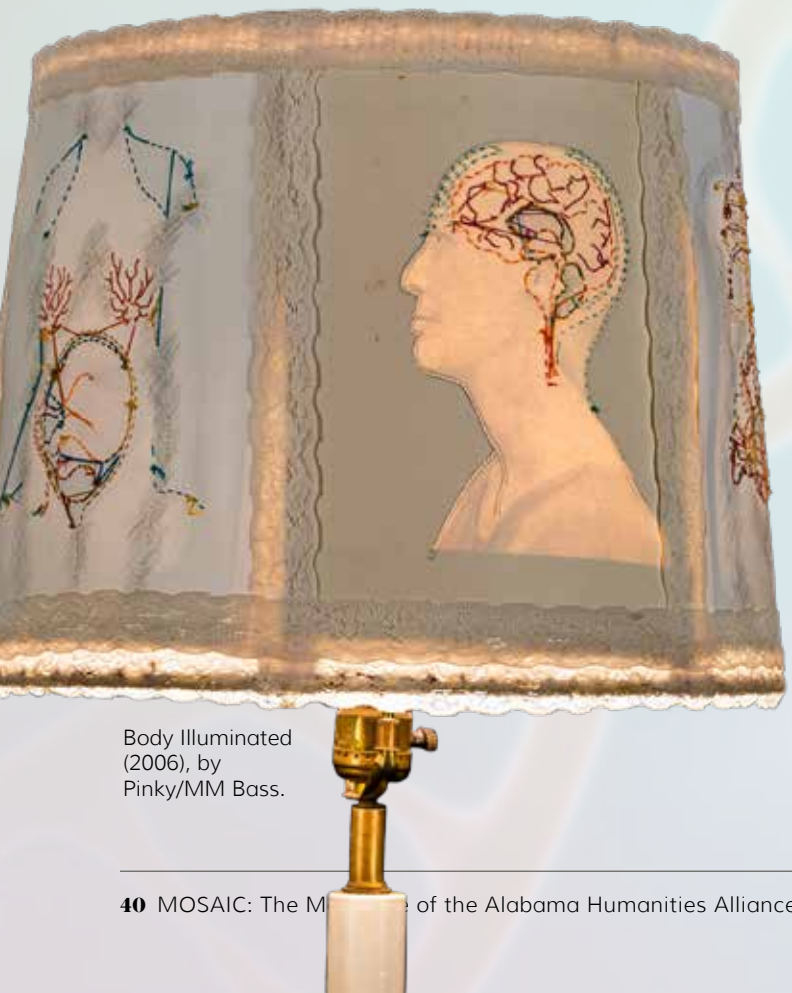
‘Etched into our being’

Geneticist Richard Myers explores what we can learn about ourselves when we study the very elements that make us human

by Richard Myers

The thirst for knowledge about the natural world seems to be a uniquely human trait, perhaps even etched into our being. From ancient times, even in human prehistory, people have explored, sampled, and recorded phenomena on our planet and beyond in attempts to understand cause and effect, not just because it’s interesting, but also because it can help us solve problems. We are especially interested in learning about ourselves, seeking to understand our bodies, brains, physiology, health, disease — as well as our history, culture, values, and our place within nature and the universe. These disciplines are labeled the sciences and the humanities, and they are sometimes, mistakenly, thought of as unrelated, or even antithetical, to each other. However, it doesn’t take much to see that these two ways of knowing are always connected, and, for many of us, deeply intertwined.



Body Illuminated (2006), by Pinky/MM Bass.

I’m one of those people. I am a faculty investigator at the HudsonAlpha Institute for Biotechnology in Huntsville. Here and elsewhere, I’ve spent much of my career studying human genetics, with the aim of understanding how our genes (what we are born with) as well as our environment (what we are exposed to and experience) contribute to who and what we each become. I have particularly sought to understand our brain — how it works, how it is different from all other organisms’ brains, and what goes wrong in neurological and behavioral disorders.

And while I am not a card-carrying practitioner of the humanities, almost all the activities of those disciplines are part of my everyday life, personally and professionally. Like many people, I have long pondered the defining characteristics of our species — our history, what makes us different from other species, and how our human characteristics differ from culture to culture, as well as from person to person. And the scientific research I do every day on finding the links between our genes and our brains is heavily influenced by those endeavors we call the humanities.

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Even though I spent almost half my life elsewhere, I am a son of Alabama who left and then came back. I was born in Selma and spent the first 10 years of my life there. In those early days, I had no burning desire to be a scientist. But, thanks to my parents, I did have a zest for learning. I loved animals and nature, music, art, history, and storytelling. I had the good fortune of living across the street from the inimitable Ms. Kathryn Tucker Windham, who frequently came to my school to tell stories to us enthralled grade schoolers.

But science? The science I was exposed to in the late ’50s and early ’60s was from (mostly) terrible movies that depicted scientists as evil and sometimes demented people bent on harming others or destroying the planet. I started reading science fiction and loved the genre because it imagined fantastic technological possibilities such as space travel and explored the future of

Richard Myers, l-r: Age 3, at home in Selma; postdoctoral researcher, Harvard University, 1984; today, chief scientific officer at HudsonAlpha, Huntsville.

humanity, often in a more positive and optimistic light, which suited me well. Still, none of this sparked even a remote interest in "doing" science. It was really chance that led me into that career.

We moved to Tuscaloosa, and halfway through college there, thanks to two professors who were gifted teachers and researchers, I discovered that, yes, people can get paid to ask questions about how the world works and then design and conduct experiments in attempts to answer those questions. To make sense of the world around and within us. Now, that hooked me. I decided to pursue the training to become a life sciences researcher. On to the University of California, Berkeley, then Harvard, for my advanced training, and then back to the San Francisco Bay Area, where I became a professor and set up my own laboratory to do research in human biology. Scientists were just beginning to identify genes that are involved in human diseases, using tools to sift through the 6 billion DNA letters that make up the 23 pairs of our chromosomes, and I became obsessed with using genetics to figure out what causes brain diseases and how to use this information to do something about them.

In 1990, the field of human genetics received an exponential boost with the birth of the Human Genome Project. This international collaboration, which included my laboratory at Stanford University, spent 13 years and billions of dollars to determine the entire genetic make-up of a human being. We called this puzzle assemblage the "sequence of our genome." By now, three decades later, the genomes of millions of people, plants, animals, and microbes have been sequenced, and our learnings, along with advanced technology, mean this sequencing can now be accomplished more quickly and much more cheaply.

Most importantly, this work has already begun to revolutionize medicine, as well as agriculture, environmental science, our understanding of our ancestry, evolutionary biology, our response to toxins and other features of the environment, infectious diseases, forensics — practically every dimension of human experience.

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Here are some examples of what we can learn from this revolution.

A few years into the Human Genome Project, my laboratory identified a gene that causes a severe type of progressive epilepsy in children when they inherit a specific DNA spelling mistake — a mutation — from both parents. Because the symptoms are not easily distinguished from other forms of epilepsy, neurologists had been treating these children with a widely used drug that is effective for most people who have seizures. However, for this particular form of epilepsy, that drug is very harmful. As soon as we found the gene, clinics started testing for mutations in this gene in children with epilepsy and using a different drug that doesn't cause harm.

A more recent and incredibly exciting example is work led by Dr. Greg Cooper here at HudsonAlpha. His group, working together with teams throughout the Institute,

has studied thousands of people, mostly children, who have unexplained neurological and other diseases. By determining the entire genetic make-up of these individuals, Greg's group has been able to identify the genetic causes in more than a third of those tested, providing extremely valuable information for the patients and their families and healthcare providers, often leading to treatments, relief, and improvement in the lives of severely affected individuals.

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And it's not just discoveries about health and disease we're turning up with this research. We're also directly learning about humanity and our place on earth. By comparing the genome sequences of multiple people, we now know that humans are incredibly similar genetically. Our DNA is 99.9% identical, regardless of where in the world you and your ancestors are from. The vast majority of the DNA differences between people appear not to have any obvious consequence, and those DNA differences that do result in different traits (like disease, resistance to infection, and skin color, to name a few) are typically found in all of the world's populations. It is striking that a smattering of only a few genetic differences appear to be specific to particular ethnicities, and these are typically superficial. To me, this is profound. We really are "the family of humankind," and I believe that embracing our similarities, along with our differences, makes the world a better place.

There is a deeply human element to the process of performing such research, too. When we talk about genetics, we are delving into the essence of our humanity, learning about the health, families, and histories of individuals and groups of people. This demands an intense level of responsibility to respect and protect the participants in such research, as well as the applications of the knowledge we learn from it. Enter the humanities again. Since the onset of the Human Genome Project, the scientific community has conducted a large amount of research into the ethical, social, and legal impacts of learning so much about our genetics. Genetic privacy, informed consent, legal protections, community engagement, cultural diversity, and other aspects of bioethics are important considerations of every study.

Learning about our genomes has also greatly helped us understand our history — where we all come from. It's no accident, of course, that genealogy and genetics share an opening syllable. If you've ever spit into the tube of a home DNA test kit then you, too, have blended the sciences and humanities to learn more about your past. But that's just the tip of the iceberg.

Archeology, anthropology, and linguistics have identified artifacts, as well as origins, of languages and human culture. Genetic studies of living and ancient humans — and our evolutionary relatives — add greatly to this type of knowledge, providing unequivocal support of our collective origins in East Africa and the migrations that subsequently populated the globe. And comparing our genomes with those of other organisms underscores what makes us distinctly human. Just considering our remarkable brains, it is striking that no other organism — including our closest living relative, the chimpanzee — has any semblance of humans' capacity for mathematics, complex language, music, art, philosophy, or for pondering our place in the universe.

In addition, the combination of genetics and behavioral sciences has taught us that, in many cases, organisms that interact and are dependent on one another have co-evolved to benefit both species. In other words, we need each other on this earth. My favorite example is our best friend, the dog. In the last 15,000 to 30,000

years, it appears that we humans began to domesticate gray wolves that hung around our campsites, leading, over many generations, to the mutual benefits of protection for us and food for them. And look at us now! Dogs are usually considered close family members, and I am convinced that they can read us better than we can read each other. This almost certainly was influenced by genetic selection in both species, as well as by our remarkable brains — our ability to think, plan, and anticipate the consequences of our actions (or maybe it was the dogs' plan all along!). In any case, dogs are also part of what makes us human.

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When I joined the Human Genome Project in 1990 — tasked with helping to determine the first entire genetic makeup of a human being — the undertaking seemed so monumental that I mostly put my head down and focused on improving and applying the technology and organizing the teamwork needed to get the job done. But within a few years, it struck me that this work and its many applications were going to change the world profoundly. Identifying genes that cause disease became much faster and easier, and improved so much that what was a trickle of discoveries before is now a downpour.

Medically, I personally benefited from these advances by learning that variations in two of my genes make me have an unfavorable response to two classes of drugs, so my doctor changed my prescriptions based on this knowledge. As a human being, I have also learned to be much bolder in my imagination, to never say never, and to expect many more "aha" moments in my lifetime.

I see a not-too-distant future where much human suffering will be diminished by new treatments for diseases, where we will gain a deeper understanding of what makes us uniquely human, and where we will make even more advances in sustainable agriculture and our stewardship of our planet. For that to come to fruition, of course, requires the best that both the sciences and humanities offer. It also requires our collective commitment to keep asking questions, to keep learning, and to remember that humanity's future, whatever it may be, is a destination we'll all share together.

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