish. More important, she was the age of the grandmothers' missing daughters and Emily was the age of their children.

King developed a test based on maternal lines of heredity. With a sample from a granny, researchers could tell if a boy or girl was her grandchild without a trace of DNA from a missing parent. *Abuelas de Plaza de Mayo*

For King, the Dirty War echoed the Chilean coup. "It seemed that as an American I owed something back," she said.

Argentine reformers had set up a human rights commission to which King was a consultant. She helped create a national genetic database of families who lost children during the Dirty War that could be used to confirm the true identities of children. Courts ordered some suspected stolen children to be tested. Others volunteered after later learning they were adopted.

But King's blood tests had shortcomings. They needed samples from all four grandparents for bulletproof confirmation.

More puzzles to solve.

King and colleagues built a more powerful test based on maternal lines of heredity. They relied on analysis of DNA from mitochondria, a component in cells that passes from mother to child, creating a kind of genetic family crest. With a sample from granny, researchers could tell if a boy or girl was her grandchild without any remains or a trace of DNA from the missing mom.

It was the first application of mitochondrial DNA analysis. And in December 1984, Paula Logares became the first child reunited with her biological family based on King's genetic evidence.

Logares was 23 months old when she was kidnapped, along with her parents who were suspected radicals. She was raised by a police officer and his wife. A neighbor became suspicious when she heard the officer's wife shout at her husband that he had killed a little girl's parents and now expected her to care for the child. The neighbor snapped some photos of young Logares and got them to her maternal grandmother. After democracy was restored, and legal hurdles cleared, King's analysis showed with 99.98 percent certainty that Logares was related to her grandmother.

King's lab was soon asked to help the American military identify remains from as far back as World War II. And her lab began to identify victims of atrocities worldwide. Her efforts helped launch the United Nations forensic team.

At last count, 130 of the estimated 500 disappeared children in Argentina had been reunited with their true families.

In all the tributes heaped on King, one of her forensic feats has received little attention. She helped identify the mangled remains of Russia's last royal family, who were executed in 1918 by Bolshevik bullets, bayonets and rifle butts, then buried and chaotically reburied in a forest.

Misinformation and mystery had long

Paula Logares was "disappeared" along with her parents when she was 23 months old. Six years later she was the first of Argentina's missing children whose real identify was confirmed by King's tests. *Abuelas de Plaza de Mayo*

shrouded the deaths of the royal Romanov family and disposal of their corpses. After their murder in Yekaterinburg, a mining hub about 1,000 miles east of Moscow, Bolsheviks admitted to Czar Nicholas' death. But they claimed Czarina Alexandra and royal heir Alexei were alive and safe. Josef Stalin then banned discussion of the family, which only fueled questions and rumors and led to a string of royal impostors.

A pair of amateur sleuths found one of the burial sites but kept it secret until after the fall of the Soviet Union in 1991. Russians hired three teams of foreign scientists to analyze teeth and bones. The various scientists all concurred that the first discovered burial site contained Nicholas, Alexandra and three of their children. (Remains of the other two children would later be unearthed at another site.)

In the meantime, King had been contacted by surviving members of the Romanov family. King said she'd be glad to perform an analysis in the same way she did for relatives of kidnapped children in Argentina—at no cost to family members. "There's not going to be anything different about your family compared to any other family," she told the Romanovs. "No money changes hands."

Her findings were consistent with other scientists' conclusions. But she didn't publish her work. "I didn't send out a press release. I didn't talk about it. I said it was up to them to talk about it." When the family later went public, she felt free to disclose her role, though it's rarely been reported.

JUST AS KING HAD IMAGINED when she was smitten by Curt Stern's lectures, genetics was proving to be the greatest puzzle of all.

The search for reliable breast cancer data was long and painstaking. She had to collect a good number of large families in which a history of the disease was well-documented. Then she and her researchers had to determine whether these women were inheriting the same stretch of DNA on a particular chromosome.

The National Cancer Institute survey eventually collected details from 1,579 patients. And King received permission to contact women who said their mother or sister also had breast cancer. She had also found families on her own over the years, often referred to her by physicians. Other women with a family history contacted her after seeing an ABC-TV news

King's quest to find a breast cancer gene spanned 17 years as she painstakingly hunted for families ravaged by the disease, as well as compelling evidence of a renegade gene. *World Science Festival*

story about King in 1987 that had aired on 127 network affiliates around the country.

She and her lab researchers dove in with questions: Can we, using the large number of families, state genetic hypotheses based on the distribution of cancer in the families? Then can we test statistically whether those hypotheses fit the data better than other theories of clustering without a hereditary effect?

King applied statistical models to the 1,579 National Cancer Institute families. The results were striking. King's analysis, published in 1988, suggested that about 4 percent of the families carried a single gene that made them susceptible to breast cancer. The best way to validate her finding about familial clustering was to track down the gene.

New technology and processes were revolutionizing genetic analysis and King's small lab, with the help of young biochemist Jeff Hall, had begun implementing the advances. Scientists were now able to find "markers," or variations, in genetic material that could point them to a region of DNA, if not the precise location, where the culprit gene might be hiding.

Still the quarry remained elusive. King's team had narrowed their focus to 23 large families with 146 cases of invasive breast cancer. In each of the families the cancer struck three or more "first-degree" relatives: sisters, daughters, mothers, grandmothers or aunts. But the results were mixed. Some families showed convincing linkage to a genetic marker on the 17$^{th}$ of 23 human chromosomes. Other families did not fit that pattern.

King's researchers took the family trees, which look something like complex sentence diagrams, and rolled them out across lab benches and floors to further study.

One morning, King's colleague Beth Newman had a brainstorm: Let's look at this by age.

They stretched the family trees, or pedigrees, out in the halls of the Life Sciences Building, organized by average age of breast cancer diagnosis in the family. The pieces began to fall into place as more and more paper blanketed the halls. For each of the seven families in which women had been stricken before 50, the abnormal marker on Chromosome 17 proved a strong predictor of risk. "It was really clear that statistically there was something there," King said.

Once King and her researchers organized families by age of breast cancer diagnosis, they found an abnormal marker on the 17th of 23 human chromosomes that proved a strong predictor of risk. *University of Washington*

IN OCTOBER 1990 King stood backstage in Cincinnati's convention center ballroom. She had been a late

addition to that night's meeting of the country's leading geneticists, so late that she wasn't on the printed agenda. Just weeks earlier, King's lab had made a breakthrough. King wanted to unveil the news in front of her peers, some of whom were deeply skeptical of her work.

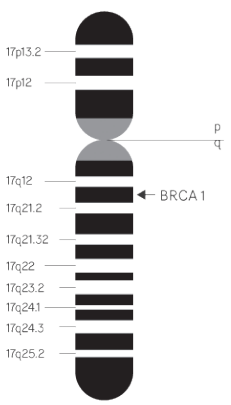
She was nervous. While friends thought she remained cheerful, she had taken each new breast cancer death personally and stumbles on her long quest had sapped her confidence. Although she had been compared to "a terrier with a bone" in her dogged focus on a single gene, she had doubts. Earlier findings she published had not held up. She was not sure her hereditary theory was foolproof. That was one reason her research had digressed to forensics and other pursuits; she thought it was too risky to bet all her chips on the breast-cancer payoff.

Cavalli-Sforza, a mentor, comforted her backstage in Cincinnati. "Show them what you showed me," he said, giving her a friendly hug.

King stepped out of the wings and into the spotlight. Displaying charts, graphs and family trees on a large screen, she explained that her team looked closely at the 23 extended families. With a scary regularity that mimicked an inherited disease, not an acquired one, roughly half of the women in those families developed breast cancer at a rate far above the overall average for women.

More importantly, the cancer tended to hit these women before menopause, unlike most women who aren't diagnosed until after the age of 50. This was most likely a result of some inborn biological error, probably a mutated gene that deprived women of a tumor-suppressing defense mechanism and pushed them onto a premature path to cancer.

And King's lab found the error in a tiny region on Chromosome 17 that was consistently altered in DNA of women with cancer. The statistical link between this abnormal stretch of DNA and breast cancer was "many times stronger than any other association that King or anyone else had yet found." King thought she had located the gene. But she still wasn't 100 percent certain. Was it possible that her families were unique in some way she didn't see? There would be no popping Champagne yet. She said her discovery needed to be reproduced by another lab.




An illustration shows the location of the breast cancer gene on Chromosome 17, at "arm q" and "band 21."

A few months later King was on her way to London. Gilbert Lenoir, director of France's International Agency for Research on Cancer, was going to present a paper on inherited breast cancer. When Lenoir became interested in a breast cancer gene several years before, a colleague suggested he contact Henry Lynch, a doctor in Nebraska intrigued by familial cancer since the 1960s. Lynch had amassed records of dozens of families with breast cancer. But scientists had dismissed his evidence as anecdotal. Lenoir visited Lynch

and plunged into the doctor's files. Lenoir was encouraged by the hidden treasure.

He was in the Cincinnati ballroom when King divulged her findings about Chromosome 17. The next day he called his French colleagues and directed them to look for the offending gene where King had pointed.

Just before Lenoir began his talk in England months later, he was coy with King. In a private aside, he asked her what she thought the chances were that she was right about Chromosome 17. She told him "fifty-fifty." Without a hint about his coming presentation, Lenoir said, "Maybe."

As the lights dimmed and Lenoir started showing slides of several family pedigrees, King thought he was offering a review of her data. She asked anxiously where his results were.

While friends thought she remained cheerful, stumbles on her long quest to find a breast cancer gene had eroded her confidence. *World Science Festival*

"Those are mine," he said.

He had applied King's methods to a set of families in France. His results were virtually identical to King's. Same markers, same age effect, but with different families.

"That," King said, "was when I believed the result was real."

Others agreed. Ellen Solomon, a top researcher who organized the London meeting, celebrated with both Lenoir and King over tea. "Lenoir's talk was very convincing," Solomon told Pulitzer Prize-winning journalist Michael Waldholz. "But, of course, Mary-Claire had gotten there first. It was a great, great moment for her."

King named the gene BRCA for breast cancer. It became BRCA1 when a similar tumor-suppressing gene with a defect was later detected on Chromosome 13 and named BRCA2. Both genes function like custodians, cleaning up mutations in other genes caused by ultraviolet radiation, tobacco smoke, or deterioration. Unfortunately, they are sometimes mutated themselves and can't repair damaged genes. Together, the two mutated genes account for about 5 percent of all breast cancers, and they increase a woman's lifetime risk of developing cancer dramatically.

King had found the neighborhood where BRCA1 resided on Chromosome 17. Now the race was on to pinpoint the exact street address amid a million subunits of DNA, a "task akin to searching for a car key dropped on the bottom on Lake Washington," wrote Paula Bock in *The Seattle Times*.*

Her lab did not win the high stakes competition to isolate, clone and patent the BRCA1 gene, which helped scientists understand how its mutations

* Francis Collins, another superstar geneticist, compared the hunt to searching all of Texas to locate a particular room in a single house in the Lone Star State.

triggered breast cancer, and how to craft diagnostic tests to look for the fugitive gene. Mark Skolnick, a Utah-based Berkeley alum, led a team of 44 colleagues from five institutions that won that prize, thought to be lucrative and glamorous. His company Myriad Genetics was awarded an exclusive patent on the gene.

But King didn't feel like a loser. Even though finding the gene "was her reason for getting up in the morning" and her "less-than-tender feelings" for Skolnick were known to colleagues, King told *The New York Times* his triumph was "lovely" and deserving of all the praise he might get.

She had pointed the way, moving science forward and changing thinking. In her view, Skolnick and Myriad cloned the gene first because "they had vastly more sophisticated equipment, so could move much more quickly through (analyzing) thousands of DNA fragments."

New puzzles awaited King, such as figuring out whether some mutations were associated more strongly with breast cancer, and others with ovarian cancer, which was also linked to BRCA1. And she felt a duty to do more.

ANOTHER REASON King didn't feel like a loser: she was being wooed by other institutions.

As her focus shifted from cloning BRCA to trying to use it for diagnosis and possible therapies, King wanted to get closer to surgeons and clinicians who saw cancer up close every day. Berkeley doesn't have a medical school and the drive to San Francisco, which does, had become intolerably gridlocked.

After more than a year of courtship by the University of Washington, King moved her lab north in 1995, along with a dozen researchers, all supported by federal grants or fellowships. King herself brought a lifetime grant from the American Cancer Society (via the Walt Disney family) to help defray research costs. Her new lab was just an indoor stroll from the UW's acclaimed medical center.

Calling Seattle the "Athens of genetics," King was impressed by its scientific luminaries such as Lee Hood, who then headed molecular biotechnology at the UW. But the most important factor in her move was Seattle's vibe. "I could've gone to many places," she says. "I came here because it was the minimal cultural move from Berkeley. I love Berkeley and I love Seattle."

Journalist Paula Bock captured the bustle of King's lab in 1998, as researchers—"who looked like a multicultural GAP ad"—removed teeth from packages postmarked Ethiopia and El Salvador, shattered them with a hammer, extracted DNA from their pulp, and then prepared tiny vials of genetic material for analysis in an oven-sized $100,000 instrument. When King was away on trips to raise money, receive an award, or help scientists on a distant continent, rock music bounced off the lab's beakers and pipettes.

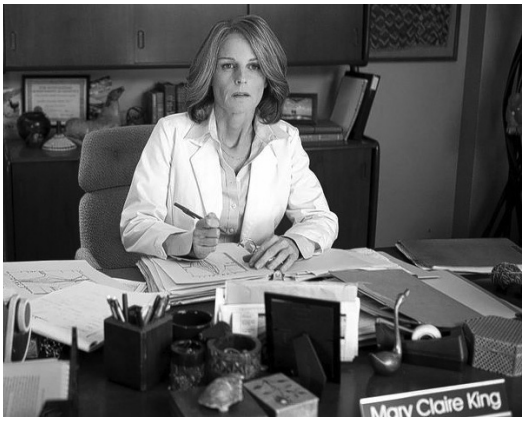
On King's return, the stereo shut down. "It is replaced by the scientist's musical laughter, her chorus of questions, her hunger for results. At 52, King is a

dynamic presence, mind leaping, hands gesturing, smile dimpling, pencil twiddling, tawny hair bobbing like a pony's mane as she nods excitedly and exclaims, "Really? That's WONDERFUL!"

King's UW lab researchers "looked like a multicultural GAP ad," wrote Paula Bock in *The Seattle Times*. "I had my own lab for 15 years before I had my first white, straight, male graduate student," King says. *World Science Festival*

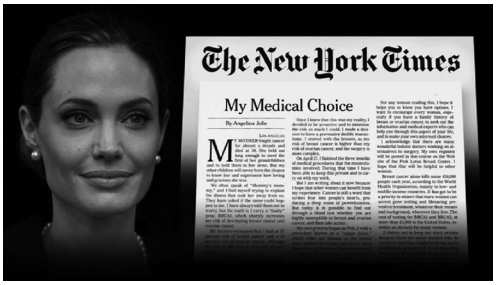
By the time of Bock's story, King had begun collaborating with both an Israeli and a Palestinian scientist in the study of inherited deafness. And in four years the trio and their affiliated universities had identified four genes associated with deafness. It was important to solve hearing loss, King said, but even more important to show "we can do this together for the sake of science and for the sake of peace."

King was back in the news in 2013 when Academy Award winner Helen Hunt played her in "Decoding Annie Parker," a movie that weaves the story of real-life breast-cancer patient Annie Parker with King's quest to find BRCA1. King wasn't consulted by the filmmakers or Hunt. "It will be my words with perfect hair," she predicted after learning about the movie from one of her students. *The Washington Post*'s review said the film didn't explore King's efforts "nearly as fully as they deserve," but it was rescued by a cast that included Samantha Morton, Rashida Jones and Aaron Paul. King deduced that Hunt watched video interviews to get her mannerisms down, such as the way her hands seem to be in perpetual motion when she talks, and her urgent efficiency that can seem chilly.




Describing King's movie character as "bordering on icy," *The New York Times* said "she is portrayed by Ms. Hunt with the simmering anger of someone so consumed by her quest that she has no room in her life for anything else." *Decoding Annie Parker*

Another Hollywood figure, Angelina Jolie, raised awareness of risk and treatment just as "Decoding Annie Parker" premiered at film festivals. Jolie




After testing positive for BRCA1 mutations and having a preventive double mastectomy, Angelina Jolie said her chances of developing breast cancer "dropped from 87 percent to under 5 percent." *PBS*

authored a column in *The New York Times* about the preventive double mastectomy she had after testing positive for BRCA1 mutations. While a harmful BRCA mutation is relatively rare, afflicting about one in 500 American women, it greatly increases risk for women like Jolie whose mother, aunt and grandmother died from breast or ovarian cancer. In the overall population, 1-in-12 women will have breast cancer by the age of 70. Among women with a BRCA1 mutation the risk rises to 6-in-10 women by age 70. The risk for a BRCA2 mutation is slightly less.

King praised Jolie's announcement as "really good, very clear, very accurate." Testing for BRCA mutations surged in what some called the "Angelina effect." But those tests cost $3,000, in part because Skolnick held exclusive rights to the genes.

With her UW colleague Tomas Walsh, King developed a one-time test in 2010 that could check for more than a dozen genes, in addition to BRCA1 and BRCA2, which scientists found to be implicated in breast cancer. Walsh and King did not seek an exclusive patent. But their test, called BROCA, could not be widely used because of Myriad's patent.

A month after Jolie's revelation, the U.S. Supreme Court ruled on an American Civil Liberties Union lawsuit challenging Myriad's patent. Unanimously, the justices said genes, as products of nature, couldn't be patented by companies. When called by Nina Totenberg of National Public Radio for reaction, King said she was "as high as a flag on the Fourth of July."

King's one-time test helped with earlier diagnosis of breast cancer and treatment through preventive surgery such as Jolie's. And her discovery of the BRCA1 gene later allowed for development of potential therapies that make it harder for some cancer cells to survive.

But curing inherited breast cancer remains an evasive goal. "To actually fix BRCA1 and 2 mutations, we would need new genetic engineering technologies that don't yet exist, or are not yet ready for human use," says Dr. George W. Sledge, Jr., chief scientific advisor to the Susan G. Komen Breast Cancer Foundation, and head of the oncology division at Stanford University School of Medicine. "We may get there, but we are a ways away."

THE UW IS A "fabulous place" to carry out her work, King says on an April morning in 2019. "There cannot be anyplace that's superior to this."

It's also a fine place for women in science, she says, on the Monday after

a "depressing" story in *The New York Times* about sexism at the prestigious Salk Institute in California. "One of the great things about working here is that interactions are straightforward. Clearly that's not universal," she says at her tidy desk, below shelves lined by white binders full of family pedigrees.

Women account for a majority of her lab's roughly 20 researchers, who include surgeons, professors, post-doctoral fellows, and graduate students. "I had my own lab for 15 years before I had my first white, straight, male graduate student," she says.

While attitudes have changed, and "young men are very modern about this kind of stuff," women scientists still face a major challenge: their child-bearing years coincide with the time they need to bear down on building a career, publishing research and earning academic tenure.

"Science is also a very demanding child—you just can't walk away from either. That hasn't changed. It's not realistic to say one can drop out of science and drop back in." Until good, reliable, affordable child-care near work is widely available, the demands of a career in science are "always going to be an impediment for mothers."*

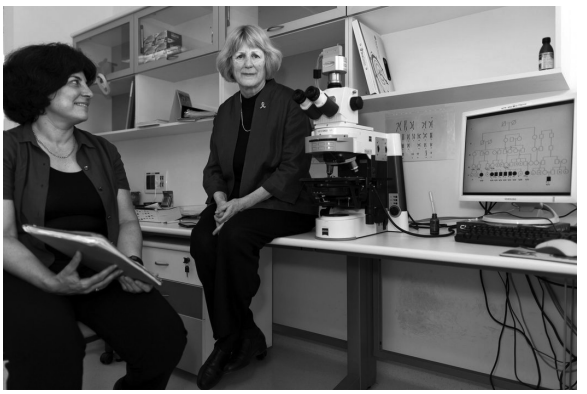
King says she "quite possibly" may have won the race to clone BRCA1 had she then been at the University of Washington which had superior technology to her lab at UC, Berkeley. *Newscom*

King once told *The New York Times* that she couldn't find time to excel in all three roles of young mother, young wife and young scientist—and wife was the one that suffered most. Then she still felt guilt as a single mother. When her daughter Emily was 6 or 7 she'd come to the lab and hang out in King's office with books and toys. Emily took to making posters that would go on the office door. When King asked why she made the posters, Emily said, "They are to keep people happy while they have to wait for you."

THE AMERICAN CANCER Society Professor of Genome Sciences and Medicine at UW, King hasn't slowed down as her career approaches the half-century mark.

Her UW lab continues to research breast and ovarian cancer with a focus on families whose genetic problems remain undetermined. Researchers in the King lab are also trying to sort out the genetics of schizophrenia, which occurs more frequently due to mutations that are acquired during life rather than inherited at birth.

* Asked in 2019 what she'd do if she weren't a scientist, King said: "I would open a daycare for the children of my lab where the kids would learn story problems while their parents do experiments."



King has long-running collaborations with both Palestinian and Israeli scientists, including Dr. Ephrat Levy-Lahad (left), saying it's important to show "we can do this together for the sake of science and for the sake of peace." *Judy Siegel-Itzkovich*

She keeps her passport at the ready. She's collaborating on breast cancer projects in South Africa and Mexico. And she's gone to Israel almost every year since 1995.

In addition to her work in the Middle East on inherited deafness, she's part of a team that established a modern lab to conduct genetic testing for women of Arab ancestry, which has led to characterizing cancer-causing mutations specific to that population. King and her colleagues also helped train Palestinian nurses and social workers in counseling for high-risk women. And she has teamed with Israeli scientists to publish research on the startling breast-cancer risk that Ashkenazi Jewish women face. In 2018, she received a $1 million Dan David Prize, administered by Tel Aviv University, for her career achievements.

She once imagined retiring to Berkeley at 80 and hosting "a salon for unrequited lefties." Maybe King, a fan of detective stories, might even find time to write that mystery novel she has all plotted out in her mind. "Needless to say," she smiles, "DNA is at the heart of that story."

But not now. She says she hopes never to retire. At 80 she expects to still be in her lab figuring out more about inherited susceptibility to breast cancer.

There are all those families waiting on her shelves. Someone's always waiting for her attention, for her to solve a human puzzle, no matter how long it may take.

**Bob Young**
**Legacy Washington**

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