



Dr. Michael Joyner monitors a patient while testing her maximum oxygen consumption.

‘This person is a cheeky heretic’

The views of Dr. Michael Joyner—on genetics research, on Precision Medicine—
don’t necessarily represent those of the Clinic.

(But the medical world wants to know what he thinks anyway.)

By Paul John Scott | Photos by Ken Klotzbach

It is early September and Dr. Michael Joyner is giving a lecture in the big hall below the Kahler, a talk entitled “Rio 2016, Observations and Lessons from the Summer Olympics.”

So he could have picked a snazzier title. Well, his audience for today doesn’t go for snazzy. The room is here at the behest of the clinic’s Center for Clinical and Translational Science, an NIH-funded initiative to bridge the gap between science and new treatments.

Joining the 300 or so doctors, administrators and students in the room are a learned contingent of Scandinavians, prominent Swedish MDs participating in the Clinic’s brain-trade with the prestigious Karolinska Institute in Stockholm. That’s the place where they hand out the Nobel prizes each year in medicine and physiology.

So if you’re the guy picked to give today’s talk, you don’t get to bring your weak sauce.

And the noted Mayo physiologist and anesthesiologist—one of the world’s leading experts on human performance and exercise physiology; the guy whose *New York Times* Op-Ed piece famously argued that the precision medicine of genomics “is unlikely to make most of us healthier”—gets right down to business.

He skips all the usual banter and opening with the blandest of topic questions: “What Can Elite Sport Teach Us About Excellence and Extreme Genetics?”

But this was being polite. Joyner should have phrased the question as “What the Gene Research We All Are So Excited About Can Teach Us About It’s the Great Pumpkin, Charlie Brown,” but then the Center for Clinical and Translational Science people would have had

to pack Pepto-Bismol with the audience’s box lunches.

Joyner, a tall, soft-spoken man who is an influential expert in exercise physiology and one of Mayo’s highest-profile clinicians, spent the next hour using the Rio Olympics as a way to highlight a problem with the organization of scientific research around genetic medicine. That’s not the company line. If you haven’t noticed, genes are big these days.

THE SLOW, SLOW RISE OF GENOMIC (NOW PRECISION) MEDICINE

The head of the NIH, Francis Collins, has been predicting the rise of genomic medicine since the 1990s. Like Linus on Halloween night, Collins keeps proclaiming the imminent approach of the Great Pumpkin, but so far no luck. No matter, so far, the medical world is waiting like Sally in that pumpkin patch with him.

Precision Medicine, the Obama administration plan to improve health care by targeting an individual’s unique genetic signature, has the support of both political parties, and last summer, Mayo received a major infrastructure grant in this effort: \$142 million to build a biobank hoping to link diseases to genetic variants.

Personalized medicine has been given a formal home at Mayo within the Center for Individualized Medicine. So anyone who questions this Manhattan Project to end all disease by targeting molecular medicine runs up against the great shared vision of our time. Rochester, especially, so. It is, in fact, written into the slogan for the University of Minnesota Rochester (“Recoding the DNA of Learning,”) and is literally tattooed on the

Dr. Joyner, one of the world's leading experts on human performance and exercise physiology, speaks at the Gold-Lab Symposium at the University of Colorado Boulder in 2015.



arm of the woman sitting next to me during Joyner's speech (it was a double helix, and it was awesome).

'ELITE ATHLETES ARE MADE, NOT BORN'

But what if focusing on genes is causing us to miss out on other discoveries?

"Someone like me gets a lot of emails, text messages, phone calls, and hallway conversations during the Olympics," begins Mayo's resident sage of the lactate threshold and other human athletic performance indicators. "Many of them go something like, 'Did you see Usain Bolt, he's a genetic freak.' 'Did you see Michael Phelps, he's a genetic freak.' 'Did you see Katy Ledecky, she's a genetic freak.'"

And as we all nod in quiet agreement—because clearly Katy Ledecky is a genetic freak, good Lord, the child had crushed the world record in the 800 meters and still had time to do her nails before other swimmers could finish—Joyner sets about dismantling our belief that elite athletes are born, not made.

As proof that specific genes have only a

weak effect on high-performance athletics (and by extension, diseases), Joyner opens with findings from a recent study of over 1,500 elite endurance athletes, an ambitious project carried out by a global consortium of scholars who in late 2015 published their giant bummer of a finding in the journal *PLoS One*.

Working with spit from an elite sampling of hardbodies—each of whom could probably crush the Med City Marathon on just four hours of sleep and with a plate full of calzone in their stomach—the researchers searched in vain for a genetic variant to link the world's greatest runners, cyclists, and swimmers. In the end, the authors "could not find evidence for a detailed genetic signature" separating elite endurance athletes from schlubs like you and me.

"But let's talk about direct-to-consumer testing," Joyner continues, shifting gears to the newly bustling trade in talent-identification DNA kits for would-be parents of future Olympians. The most prominent of these testing companies, Joyner explains, "will offer a cheek swab in your child to see what your child will be good at."

But as a 2015 paper published in the *British*

Journal of Sports Medicine determined, even the genotype most likely to be tested by these companies, a sure thing in the eyes of the commercial genetics industry, held but a "trivial" contribution to athletic potential. The authors concluded no child should ever have his or her DNA taken under the premise of his parents' or coaches' determined search to groom the next Michael Phelps.

Joyner then debunks a familiar set of beliefs we all hold about the role of genes in Olympic medals.

"How many people here believe there is something special about Afro-Caribbeans and sprinting?" he begins. The woman next to me with the double helix tattoo picks quietly at her salad. Everyone in that room believes there is something special about Afro-Caribbeans and sprinting—how could you not, the medal round for the sprint events has so much Jamaican green and yellow in the uniforms that it looks it like the front four of the Green Bay Packers. Wisely sensing a trap, no one puts up their hand to affirm the premise. Joyner then shares with the room a picture of the 2016 silver medalists in the 4-by-100. They were from Japan.



"Not too many Afro-Caribbeans in this picture," he remarks.

"We all know white women can't jump, right?"

Don't answer that, because this last question is accompanied by a clip of a white woman sticking a standing vertical onto a platform near her breastbone. (It was a YouTube of the elite Australian cyclist Anna Meares.)

Concluding his brief tour of facts that defy our biases about genes, Joyner points out there are more world record holders in the mile from Kansas than from Kenya. And here is where things get just slightly personal. "When will the [Mayo] Center for Individualized Medicine fund a study to search for endurance genes in Kansas farm boys?" he asks. He is being facetious. The remark draws scattered laughs. No one throws their hard roll at him.

'[JOYNER] IS A HUGE RESOURCE TO ... HUMANITY IN ITS ENTIRETY.'

Lest you think these are the thoughts of an upstart med student on his way to professional obscurity in Topeka, Joyner's opinions have become highly sought-after by the nation's health press. The 58-year-old father of four and Arizona native has been quoted in the *New York Times*, ABC News, the *Wall Street Journal*, Five Thirty-Eight blog, and on National Public Radio.

During the Olympics, BuzzFeed called to find out if Joyner thought all the biggest track records had been set and Business Insider called to ask if Joyner thought Phelps had the perfect body for swimming. His writing has appeared in *Outside Online*, at *Health News*

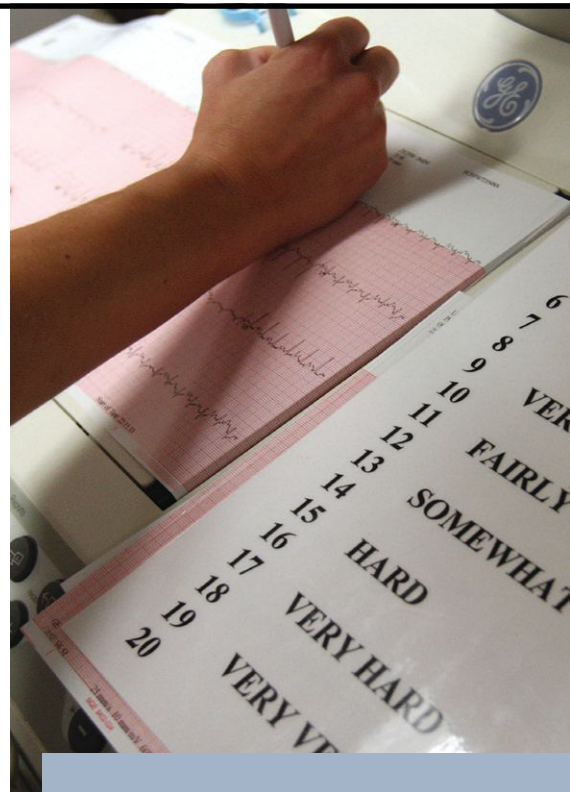
Review, in *Sports Illustrated*, and the *New York Times* opinion page.

"He could isolate himself and only take calls from Olympic Committees around the world," says fellow anesthesiologist Dr. Brad Narr. "He is a huge resource to our clinic, medicine, and humanity in its entirety."

Mayo's leading editorial professional agrees. "Dr. Joyner has tremendous energy and intellect, and he is an independent thinker," says Dr. William Lanier, professor of anesthesiology and Editor-in-Chief of *Mayo Clinic Proceedings*. Lanier says Joyner "is what the author Malcolm Gladwell describes as a 'maven' personality—a person we rely upon to connect us with new information. Whether you agree with him or not, it is always entertaining to hear his ideas, and he is the type of scientist and colleague who constantly encourages us to challenge our thinking as he challenges his own thinking."

A former Division I distance runner (he was a walk-on at the University of Arizona), the athlete-turned-deep-thinker takes a special interest in the physiology of endurance training. Joyner likes to study how the body performs under stress, but largely as a means to learning about the interconnected nature of physiology. That's a fancy way of saying a variety of systems divide up control of the functions that keep us alive. Joyner calls the body redundant in this way, and says this redundancy—the potential for all systems to chip in and help a little bit with the other guy's job—is critical to our survival as a species.

"Humans evolved to run away from predators, or chase prey, or to move around for whatever



Left: Dr. Joyner (far right) and Dr. Sarah Baker (center) monitor oxygen levels during an exercise test for patient Mary Liffbrig. Right: Results are also assessed based on a perceived exertion scale.

reason, and so you have to have blood flow to your muscles to be able to move for long periods of time," he says. He is at the time taking me to see an experiment in which a volunteer was having the blood suctioned (from other areas of his body) into his legs. The goal of that project—it is research funded by the Department of Defense—is to discover the exact point at which a human being passes out from blood loss. It seems like an esoteric matter of physiology, until you realize it could determine the best use of transfusions on the battlefield.

But back to the subject of redundancy.

"If there was only one thing that controlled all that blood flow, and something went wrong with it, you'd be in big trouble," he says. "So there's tremendous physiological redundancy to the control of breathing, control of blood pressure, control of temperature regulation. That's one of the reasons I've challenged the reductionists. When you say one thing is responsible for everything, you typically run into dead ends. One thing might control ten or twenty percent, but not much more than that. Other systems kick in to help."



A computer charts the O2 and CO2 exchange during a VO2 exercise test.

'CHEEKY HERETIC'

Here's the thing: When it comes to genes, this redundancy principle seems to be holding firm. The search now underway within Precision Medicine for singular genetic variants in switching off diseases has run into an inconvenient truth about the body—dozens or even hundreds of different genes are involved in any given disease or condition.

This complexity is why singular genetic variants have been identified in connection to only a few illnesses, and despite years of searching, why no gene therapies have emerged to “recode” our DNA, as the UMR has invoked in that sign over the Peace Plaza.

It is also why Joyner wrote “Moonshot Medicine Will Let Us Down,” a widely-shared *New York Times* opinion page piece that followed the announcement in 2015 of the president's Precision Medicine initiative.

“Given the general omertà about researchers' criticizing funding initiatives, you probably won't hear too many objections from the research community about President Obama's plan for precision medicine,” as Joyner put it at the time. “But I am deeply skeptical. ... Medical problems and their underlying biology are not linear engineering exercises, and solving them is more than a matter of vision, money, and will. We would be better off directing more resources to understanding what it takes to solve messy problems about how humans behave as individuals and in groups. Ultimately, we almost certainly have more control over how much we exercise, eat, drink, and smoke than we do over our genomes.”

Joyner elaborated on this theme again in October, writing with the influential Stanford University medical evidence critic John Ioannidis for JAMA about “What Happens When Underperforming Big Ideas in Research Become Entrenched.” That article argued that medicine's reluctance to let go of ideas that don't pan out is a drain on open-ended or even failed drug research, work that sometimes does pan out. The antivirals that tamed HIV

were the result of failed cancer research. Viagra was a failed heart pill. “Public funders such as NIH should expand the funding for basic, ‘blue sky’ science for which it is impossible to set, predict, and promise specific deliverables,” as they argued.

Joyner knows this position gives his critics indigestion. He says his well-received talks on the limits of genetic breakthroughs always seem to leave a handful of listeners ready to burn him in the review cards.

“I gave this talk in Dallas where they have six Nobel laureates. Maybe 80-90 percent said ‘This is great,’ and 10-20 percent said ‘This person is a cheeky heretic,’” he says.

After a recent piece in JAMA, Joyner said he received hundreds of supportive emails with “only a couple of them hostile.” More troubling, he says, is the climate of silence within the research community thanks to “all-in” programs like Precision Medicine. He says that a large portion of the emails he receives are from allies in hiding. “They say I agree with you completely, but unfortunately I can't say so because I don't want to commit career suicide,” he says.

Which makes this a good place to return to that talk last fall in the Kahler.

To its credit, Mayo does not burn its heretics at the stake, which is what allows Joyner to remind the room that it has been improvements in training, equipment, and technique that have transformed elite athletics, not the identification of genetic super-heroes (or anything else about the gene revolution).

Michael Phelps, it turns out, has clearly hit the weights a lot harder than Mark Spitz ever did, and has tweaked his turning technique to his advantage as well (he dives deeper in his turns, surfacing last but far ahead of the pack).

Were the 1930s American sprinter Jesse Owens to run with today's faster tracks and spikes, Usain Bolt might only tie him. Kenyans do run farther in general than Americans, but more Kenyan kids run to school every day while more American kids climb into the minivan.

“DNA variants will be useful in helping with selective patients and selected diseases in terms of diagnosis and potentially therapies,” Joyner says about the modest expectations of Precision Medicine that make up his cynicism about the plan. “There's no question about it. But [Precision Medicine] is unlikely to transform human health ... this idea that it's something were going to conquer Type 2 diabetes with, or reduce the incidence of cancer by 70-80 percent, that's probably a little bit wishful thinking.”

This is where Mayo's high profile anesthesiologist hopes we think less about molecular magic, and more about the easy things we can do to fight disease, like quitting smoking, eating better, and getting more exercise. ■