CHEATING IS SO 1999

OUTSIDE THE LINES

WHICH IS WHY *THE MAGAZINE* SPENT A YEAR SEARCHING FOR THE ATHLETIC HOLY GRAIL: A SPORTS GENE.

BY SHAUN ASSAEL

PHOTOGRAPHS BY SARAH A. FRIEDMAN
3-D ANATOMY BY ZYGOTE

MMP3 GENE

A gene linked to strength or weakness of the Achilles tendon. People who carry the CC genotype combination are twice as likely to injure their Achilles as those without it.

COL1A1 GENE

A gene with just one task: cue the body to manufacture collagen, the protein that keeps ligaments and tendons strong. Those with the CC or CA combination have decent collagen production. Those with the AA variant, our "Superman" gene, have an 85%-reduced risk of ACL injuries.

Chiefs lineman Andy Alleman embraces genetic analysis: "I'm all about information I can act on."

THE QUESTION THAT BROUGHT ME TO THE BUCK INSTITUTE, OUTSIDE SAN FRANCISCO, LAST FALL SEEMED SIMPLE ENOUGH: WHY DO SOME ATHLETES SEEM TO AGE MORE SLOWLY THAN OTHERS?

Swimmer Dara Torres had just completed her fifth Olympics, at age 41. Brett Favre was coming out of retirement at 38 to play for the Jets. Driving up the winding road, past parking gates and security checkpoints, I listened to sports talk-radio chatter about how far that trend might go. Could a quarterback play until 50? Will we see a gold medalist at 65?

If there were answers, they'd surely be found in the flying saucer-shape building at the top of the hill. It has no sign on the outside. But visitors don't arrive by accident. Anyone who comes this far knows he's at the country's leading think tank devoted to age and chronic disease research. I had come to see its president, former Saints linebacker Jim Kovach. He had already earned a medical degree, and then, after retiring from the NFL in 1986 following a seven-year career, earned a law degree, too. Today the 53-year-old still looks like he can chase a QB out of the pocket. As we walked through the building's polished halls, he spoke excitedly about the work unfolding behind its high-security doors. One researcher had quadrupled the life expectancy of a worm by altering its genes. Another conducted experiments showing that it's possible to predict a worm's life span based on what's contained in its DNA.

Yet when I asked Kovach a fairly basic question—What do we know about how genes impact athletic performance?—he simply shrugged. "I have no idea," he said. "Athleticism is a complex trait. How our genes interact is still a mystery."

According to Kovach, studying genetics is like opening a series of those Russian nesting dolls where a small soldier fits within the body of a larger one, and so on. The big soldier is the human body. A small soldier inside represents one of the trillions of cells that make up our body. And inside that is an even tinier doll. That one, Kovach said, is our DNA—a wondrous strand of three billion microscopic pieces of data that control every aspect of human life.

The whole genetic alphabet, he continued, can be represented by just four letters: A, C, G and T. Each stands for something called a nucleotide—the building blocks of DNA—and they repeat in pairs along our strands of genetic material. The pattern in which pairs of these four letters repeat accounts for all the differences between us. A pair of C's along one side of the chain might create dark hair, while a pair of T's in the same spot could turn it red. "Athletic performance might involve a thousand of those letters scrambled in different ways," Kovach said. And who knows which of them could explain why Favre and Torres were still going strong? Finding out, he said, would require a study that Buck Institute geneticists had never done, a study that would examine the DNA of the pros themselves.

OUTSIDE THE LINES
WATCH THE IN-DEPTH TV REPORT ABOUT THE SEARCH FOR THE SPORTS GENE, OCT. 18, ON *OTL*.

The more Kovach thought about that idea, the more intrigued he became. At a minimum, he said, you'd need about 100 elite athletes with very distinctive physical traits that make them stand out from the crowd, implying that there was something unique about their underlying genetics.

Like 350-pound NFL linemen.

I wondered, how hard could it be to pull that off?

UP TO THIS POINT, RESEARCH HAS FOCUSED ON IDENTIFYING THE GENES THAT CAUSE DISEASE. BUT WHAT IF WE COULD FIND THE GENES THAT EXPLAIN ATHLETIC PERFORMANCE?

This was a new frontier, real cutting-edge science. Surely, guys who measured athletic advantage in milliseconds would want to be a part of it.

By the time I left Kovach six hours later, we'd agreed to recruit 100 NFL linemen to cooperate with our own study—one that, if successful, would be the largest-ever genetic examination of professional American athletes.

I'd walked into the Buck Institute wondering why some jocks age better than others. I walked out in search of the athletic holy grail: a sports gene.

GETTING PLAYERS to cooperate with our little scheme was only half the battle. We also needed a way to examine parts of the code of the athletes'

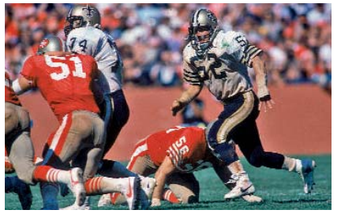
OPENING SPREAD: ILLUSTRATION BY JASON LEE

DNA, which means identifying the placement of those pairs of genetic letters along the three-billion-character strand.

It took roughly two decades and $3 billion for scientists to decode the first human genome. And when it was unveiled, in 2000, it was a game-changer. From it, scientists have identified genes responsible for everything from hair or eye color to those that trigger diseases such as Alzheimer's and various forms of cancer. As more companies have learned how to sequence DNA, the cost has tumbled. Some biotech firms can now sequence a full genome for a million dollars—which would have seemed cheap 10 years ago. But there are also companies today that, rather than do a full analysis, will look for a handful of genetic markers, usually those related to a person's likelihood of developing common diseases. A test like that can cost as little as a few hundred dollars.

After my meeting with Kovach, I called one such company, 23andMe. The Silicon Valley start-up has good genes of its own: It was launched in 2006 by Anne Wojcicki, who is now the wife of Google co-founder Sergey Brin. For $399, the company will scan the DNA in a customer's spit sample for genetic variants that show a predisposition to things like arthritis and diabetes. I asked whether they might be willing to take their science in a whole new direction—a hunt for variants that explain athletic performance.

Kovach is learning as a research executive what he never knew as a player (No. 52): how to use genetics to extend careers.



GENETICS 101

DON'T WORRY, NO ONE REMEMBERS HIGH SCHOOL BIO. FORTUNATELY, WE HAVE A REFRESHER COURSE:

DNA Your body holds trillions of cells that contain genetic material called DNA. It's the blueprint that contains the information for what traits and characteristics are possible, from hair and eye color to our likelihood of developing various diseases. The code itself is so intricate and complex that if you were to write out its components, it would stretch from the North Pole to the equator. Yet DNA itself is coiled so tightly in our cells that it barely measures a thousandth of a millimeter.

THE ALPHABET So how does DNA tell your eyes what color they'll be? It's made out of chemical units called nucleotides, also known as the building blocks of DNA. Each nucleotide is represented by one of four letters (A,C, G and T), which repeat in pairs along our strands of DNA. The order of these letters, and the pattern by which they repeat, dictate the way our genes express themselves—blue eyes or brown, for example—in our bodies.

BASE PAIRS Those pairs of nucleotides? They're called base pairs, and a single copy of DNA is three billion pairs long. One set of letters comes from your mom, the other set comes from dad. That combination is what makes you unique.

GENES It takes between 10,000 and 15,000 base pairs to create the unit which tells the body to develop a particular characteristic. That unit is called a gene.

GENOTYPE Your particular version of genes is known as your genotype.

THE GENETIC INFORMATION NONDISCRIMINATION ACT (GINA) GOES INTO EFFECT NOV. 21, WITH BIG IMPLICATIONS FOR HOW PRO SPORTS LEAGUES WILL BE ABLE TO USE PLAYERS' GENETIC INFORMATION IN THE FUTURE. FIND OUT HOW IT WILL ALL PLAY OUT, AT ESPN.COM/INSIDER.

FROM TOP: COURTESY BUCK INSTITUTE; CHUCK SOLOMON/GETTY IMAGES

Wojcicki and co-founder Linda Avey loved the idea, and they agreed to donate 100 testing kits. Athletes would spit into the provided plastic tubes and mail them back to 23andMe. The firm's staff would then search across the 20,000 known individual genes for something unique in the players' codes, something that wasn't common in the average Joe and might give us insight into the source of their prowess.

Through last winter and spring, as Kovach worked the phones to find subjects, he discovered an eager audience among retired players. (Since DNA rarely changes, retired guys' genetic material is the same today as when they played.) The NFL is hard on players' bodies. So hard that the league paid out $20 million in disability claims between April 2006 and March 2007. Most retirees, he discovered, were ready to jump at the chance to discover anything that could help them manage their long-term health.

Hall of Fame defensive tackle Merlin Olsen agreed to participate, along with his brothers, Phil and Orrin, both of whom played in the NFL. Lomas Brown, who won a Super Bowl ring with the Bucs, signed on, as did ESPN's Marcellus Wiley and Mark Schlereth.

Recruiting current players wasn't quite as easy. Genetic testing has a different ring to those still collecting a paycheck, and who may worry about what their employers might discover. Fortunately, longtime NFL agent Joe Linta saw the benefit of having his guys get a free genetic checkup. On March 7, he invited *The Magazine* to a retreat so we could give our pitch to his guys. "You can be pioneers," I told eight stone-faced linemen. "No one has ever tried this before." They looked skeptical.

"And you'll have an edge," I continued. "We don't know what we'll find, but whatever it is, you'll be the only ones in the NFL who know it."

All eight agreed to join the study. And by the middle of June the first results began pouring in. When they did, we learned what scientists have known for years: The first question you ask rarely leads you to the answer you seek.

Our theory that NFL linemen might be genetic outliers was flat-out wrong. Every way that 23andMe looked at it, the pros were just like the Joes.

Consider ACTN3, a gene that helps manufacture fast-twitch fibers. It comes in two types: the C type, which produces power, and a T version that fosters endurance. With potential CC, CT and TT combinations, we figured most of the pros would have the CC power combination. Not so. Only 32.8% had a CC genotype—almost exactly the same proportion as the Joes. The CT and TT comparisons between pro athletes and civilians were also too close to call.

"Right now, genetics isn't a good predictor of success," says Stanford University's Stuart Kim, a genetics professor who reviewed the data for us.

That's good news for anyone who might worry about a future where scouts troll maternity wards looking for franchise quarterbacks or who fear that college coaches will one day hand out scholarships to preschoolers based on genetic report cards.

But it was bad news for us. We had undertaken one of the largest-ever studies of genetics and sports and had nothing to show for it.

At least that's what we thought.

HUNTINGTON WILLARD is a trim, thoughtful man who grew up in New England as a rabid fan of all Boston-area teams. He now runs Duke University's renowned Institute for Genome Sciences & Policy. Several years ago, he and Kovach became friends when both worked in Cleveland, at Case Western Reserve University.

One afternoon this past February, as Kovach prepped for the study, he called his old friend and asked for help. Willard had his students scour every study they could find in which a gene was proved to influence an athletic trait. The students came up with about three dozen, including obvious qualities such as size and speed. But there were more subtle traits, too, like grip power and oxygen-intake capacity. Problem was, not every gene has a crystal-clear role in producing a trait; some genes and traits seem linked but those links require further study. By April, Willard whittled the list down to 18 genes whose variants played a clear and convincing role in specific sports-related traits.

At the time, this provided an interesting sideline to our study. After our roadblock, it became a vital piece of information. In fact, it offered us a new direction. As a group, pros might not be genetically different from the Joes. But using Willard's new guide, we could now see how they are different from one another.

One of the most important genes Willard and his students isolated is called COL1A1, which has a singular task: manufacturing collagen, the protein that keeps ligaments strong.

The gene comes in three combinations, coded by the letters C and A. The most common, CC and CA, do a good but not great job of lining ligaments so they don't tear. But a few people carry an AA variation—what we began calling a Superman version—of the gene. Extensive research about ligaments has been done on ACLs, since tearing the ligament is so common in sports (see page 136). Studies show that carriers of our Superman gene have an 85%-reduced risk of hurting their ACL. Only 1.7% of the linemen in our group had that rare version.

One of them was Hoby Brenner, an ex-Saint who retired in 1994. Kim, the Stanford professor, called to ask if Brenner had ever injured his ACL. "Nope, never," the ex-tight end said. "I played 13 years and retired in peak shape. The Saints didn't want me to go, but I wanted to go out on top." When Kim told him he'd hit the ligament lottery, Brenner answered, "I wish I'd known. I might have played another year or two."

Brenner illustrated the significance of our first major finding. Knowing about a single tiny genetic variation might change a thoughtful player's decisionmaking about how long to play.

And if you're not someone with a Superman gene? The reality is that most NFL players would play until their bodies gave out, regardless of risk. Which is why our biggest revelation was yet to come.

AT 6'4" and 310 pounds, Chiefs offensive lineman Andy Alleman has always surprised his coaches with his speed and endurance. From his time as a star lineman at his Ohio high school to his senior year at the University of Akron, Alleman outlasted most teammates on running drills, then outdid them in the weight room. His 5.07-second 40-yard dash at the 2007 NFL combine sealed his status as a legit prospect who deserved a shot at the big time. "Even though I'm not 350 pounds, I'm one of the stronger guys on the team," he says. "I don't struggle in the weight room like some guys."

As one of the eight linemen who'd signed up for *The Mag*'s study at his agent's retreat in March, Alleman was able to learn the reason why. He has

DUKE FOOTBALL HOPES GENETIC RESEARCH WILL HELP TURN AROUND ITS PROGRAM.

half a dozen genetic variations that give him an intense capacity for exercise. One lets him reach a greater peak exercise level than others. Another lets his blood absorb ultrahigh levels of oxygen. No surprises there for Alleman: "I've always done well with running," he says.

But Alleman also learned something he didn't expect. His genetic profile revealed a version of a gene, MMP3, that might give him trouble with his Achilles tendon. A study of South African athletes showed that runners with Alleman's variation are at least two times as likely to get an Achilles injury as those without it.

An Achilles injury would be a disaster for a guard like Alleman, who is still fighting for a regular starting position. But armed with this information, Alleman is now working to beat his genetic odds. He's already added rubber-band stretches to his workouts to increase flexibility and started using a board placed at steep angles to help him flex his foot and increase range of motion in his Achilles.

The changes Alleman made to his workout regimen might seem minor, but they are at the core of the study's breakthrough. Rather than

simply letting nature take its genetic course, players can use information gleaned from their own DNA to create training plans that will keep them healthy longer. "I'm all about information I can act on," Alleman says. "You don't want to let it run your life, but you want to be proactive."

He's right. And if the broader sports world takes the same attitude toward genetic information, the effect could be profound. Each year, 100,000 ACL injuries occur, mostly among young athletes. The National Athletic Trainers' Association funds studies of ACL injuries, but Mark Hoffman, the president of its Research and Education Foundation, says that no one is quite sure why some kids benefit and others don't. "It's still kind of a mystery to us," he says.

How easily might that mystery be solved if trainers tested those kids for the COL1A1 collagen gene to see who's at the greatest risk? At the very least, it could focus resources by targeting those who need help most. "It might be an interesting tool," Hoffman says.

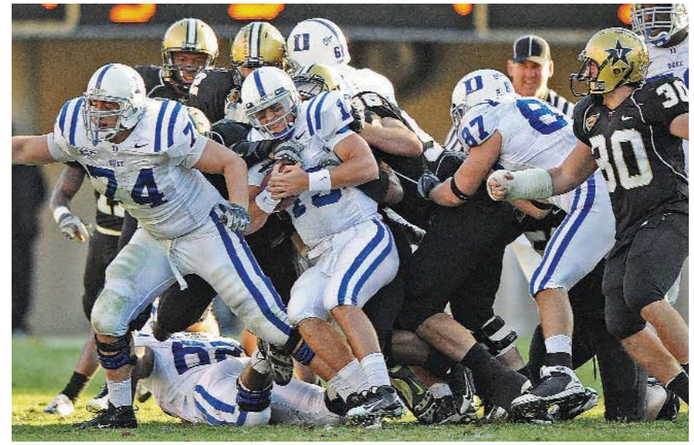
Pete Koch, a certified strength coach who retired in 1989 after playing in the NFL for five seasons (and who donated his DNA to our project), certainly sees a future for genetic trainers. "It's addition by subtraction," he says. "You only have a certain amount of time to train. If you know what you need, you won't waste time with the other stuff that matters less." Add to that an emerging discipline known as nutrigenomics, which uses DNA to personalize nutrition, and soon we could see athletes being able to send their spit samples to Gatorade, then get back a genetically calibrated sports drink. "It's at least theoretically possible," says Bob Murray, co-founder of the Gatorade Sports Science Institute. He retired last year, but already GSSI scientists were closely monitoring the field. "I think this is seen as something that might become reality in five years."

It's easy to imagine that by 2015 NFL teams will have geneticists on their training staffs and kids will be coming to the combine with their DNA on memory sticks. But this fast-moving world will also make athletes face hard choices.

Take the much darker legacy of still another gene on Willard's list, APOE. It comes in T and G varieties, and previous studies of athletes show that the risk of long-term neurological damage doubles for those with a TT code, especially among players who suffer from multiple concussions. If athletes know they carry the TT, they may take extra steps to protect themselves, either by wearing extra protective gear or taking time off after an injury.

But deciding to seek that knowledge is a tough call. A variant of the gene—known as APOE4—has been linked to the onset of Alzheimer's. How will an active player be affected by learning he can probably look forward to dementia in retirement? "I don't know how I feel about all of this," says Jonathan Feinsod, a veteran NFL agent whose clients include Atlanta wide receiver Roddy White. "Big-time players are all warriors. They think they're infallible. This is exactly the kind of thing that would spook them. And I don't think spooking them would accomplish anything."

Kovach will confront that issue soon. In September, he spun off his work from *The Magazine*'s project into a company called Athleticode, which will test athletes for the same genes we targeted and provide them with counseling and personalized training plans based on their results. But he plans to handle the issue of APOE delicately, making it an option for customers to learn about, not a standard part of Athleticode's genetic review. "Some of this is going to take time for folks to get used to," Kovach says.



A YEAR into my search for a sports gene, I found myself watching a dozen Duke Blue Devil football players line up for a blood test in the training room at the school's Wallace Wade Stadium. The $10 procedure determines whether the players have a genetic mutation known as the sickle cell trait, which causes oxygen-carrying red blood cells to change shape and get stuck in arteries during intense physical exertion, sometimes resulting in death from cardiac arrest, heat stroke or kidney failure. The trait is carried by one in every 12 African-Americans, and since 2000, seven college football players, all African-American, have died from the condition.

To settle a lawsuit brought by the family of one of those players, the NCAA recently suggested that all schools test student-athletes for the sickle cell trait. But the reaction to that announcement shows what a hot-button issue genetics can be. Critics are lining up to suggest it will lead to discrimination against the trait's largely minority carriers. "A coach is going to be able to say, 'Even though this kid is great, do I really want to put him out there as the quarterback and take the risk of something happening?' " Elliott Vichinsky, a doctor from Children's Hospital Oakland, recently told the *San Francisco Chronicle*.

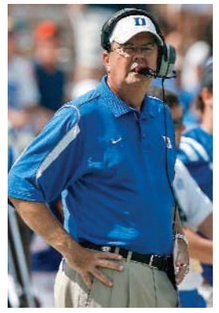
The NCAA is squeamish about even calling it a genetic test. "This blood test is not considered genetic or DNA testing," a spokesman e-mailed *The Mag*, pointing out that no one was being asked to spit in a tube.

On the other hand, knowledge of the trait could simply change the way coaches train players who carry it. At Duke, Blue Devils football coach David Cutcliffe is asking players to embrace that broader view of genetic testing. Ever since Willard's class crossed campus to visit him last spring, Cutcliffe has been fascinated by their research work. "From an injury-prevention standpoint," he says, "what those kids are studying could be huge for my kids."

In our search for a sports gene, we saw how even a small bit of genetic information can give a player like Andy Alleman an edge. Cutcliffe wants to consider taking the next step by including his whole squad in a study that would help Willard compare the DNA of the individual players with their injury reports, allowing him to get a better understanding of which variations may account for the most muscle tears or joint breakdowns. (Players' individual data would be kept anonymous. The project is currently pending approval by a Duke institutional review board.)

FROM OUR STUDY, HOBY BRENNER FOUND OUT HE CARRIES THE SUPERMAN GENE FOR ACL STRENGTH. "I WISH I KNEW," HE SAID. "I MIGHT HAVE PLAYED ANOTHER YEAR OR TWO."

THIS JOURNEY is far from over. The staff at 23andMe continues to pore over our pro linemen's DNA, looking for ever smaller connections and adding to our base of knowledge. Willard continues to train and graduate waves of students who are now equipped to join the search. "The landscape will be unrecognizable when today's freshmen graduate," he says. And in 10 or 20 years—how far will genetic testing have taken us then? Will it be able to find the one trait that Cutcliffe values most?



Coach Cutcliffe wonders how far DNA studies of his Blue Devils can go: "I'm trying to find intelligence, focus and attitude."

"I'm trying to find kids who are gifted athletically," says Cutcliffe, who once worked as Peyton Manning's offensive coordinator at Tennessee and as his brother Eli's head coach at Ole Miss. "But I'm also trying to find intelligence, focus and attitude."

Willard is philosophical. He has to be. If predicting an ACL tear is so difficult, how do we begin to use genes to quantify such deeply abstract traits as logic, emotion and leadership? "We're starting with a simple code for things like size and speed and then adding in things we barely understand until we end up with poetry in motion," Willard says. "I think figuring it all out will be a 20-year project.

"But when we're finished, I also think we'll know a lot more about what makes us more human."

Got ideas, gripes, something nice to say? E-mail the writer at shaun.assael@espnthemag.com.

PROS VS. JOES
THE GENETIC HOME GAME

When *The Magazine* decided to genetically test 100 current and ex-NFL linemen, we figured that a 350-pounder who runs a five-second 40 has to have something special in his DNA. But what? To find out, we asked genetic testing company 23andMe to compare the DNA of our pros with that of 40 regular Joes with similar sizes and builds. It was looking for different gene combinations on each guy's DNA that might explain why one is wearing an NFL uniform while the other quarterbacks from the couch. If there were anything special about the NFL genes, it should be obvious in the comparison. But when the results came in, we got a lesson in jumping to conclusions: In every major category examined by 23andMe, the Joes were virtually identical to their NFL counterparts.

The Mag's project continues to add new data to the study every day and will continue to search for differences between the groups. But for the moment, the verdict in the nature vs. nurture debate is in: Score one for nurture.

ACCORDING TO 23ANDME, ALL SPREADS ARE STATISTICALLY INSIGNIFICANT DUE TO OUR SMALL SAMPLING SIZE.

PHOTO COMPOSITE: STEVE MITCHELL/US PRESSWIRE (MANNING); JORDAN STRAUSS/GETTY IMAGES (ROGEN)

FROM TOP: DON MCPEAK/US PRESSWIRE; KEVIN C. COX/GETTY IMAGES