IN OTHER NEWS

PIG LUNG WORKS, BRIEFLY, IN HUMAN

In a small step forward for the long-struggling field of xenotransplantation, surgeons in China have put a pig lung into a brain-dead man and shown it can function, although the organ only lasted 9 days before succumbing to an immune assault. The organ came from a miniature breed of pig with three of its genes for cell surface sugars deleted and three human genes added, changes made to help the lung work in a person without being rejected. The lung delivered oxygen to the man's blood and removed carbon dioxide, according to a report this week in *Nature Medicine*. The organ also avoided an initial antibody attack, but soon swelled with edema as immune factors reacted to the foreign tissue. The experiment "clearly illustrates that lung xenograft survival in humans will require more genetic engineering and optimized immunosuppression," says animal cloning specialist Dengke Pan, a co-author of the study and founder of Chengdu ClonOrgan Biotechnology, which makes the pigs. Meanwhile, a gene-edited pig kidney has continued working in a U.S. man for 8 months, nearing the 9-month record for a xenotranplant in a human. —Jon Cohen

PHOTO: RICH VON BIBERSTEIN/ICON SPORTSWIRE VIA AP IMAGES

GENETICS

Gaps remain in college sports' 15-year-old sickle cell policy

Report recommends education, genetic counseling with NCAA screening

RODRIGO PÉREZ ORTEGA

In September 2006, Dale Lloyd II, a first-year football player at Rice University, collapsed during a routine team workout and never got back up. The 19-year-old's death was later linked to sickle cell trait (SCT)—a genetic condition he hadn't known he carried, and that can make intense exercise dangerous.

The tragedy was a turning point in college sports. Lloyd's parents sued the university and the National Collegiate Athletic Association, and, as part of a settlement, NCAA mandated in 2010 that all Division I athletes either show proof of prior screening for SCT, undergo new testing, or sign a liability waiver. The policy soon expanded to all NCAA sports. At the time, it was one of the most ambitious genetic screening efforts by a private organization in the United States.

The policy has likely saved lives, but a comprehensive new study funded by the National Human Genome Research Institute also finds shortcomings in its implementation. Conducted by researchers at Duke University and the University of North Carolina at Chapel Hill and described in a report published this week on a Duke website, the study finds the testing itself can be inadequate, and that many athletes who test positive don't get comprehensive advice about how to reduce their risk, or genetic counseling about the implications of the trait for future generations.

"I'm really impressed" with the report, says Lakshmanan Krishnamurti, a pediatric hematologist at the Yale University School of Medicine. The findings are "not a surprise," he adds. It's particularly troubling that protocols long used in the military to mitigate SCT-related risks, such as ensuring good hydration and not exercising outside on very hot days, are still not universal in college sports, he says.

A spokesperson for NCAA's national office declined to comment on the study.

SCT is caused by a mutation in the gene for hemoglobin, the oxygen-carrying protein in red blood cells. The condition disproportionately affects Black people, about one in 13 of whom carry the mutation. People with two copies have sickle cell disease (SCD), in which misshapen red blood cells can lead to chronic pain, anemia, and organ damage. But those with SCT carry a single copy and often have no symptoms or health risks—unless they engage in extreme physical exercise. Most of the reported deaths related to SCT are from exertional rhabdomyolysis—a condition in which muscle breaks down, releasing toxic proteins into the bloodstream that can damage organs. A 2012 study in the *British Journal of Sport Medicine* reported that athletes with SCT had a risk of exertional death 37 times higher than those without the trait.

Duke University defensive tackle Aaron Hall tested positive for sickle cell trait in a screening program mandated by the National Collegiate Athletic Association.

Since the NCAA policy was implemented, the number of football players who died of complications related to SCT has plummeted, according to a 2020 paper in *Sports Health: A Multidisciplinary Approach*. Nine players died in the 10 years before July 2010, and only one in the 9 years after. But deaths still happen: Last year, 18-year-old Calvin "C.J." Dickey Jr. collapsed during football practice at Bucknell University and died 2 days later from exertional rhabdomyolysis. He had tested positive for SCT weeks earlier.

In the new study, Duke geneticist Charmaine Royal and her colleagues interviewed nearly 1900 athletes, trainers, coaches, and team physicians across 172 schools about their experiences with the NCAA policy. About 2% of the participating athletes carried SCT. And even though newborns in the U.S. have been routinely screened since the mid-1970s for hemoglobin abnormalities, more than 40% of those athletes found out they had SCT during the NCAA screening.

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>
> **Lainie Ross**
> University of Rochester

More than 85% of participants supported SCT screening. But the report raises concerns about the testing method. NCAA recommends a "solubility test," which detects the presence of abnormal hemoglobin caused by the sickle cell mutation in blood with very high sensitivity but can miss abnormalities from other harmful gene variants that can pose risks to athletes. The report says players who test positive should have a confirmatory "electrophoresis" test, which uses electrical current to separate different types of hemoglobin and can distinguish SCT, sickle cell disease, and other hemoglobin disorders such as beta thalassemia. "I think it's unconscionable to test these kids with solubility testing and not do hemoglobin electrophoresis," says pediatrician and philosopher Lainie Ross of the University of Rochester, who attended summits convened by the study's authors to discuss the NCAA policy.

The researchers also found that many schools don't have clearly documented protocols for athletes with SCT. An NCAA fact sheet recommends precautions, including limiting all-out exertion to 3 minutes without resting, but the organization doesn't say how coaches and athletes should handle SCT-related complications.

Aaron Hall, a Duke student athlete who participated in one of the summits, found out he carried SCT during the NCAA screening as a freshman. He says coaches and staff gave him and his teammates plenty of information about the trait. "If I ever do encounter symptoms, I kind of know what to do myself," he says. But he may be an exception; the study found that only 21% of coaches felt knowledgeable about SCT facts, and only 11% of all athletes did.

The surveys also revealed that although NCAA recommends that people with positive results seek genetic counseling, only 20% of the colleges offered it, and no athlete in the study had received it after a positive SCT test. Schools have "an obligation to do pre- and post-test counseling," Ross says. "We shouldn't just treat these people as football players. ... You should treat them as whole, holistic human beings."

On the positive side, the report finds little evidence to support concerns that screening players might lead to discrimination based on SCT status. At Duke, athletes are required to wear red wristbands to alert staff and teammates they have SCT. "I am totally against those bands," Ross says. "This is private health information." But Hall says he's "extremely comfortable" wearing a risk band because it allows teammates and staff take care of each other.

Royal hopes NCAA takes the report seriously and doesn't "throw the baby out with the bathwater" in addressing the recommendations. "We propose a whole bunch of strategies" for improving the policy, she says, "so they have lots of options." □

ARTIFICIAL INTELLIGENCE

AI hypotheses lag human ones when put to the test

Machines still face hurdles in identifying fresh research paths, study suggests

JEFFREY BRAINARD

In May, scientists at FutureHouse, a San Francisco–based nonprofit startup, announced they had identified a potential drug to treat vision loss. Yet they couldn't fully claim the discovery themselves. Many steps in the scientific process—from literature search to hypothesis generation to data analysis—had been conducted by an artificial intelligence (AI) the team had built.

All over the world, from computer science to chemistry, AI is speeding up the scientific enterprise—in part by automating something that once seemed a uniquely human creation, the production of hypotheses. In a heartbeat, machines can now scour the ballooning research literature for gaps, signaling fruitful research avenues that scientists might otherwise miss.

But how good are the ideas? A new study, one of the largest of its kind, finds the AI-generated hypotheses still fall short of human ones, when researchers put them through real-world tests and get human evaluators to compare the results. But not by much. And maybe not for long.

A paper describing the experiment, posted to the arXiv preprint server in June, suggests AI systems can sometimes embellish hypotheses, exaggerating their potential importance. The study also suggests AI is not as good as humans at judging the feasibility of testing the ideas it conjures up, says Chenglei Si, a Ph.D. student in computer science at Stanford University and lead author of the study.

The research is drawing praise but also caution from others in the field, in part because judging originality is so difficult. "Novelty is the bugbear of scientific evaluation and one of the most difficult tasks in peer review," says Jevin West, a data scientist at the University of Washington.

The study examined hypotheses about AI itself, in particular natural language processing (NLP), which underpins AI tools called large language models (LLMs). The researchers tasked Claude 3.5 Sonnet, an LLM developed by the startup Anthropic, with generating thousands of ideas based on an analysis of NLP studies in the Semantic Scholar database and ranking the most original ones. The researchers then paid human NLP specialists to come up with compet-