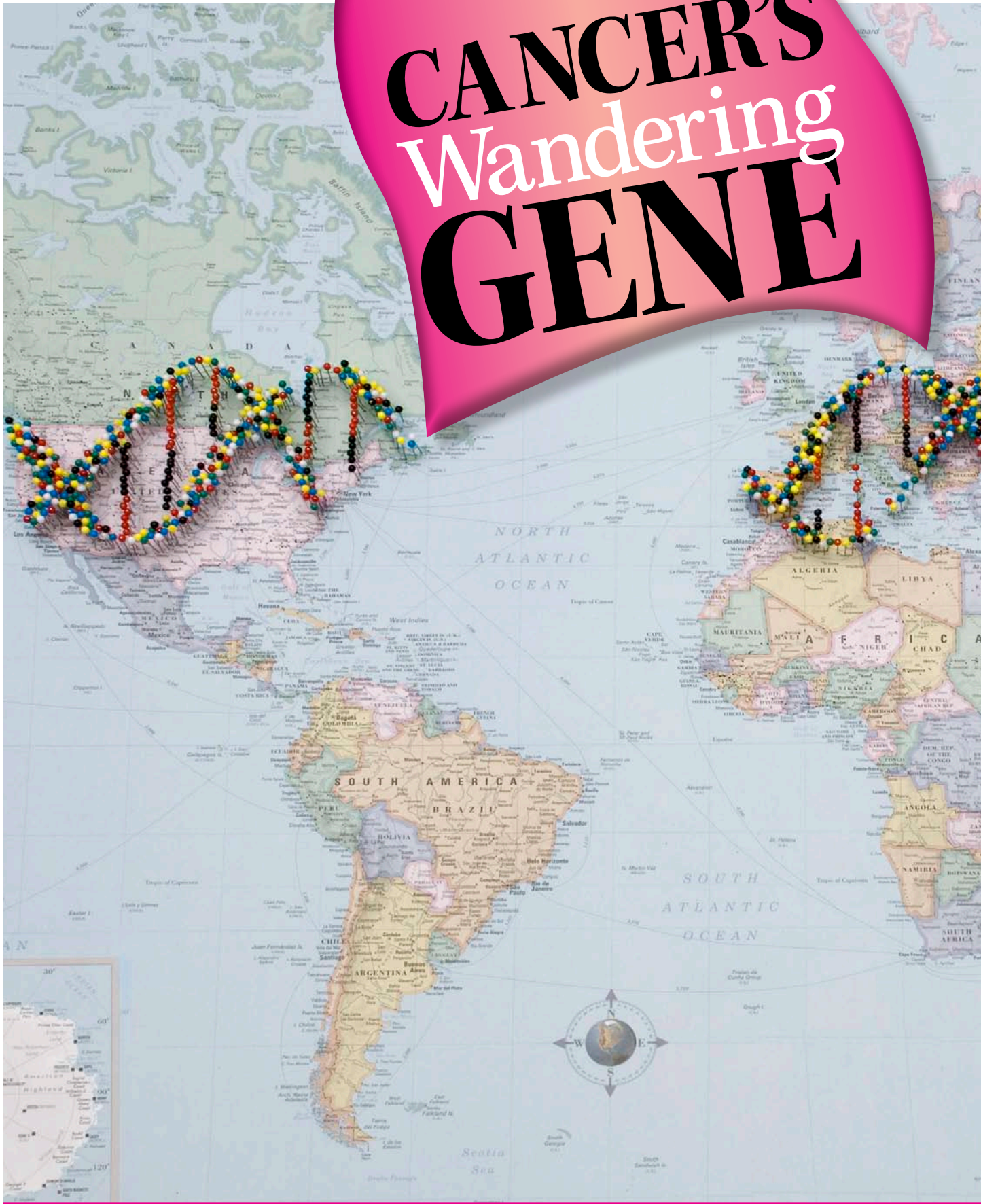
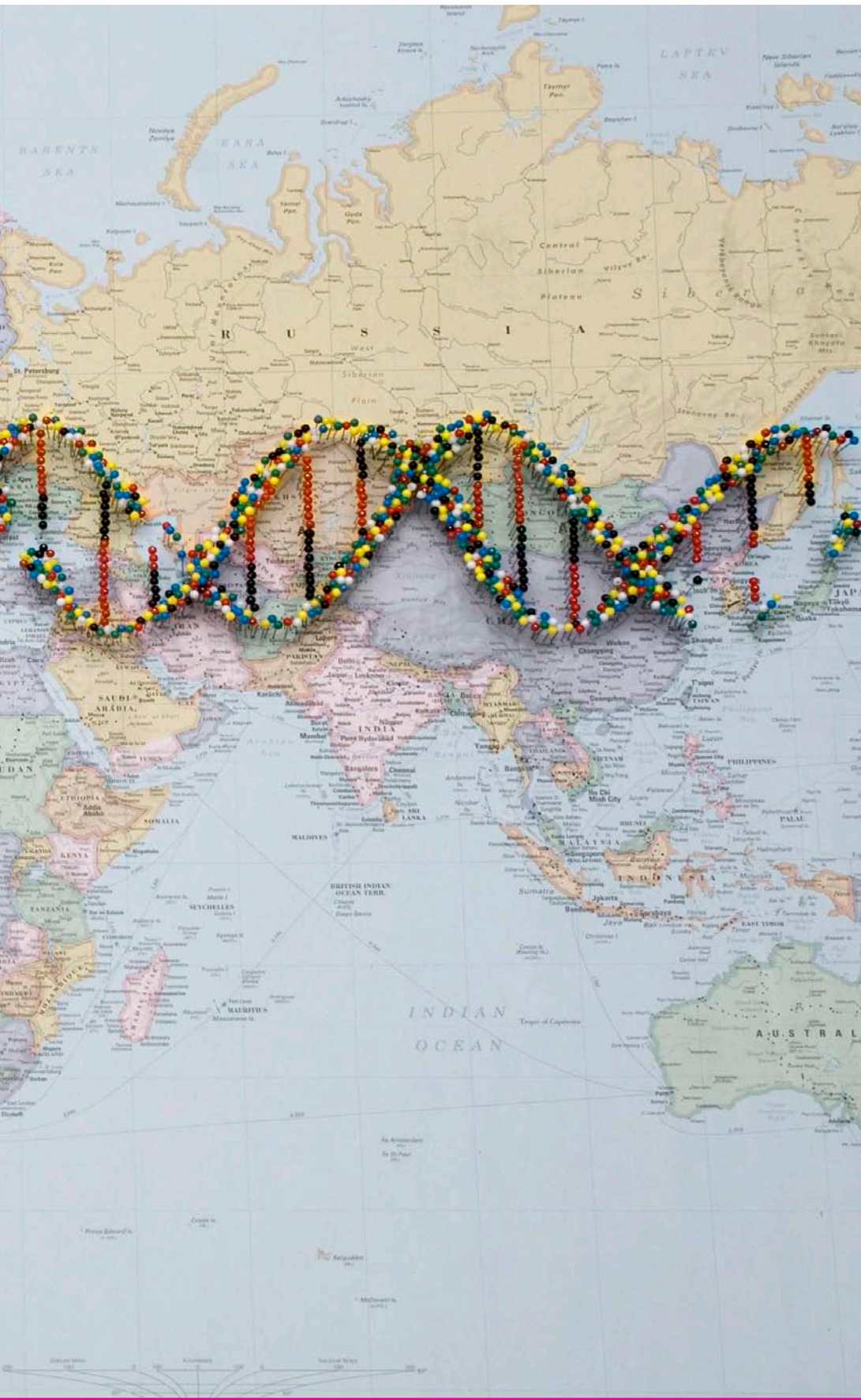


# CANCER'S Wandering GENE





The world's most studied piece of DNA—a mutation that causes breast cancer—has followed an amazing journey from ancient Palestine to the American Southwest.

BY JEFF WHEELWRIGHT

SHONNIE MEDINA WAS A HAPPY girl who felt she would die young.

Her physical beauty, when she was a young woman in Culebra and a young wife in Alamosa, was the primary thing that people mentioned about her. Photographs and snatches of videotape don't quite capture it because fundamentally what people were talking about was charisma. It came through her looks when she was in front of you, tossing her full head of dark hair and giving you her full attention. Then her beauty acted like a mooring for her other outward qualities, undulating from that holdfast like fronds of kelp on the sea. Then Shonnie was magnetic, vain, kind to others, religious without reservation, funny, a little goofy, and headstrong.

Being headstrong or unreasonable was the quality that the doctors in Alamosa and Denver blamed for her death—for Shonnie was right about dying young. She carried in her cells a dangerous genetic mutation and died when she was 28, after refusing surgery for her aggressive, inherited breast cancer. Jealous of her body, oblivious to the gene, she insisted on another style of care.

Shonnie Medina grew up in the San Luis Valley of Colorado.

# The gene had followed Shonnie from Palestine to Spain, and

Her family is Hispano, a mix of Spanish and Indian people. Older than other Hispanics in North America, the Hispanos claim a 400-year history in northern New Mexico and southern Colorado. Their villages, dotting the northern reach of the Rio Grande, were once as lively and insular as the shtetls of Eastern Europe.

The gene Shonnie inherited, known as *BRCA1*.185delAG, also has a long pedigree. Its discovery in the Hispano community confirmed events of half a millennium before in Spain that are echoing still. Most likely the mutation arrived by way of Sephardic Jews who converted to Catholicism under pressure from the Spanish Inquisition. From Spain they traveled to the New World, where

gene; the deletion of the two letters disabled its protective function. But the mutation wasn't immediately harmful to the founder because he or she had another copy of the gene that worked.

Researchers have no idea who the founder was, but they can deduce from historical evidence when he or she lived. When Jews were permitted to return to Jerusalem after their captivity in Babylon, not all the exiles went home. The ones who stayed behind are the ancestors of Iraqi Jews, whose numbers are today much reduced but who for centuries constituted a venerable center of the faith. In addition to the Jews living in Mesopotamia and Jerusalem, satellite immigrant communities sprang up elsewhere in the Middle East.



Goya's 1823 painting *Pilgrimage to Saint Isidore's Well* depicts the Spanish Inquisition that helped disperse the Jewish *BRCA* genes worldwide.

eventually they seeded the modern Hispano population. Indian blood and new terrain erased part of the history those emigrants carried, assuming they were even aware of their Jewish legacy. For the Hispano Catholic people of northern New Mexico and southern Colorado, Jewish ancestry was a will-o'-the-wisp of memory and culture, which many people had heard about without knowing if it was true. Shonnie's mutation shows that it is.

The breast-cancer mutation 185delAG entered the gene pool of Jews some 2,500 years ago, around the time they were exiled to Babylon. Random and unbidden, the mutation appeared on the chromosome of a single person, who is known as the founder. In the same sense that Abraham is said to have founded the Jewish people, scientists call the person at the top of a genetic pyramid a founder. This particular founder was born missing the letters A (for adenine) and G (guanine) from the DNA chain at the 185 site on one copy of his or her *BRCA1* gene. *BRCA1* is a tumor-suppressor

A decentralization of the gene pool had begun, and the distances between groups acted as barriers to the exchange of DNA, barriers that have persisted into the modern day. When scientists in Israel tested *BRCA1* carriers from the dispersed Jewish populations, they discovered that all shared the same basic spelling in the genetic region of 185delAG. But some of the matches between Jewish groups were off by a letter or two, which indicated minor changes since the groups had split. Rolling back the demographic clock, the scientists inferred that its founder must have lived before the groups divided—that is, prior to the Babylonian watershed.

Given that the 185delAG mutation originated among Jews, scientists think that when the mutation shows up in another ethnic or racial group—like Shonnie Medina's Hispanos—it is because a Jew or a descendant of a Jew has married in. Beyond the bounds of Jewry, sightings of 185delAG are few. There are scattershot reports in the medical literature of gentile carriers in Spain, Chile, Slovakia, the

## then from Mexico up the **WINDING AISLE** of the Rio Grande.

Netherlands, Pakistan, India, even Africa, but most of these areas have or used to have Jewish enclaves. There are many American carriers who are not Jewish, but these people, like the Medinas, very likely have at least some Jewish ancestry.

So the gene that had followed Shonnie from Palestine to the Iberian Peninsula, and then to Mexico after Jews were expelled from Spain, and then from Mexico up the winding aisle of the Rio Grande, caught up with her at last in the remote, mountain-rimmed San Luis Valley. In 1998, hospitalized and close to the end of her life, Shonnie was advised to have a *BRCA* test. Her parents, Joseph and Marianne, went into their depleted savings and paid \$2,800 for the analysis, which was not covered by her insurance. “Hmm,” said the genetic counselor, “your daughter is a carrier of 185delAG . . . but that’s the Ashkenazi mutation.” This was before the mutation’s link to Spanish or Sephardic Jews was known.

Given all that was going on with Shonnie, the Medinas put it out of their minds. The test was of no use to the patient anyway—it was a cancer alert to female relatives, but either the information wasn’t delivered properly to the family or else it didn’t sink in.

**T**HE ASHKENAZIM, WHO ARE ORIGINALLY from central and Eastern Europe, are the world’s most numerous population of Jews. Five and a half to six million Americans have Ashkenazi ancestry. Before they had to deal with heritable breast cancer and its lead agent, the *BRCA1.185delAG* mutation, a previous generation of Ashkenazim had confronted Tay-Sachs, another genetic disease. Tay-Sachs was (and is) a very grim neurological condition. Affected infants start life healthy but begin to lose muscular control at six months. Their heads loll helplessly and their vision dims; after a period of convulsions, they slide into coma and death.

Although Tay-Sachs was rare, affecting fewer than one in 2,000 Jewish babies, the suffering of the children was shocking, and the predictability of the inheritance pattern was maddening to the community’s doctors. Tay-Sachs is a recessive disorder, entailing two parental carriers who together have a one-in-four chance of producing an affected child. The math is cruel in its simplicity. Genes come in pairs. The two parents are healthy because each carries a copy of the gene that works, but their child inherits two damaged copies. If Tay-Sachs carriers could recognize their status, Jewish parents realized, the condition would have no place to hide. Like a dybbuk wrongfully possessing a soul, the disorder could be exposed and perhaps eliminated.

When the Tay-Sachs gene is faulty, it fails to make a critical enzyme, called hexosaminidase A. In the 1960s, long before the causative mutation was pinpointed, researchers were able to measure that enzyme in blood. A Tay-Sachs carrier expressed about half the normal amount of the enzyme, enough to preclude the disease;

an affected child showed no enzyme at all.

Population screening for the enzyme began in the early 1970s. First in Baltimore and Washington, D.C., and then in other cities, Jewish men and women found out whether or not they were Tay-Sachs carriers. Fired by pride and educated to the need by their rabbis, doctors, and local health departments, thousands gathered at synagogues to be tested. Eighteen hundred men and women braved the rain in Bethesda, Maryland, one Sunday in May 1971. On a single day in 1975, a medical school student named Harry Ostrer and a classmate drew blood from 500 people in Riverdale, New York. The experience inspired young Dr. Ostrer’s decision to specialize in medical genetics; he went on to become the director of the Human Genetics Program at the New York University School of Medicine, where he championed DNA testing for Jews’ genetic disorders.

Local hospitals responded to the Tay-Sachs screening programs. The pregnancies of carrier couples could be monitored by amniocentesis and terminated if the fetus was affected. Soon the statistics registered a sharp drop in Tay-Sachs, from about 40 to 50 cases a year among Ashkenazim to fewer than 10. By the turn of the 21st century, almost a million and a half American Jews had undergone carrier testing. Hundreds of fetuses were aborted, but during the same period some 2,500 healthy children were born to couples in which both husband and wife were carriers. Group screening having accomplished all it could, the testing for Tay-Sachs takes place today in outpatient clinics, on college campuses, and via online services. The handful of cases that still occur are most likely to affect non-Jews, families carrying mutations other than the distinctly Ashkenazi variants of the Tay-Sachs gene.

Orthodox and especially ultraobservant Hasidic Jews, who considered childbearing an essential duty not to be interfered with, were the last branch of Ashkenazim to take advantage of Tay-Sachs screening. Carrier testing not only opened the door to contraception and abortion but could also destroy a person’s prospects of marrying. In the close-knit urban wards of the Hasidim, the rabbi wielded more authority than the doctor, and medical information was not private. When two families were sizing up a match, just the whiff of a genetic problem could taint everyone on one side. “The concern with stigmatization should not be underestimated,” Harry Ostrer says. “Once the neighbors hear that Shmuel has been to the geneticist, they assume the worst about his having a genetic condition and might conduct a whisper campaign.”

Orthodox rabbis initially refused to cooperate with Tay-Sachs screening. Then in the early 1980s, Josef Ekstein, a Hasidic rabbi in Brooklyn, devised a testing method that brought the Orthodox into the DNA age. The reclusive Ekstein had firsthand knowledge of Tay-Sachs disease. He and his wife were carriers. Their first two children died of the disease before the age of 4. Exceeding the odds, the couple eventually produced a total of four sick children within a brood of 10. In shame, Ekstein had hidden his fourth doomed child from view; after the boy died, the rabbi was all the more ashamed for having done so.

An expert on the intricate dos and don’ts of kashruth, the Jewish

## EKSTEIN took it upon himself to **STUDY** Mendel's laws.

dietary laws, Ekstein took it upon himself to study Mendel's laws of heredity. Genetics, after all, was about applying the letter of the law of nature. The rabbi believed that God had created an order, a natural course of events, which scientists and doctors ought to investigate. "Everything is managed from upstairs," he explained in a gravelly voice, "but nature also has its rules." As before the great Flood—when the subdivisions of nature, two by two, marched up the ramp beneath Noah's discriminating gaze—this one goes with that but never with this, the wonderful hairsplitting order of life, of which there was no more wonderful example than the biochemical rule pairing A with T but never with C or G, and the complementary rule matching G with C but never with T or A.

Ekstein's idea was to dissuade the Tay-Sachs carriers in his community from getting together in the first place. Under his program, high school boys and girls submitted their blood for testing, but the results were withheld from them. Later, when a pair started to date in earnest or their families were exploring a match, they contacted the database to learn whether they were genetically compatible. Most of the time they were. If incompatible, they were strongly urged to part and find someone else. Everything was handled confidentially: No names were recorded, only an identifying number and birth date for each youth. Ekstein called the program *Dor Yeshorim*, meaning Generation of the Righteous. By the late 1980s, the decline in Tay-Sachs births was more dramatic within Orthodox neighborhoods than outside them.

Dor Yeshorim occupies a small, graffiti-splashed brownstone just south of the rumbling Williamsburg Bridge, near Brooklyn's East River waterfront. On the first floor of the office, half a dozen young women, all wearing head scarves, fielded phone calls at computer terminals. It looked like a telemarketing operation that has taken a deadly-serious turn. "We took the medical science and we applied it to the needs of the community," Ekstein said, gesturing proudly.

The rabbi believed he was born a Tay-Sachs carrier for a reason. "I had to find out the hard way," Ekstein explained, "but we think everything happens for a divine purpose. We can override, with good deeds, the bad things in the universe. If you're a carrier of a disease, it's predestined, but it's also for a purpose. You were also given the means to protect yourself. It is like clothing against the weather. You have to protect yourself, with whatever tool you're given by the Almighty."

Ekstein went after the other recessive diseases affecting his

community, such as Niemann-Pick, familial dysautonomia, and Canavan disease. Neurological disorders with symptoms different from those of Tay-Sachs, they are crippling and usually fatal. By adding carrier tests to his program, he in effect expanded the grounds for incompatibility among Orthodox young people. Still, 99 of 100 pairs received Dor Yeshorim's blessing to proceed with courtship or dating, their carrier profiles unrevealed to them. Meanwhile, the hundreds of thousands of blood samples that Dor Yeshorim gathered have been a great resource for DNA research. Dor Yeshorim contributed to the discovery or confirmation of the genes for Canavan disease; Gaucher disease, which attacks the spleen and liver, causing pain and fatigue; and Fanconi's anemia, a failure of the bone marrow.

**I**N THE 1990S, DURING A RACE TO DISCOVER THE gene for familial dysautonomia, Ekstein and his scientific collaborators competed with a rival group that included Harry Ostrer. That didn't help the relationship between the two men, which was already strained by their opposing views about the reporting of genetic information.

The Hasidic rabbi would spare Jews the psychological burden of knowing their DNA so that they would focus on making a good marriage and a healthy family. They would be fruitful and multiply as the Almighty had commanded, while he worked to rid the community of genetic disease. But for Ostrer, a Reform Jew, a scientist, a liberal, the primary commandment was informed consent. Ostrer wanted to eradicate the Ashkenazi disorders as much as the other man did, but not through a secretive program. "Rabbi Ekstein wants to control who does and doesn't get information," Ostrer has said. "As you know, that is contrary to the egalitarian and participatory style of genetic counseling."

Genetic counseling of that sort, countered Ekstein, "is not there to take away the worry but to increase the worry." After working with a good many doctors and scientists over the years, he decided that the professionals made it more difficult for a man and a woman having a baby, not easier. There was too much unnecessary testing, too much technical information being generated that was not supportive of the persons who had generated it. Through tests and scans, the doctor offered parents a sense of control over the birth and health of their child, but in Ekstein's view he also caused tremendous anxiety in the interim—and in the end it wasn't the doctor's problem. "The science of genetics is a tremendous tool. It can be very good," Ekstein said, "but most doctors are not using it the right way. They lack compassion for their patients."

Harry Ostrer did not lack compassion. He winced at stories of congenitally damaged children, and his global interest in the DNA of Jewish populations sprang from a desire never again to hold the hand of a distraught Jewish parent. At New York University Medical Center, a sprawling complex in Manhattan just across the East River from Ekstein's redoubt, Ostrer offered genetic testing to Jews and non-Jews



# EIGHT first cousins had cancer and THREE were dead.

alike, about 5,000 patients per year. Many of the patients were pregnant, educated white women who were concerned about something going wrong and who wanted answers fast. His team of genetic counselors provided information and referrals before and after the testing.

The information could have harsh consequences, but Ostrer believed that if a person wanted a test, it should be provided, as long as the patient understood the implications. “Consumers don’t want to be told what to do,” he said. “We are adding value to patient care—it is a growth business. Let the marketplace decide.”

The doctor wholeheartedly agreed with the rabbi that a couple shouldn’t be exploring their genetics during pregnancy, which was already a stressful time. Carrier status should be factored in much sooner. So periodically Ostrer went to college campuses to screen Jewish students, intending to intervene before they married, as Ekstein did. On religious campuses like New York’s Yeshiva University, Ostrer and his helpers competed directly with Dor Yeshorim to raise student awareness of the recessive disorders. “I am trying to prevent Tay-Sachs disease,” he said stoutly. “People are still falling through the cracks. . . . The modern Orthodox kids want to know their results.” Like Dor Yeshorim, he saved the blood samples for his own research, although for that part of the work the subjects signed consent forms stipulating that their names will be stripped from the samples. He kept up a stream of publications. In 2011 Ostrer moved from NYU to the Albert Einstein College of Medicine in the Bronx, not slowing down.

In the San Luis Valley, the response of the Medina family to their newly revealed Jewish genetic legacy was more tentative. They did not realize they were part of a long hereditary chain. After Shonnie died, Marianne Medina would take out the piece of paper with her daughter’s DNA test result. Brooding over the finding—the *BRCA1*.185delAG mutation that triggered the cancer—she made a mental list of the cancers she’d heard about among her husband’s female relatives. About the same time but acting independently, two of Joseph Medina’s cousins in the Denver area started to collect health histories from relatives. When the

cancer records were superimposed on the family tree, the picture was terrifying. Of Joseph’s eight aunts, five had died of either breast or ovarian cancer. (A *BRCA1* mutation predisposes a woman to either breast or ovarian tumors, in some cases both.) Eight of his first cousins, women in their thirties and forties, had had cancer, and three were dead. Two of his sisters, unaware of being carriers, were soon to be diagnosed. And then there was Shonnie, who must have acquired the mutation from her father.

In 2002 Marianne and the remaining daughter, Iona, who was 29, met with a genetic counselor in Colorado Springs. Should Iona be tested for the mutation? She was manifestly at risk, but Iona asked for more time to decide. Unlike Tay-Sachs and other recessive disorders, heritable breast cancer is a dominant condition. In dominant conditions, the malfunctioning gene overrides its healthy counterpart sooner or later. Five years went by, then six. Like many women in her situation, Iona imagined the gene, if she carried it, as a tiny bit of cancer in itself, but one so small that it might be repressed into nothingness.

The gene plaguing her family was identified by geneticists Mark Skolnick and Mary-Claire King in 1994 after an intense search. It was located on chromosome 17, and was so long that thousands of possible misspellings can occur within its sequence. Since then, more than 2,000 *BRCA1* mutations have been recorded, affecting all ethnic groups, but one mutation quickly emerged ahead of the others.

Although the codiscoverers of *BRCA1* hadn’t keyed in on Ashkenazi Jews, other researchers, now that they knew where to

look, soon noticed the prominence of the 185delAG mutation in their study samples. They immediately established its Jewish tie. Those samples had come from Ashkenazi families with a lot of cancer.

The next step was figuring out how prevalent the mutation was in the general population of Jews. Researchers went back and looked for the *BRCA1* mutation within the DNA samples that had been stored from the Tay-Sachs screening programs a generation earlier. The prevalence of 185delAG was 1 percent—meaning that one of 100 Ashkenazim was walking around with



Shonnie Medina died of breast cancer in 1999.



# A single bite of the apple tempted another, as sisters, aunts,

a gene that could kill by itself, unlike the recessive mutations. Commenting on the surprisingly high frequency of the mutation, geneticist Francis Collins, now director of the National Institutes of Health (NIH), said that the breast and ovarian cancers attributable to 185delAG might be the most common serious single-gene disease yet identified in any population group.

A less-frequent *BRCA1* mutation, called 5382insC, was identified next, followed by 6174delT on a second gene, *BRCA2*, making for a trio of characteristically Jewish breast-cancer mutations. They evidently had stemmed from three different founders in Jewish antiquity. In most other ethnic groups, the prevalence of *BRCA* mutations is low, about one in 400. The *BRCA* carrier rate among Ashkenazi Jewish men and women is one in 40—10 times the background rate. Comprising only 2 percent of the American population, Ashkenazim learned they represented up to a third of the country's *BRCA* carriers.

Being the first mutation to enter Jewish consciousness, 185delAG became the best-studied, most worried-over piece of DNA in the world. Largely because of it, more people have been tested for *BRCA1* than for any other human gene. An initial screening of the broader Jewish population, conducted by the NIH in 1996, followed the procedure that had succeeded with Tay-Sachs testing. Some 5,000 volunteers in the Washington, D.C., area were recruited with the aid of rabbis and community health officials. They

provided researchers with DNA samples and histories of any cancers in their families. As before, the people who stepped forward offered to help even though, in this first snapshot of the problem, they were not given their individual test results.

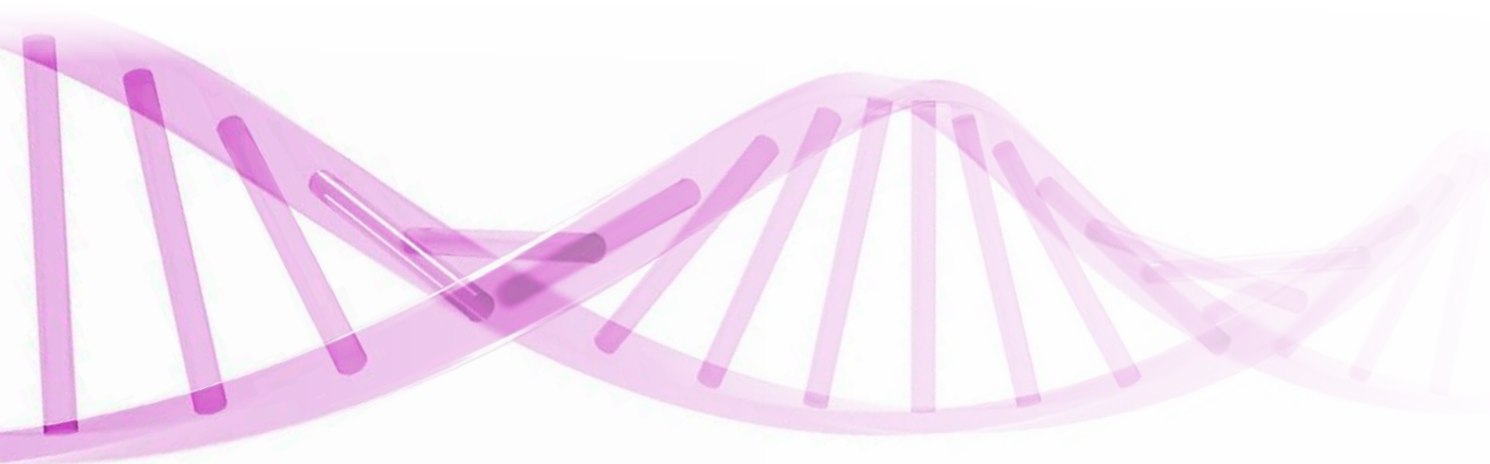
**F**ROM THE NIH study and others, scientists determined that not every *BRCA* carrier was going to be affected, because the mutations were not fully penetrant. Penetrance is a technical term signifying that a powerful gene may pull its punches. Because of incomplete penetrance—because of healthy elderly carriers like Shonnie Medina's grandmother, Dorothy—the risk of cancer from 185delAG and other *BRCA* mutations must be expressed in terms of probability. The range of estimates is wide. The most hopeful studies suggest that just half the carriers will get breast cancer during their lifetimes, the least hopeful that 90 percent will. The number given most often is 80 percent. The penetrance of ovarian cancer is lower, in the neighborhood of 40 percent. Something blunts the thrust of the gene, but no female who is a carrier can count on that happening.

When news of the Ashkenazi *BRCA* was conveyed to the Jewish community, it was often oversimplified in the direction of

alarm. Women tended to overestimate their risks of carrying a mutation if there were any reports or hints of breast cancer among their relatives. Newspapers and magazines published articles by or about Ashkenazi women agonizing over *BRCA*. According to surveys, Jewish women were much more likely to visit a genetic counselor than other minorities were. The women knew that if they took the test and it was positive, the next dilemma would be whether to have a preventive mastectomy or to try to circumvent the risk with extra mammograms and closer surveillance. The knowledge was like the apple that Eve offered Adam. A single bite of the apple tempted another, as sisters, aunts, fathers, and daughters submitted their DNA for analysis. Positive results brought fear and shame, and negative results, relief and guilt, the riptides of emotion dividing families.

Pressing to save lives, some scientists recommended large-scale screening of the Ashkenazi population. Others said no, it is too soon, better wait for additional studies to be completed. But how would such studies be used? Would health insurance companies call *BRCA* a preexisting condition and deny coverage? There were laws against genetic discrimination in health policies, but they didn't apply to life insurance policies. Would Jews become an uninsurable class of people?

Orthodox Jews wrestled with all of these anxieties and more. Within their circle, as Rabbi Ekstein knew better than anyone, a diagnosis of breast cancer could prompt a woman to seek treatment in another city,



# fathers, and daughters **SUBMITTED** their **DNA** for analysis.

lest the people at home find out. High in her mind were her children's marital prospects. If a young person was told that a *BRCA* mutation had been detected in her family or, G\_d forbid, that she carried a mutation herself, at what point in her courtship was she obliged to disclose the information to her potential spouse? Should she then be rejected? Ekstein, unable to devise a work-around for couples in his care, found the situation deplorable. "What is the advantage of screening for a condition, a mutation, that has no treatment?" he demanded to know. "It is just making more tragedy. For the rest of her life and her future generations, she will be burdened with worry," Ekstein came out strongly against the *BRCA* test.

But like it or not, the Jewish *BRCA* carriers were the vanguard. Thanks to the 185delAG mutation and its two companions, *BRCA* has become a metonym of cancer risk for every woman. When Jewish women enrolled in research to test the gene's penetrance, the results were applied to all other ethnicities, where mutations were not as common. A genetic aberration conceived in isolation from the rest of the world was donated to the world through science, adding to knowledge of *BRCA*'s universal behavior. If there was one disadvantage to using Ashkenazim in genetic studies, it was that their blood relatives were harder to come by than in other groups. Their extended families tended to be smaller, their pedigrees pinched off because of Jewish losses in the pogroms of Eastern Europe and, more recently, the Holocaust.

In New York, Chicago, Los Angeles, and other cities, demand for the tests surged, in part because Myriad Genetics, the company that owned the patent for *BRCA* testing, promoted the service directly to doctors and consumers. The company reported in 2008 that the number of people taking the test was growing by 50 percent every year. The negative findings well outstripped the positives, but that didn't dent the demand to know. Myriad estimated that half a million *BRCA* carriers in the United States remained to be detected, including 150,000 who were Jewish. Among 5 million American Ashkenazim, you could figure on 50,000 carriers of 185delAG. Nobody in the genetics profession

was calling 185delAG an Ashkenazi mutation any longer. By this time it had turned up in a dozen distant places along the spidery trail of Jewish migration, including New Mexico and the San Luis Valley.

Iona's aunts Wanda and Lupita, who had tested positive for the mutation in 2007, were diagnosed with breast cancer in 2009. Wanda's case was advanced, and she died that spring. The spate of bad news made it impossible for Iona to put off her *BRCA* test any longer. She was having trouble sleeping. "I realized I was being selfish," Iona said. "It would be selfish of me to put people through what Wanda and Shonnie did, if I could do something about it."

Leaving a blood sample at the lab, Iona went home to await the result. Her heart started beating rapidly. To work off steam, she did kickboxing exercises against a heavy punching bag. One day she felt a stabbing pain in her chest and was taken to the emergency room, believing she'd had a heart attack. Instead, she had pulled a muscle. Then the genetic counselor phoned: Iona, like her late sister and at least 10 of her close relatives, was positive for 185delAG.

In 2010 Iona enrolled in a new program at Penrose Cancer Center in Colorado Springs. Called the High Risk Breast Clinic, it offered *BRCA* carriers a free consultation with a breast surgeon, along with mammography or an MRI scan. Signing up for the program made Iona feel better. Her first MRI was negative. In her mind, she had taken her breast- and ovarian-cancer risk under control not through surgery but through watchful waiting, the strategy Rabbi Ekstein favored. Preventive mastectomy was off the table, and after learning more about ovarian removal (another preventive measure) Iona decided she didn't want that operation either. The fact that she had taken birth-control pills for years was somewhat protective against ovarian cancer.

The anxiety attacks, the sense of being overwhelmed, were past, but in relating this, Iona spoke rapidly, giving wide berth to her emotions. "Experience shows," Ekstein says, "that even the most highly educated of individuals have difficulty using intellect to dominate emotions."

Iona knew the answer deep in her DNA, knew the 2,500-year-old mutation that had found its way into her body, yes, she knew. She knew what her headstrong sister hadn't. Though Shonnie would not have cared. **D**

**Jeff Wheelwright is a longtime contributor to DISCOVER. His new book, *The Wandering Gene and the Indian Princess: Race, Religion, and DNA*, will be published in January. Excerpted with permission of the publisher, W.W. Norton & Company, Inc.**

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(2) Mailed In-County Paid Subscriptions Stated on PS Form 3541		
(3) Paid Distribution Outside the Mails Including Sales Through Dealers and Carriers, Street Vendors, Counter Sales, and Other Paid Distribution Outside the USPS®	89,033	75,600
(4) Paid Distribution by Other Classes of Mail Through the USPS (e.g., First-Class Mail®)		
c. Total Paid Distribution (Sum of 15b (1), (2), (3), and (4))	678,715	568,588
d. Free or Nominal Rate Distribution (By Mail and Outside the Mail)		
(1) Free or Nominal Rate Outside-County Copies Included on PS Form 3541		
(2) Free or Nominal Rate In-County Copies Included on PS Form 3541		
(3) Free or Nominal Rate Copies Mailed at Other Classes Through the USPS (e.g., First-Class Mail)	500	500
(4) Free or Nominal Rate Distribution Outside the Mail (Carriers or other means)	28	
e. Total Free or Nominal Rate Distribution (Sum of 15d (1), (2), (3), and (4))	528	500
f. Total Distribution (Sum of 15c and 15e)	679,243	569,088
g. Copies Not Distributed	215,131	204,113
h. Total (Sum of 15f and g)	894,374	773,201
i. Percent Paid (15c divided by 15f times 100)	99.92	99.91
16. Publication of Statement of Ownership If the publication is a general publication, publication of this statement is required. Will be printed in the DECEMBER 2011 issue of this publication.
17. Signature and Title of Editor, Publisher, Business Manager, or Owner:  
Michael Barbee, corporate circulation director.