

MEDICINE

From Race to DNA

Thinking about patients as ongoing products of evolution **BY SALLY LEHRMAN**

Even as biomedical researchers generate and dig through mountains of gene sequence data, physicians proceed in the clinic as they always have. They design preventive care, plan treatments and select drugs by assessing patient type—frequently with race and ethnicity central. Molecular biologists often look to these categories, too, as a means to sort out the ways in which gene variants influence patient response to drugs and disease. And if they get federal funding, investigators must divide the groups they study by race.

Now evolutionary biologists are leading a shift in perspective. Lumping people by the social categories of race, they argue, can hide patterns of biological variation

and lead to misinterpretation. And although ancestral population groups may be important, more comprehensive evolutionary thinking would help doctors and researchers predict patient response, design studies and interpret the associations seen between genes and disease susceptibility. Race isn't meaningless, says Lynn Jorde, an evolutionary geneticist at the University of Utah, but "those categories are only marginally useful."

Evolutionary medicine has long served to explain how some genes can be harmful in one context but beneficial in another. In one iconic example, having two copies of a mutated hemoglobin gene causes sickle-cell anemia, but having one copy protects

against malaria. Now the field aims to offer insight that might lead to a true "personalized" medicine—one that takes into account not just population history but also the dynamic of human variation, environment and selection pressures that acts on each individual today.

Genetics researchers have begun to move in this direction by replacing "race" with "ancestry." As early humans spread out from Africa, some variation arose in human DNA that remains today. By sampling enough groups from enough locations, investigators hope to identify adaptive changes that might differ by ancestral location and be important to health.

Even that approach, however, might



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oversimplify human variation and whatever functional meaning it has. Many population studies divide the world into three primary ancestral groups—usually sub-Saharan African, East Asian and European—roughly representing migrations out of Africa. But these categories not only can be hard to distinguish from “race,” they also ignore the overlap between groups and the continuous nature of the way people and genes spread today. “What we see is this wonderful, intertwined history,” Jorde remarks.

Evolutionary theory would predict that most genetic variants important to health are common, ancient and thus shared, whereas some rare variants may be quite population-specific. Even so, more recent “microevolution” caused by mutations, selection and genetic drift in each generation continues to shape our genes beyond the template set by ancient migrations. One example comes from Steven J. Mack of the Children’s Hospital & Research Center Oakland in California, who explores HLA, a cell-surface molecule that plays a role in self-non-self recognition and several kinds of disease. Mack and his collaborators studied 20 populations and found that the greatest diversity in the frequency of gene variants lay outside Africa. Surprisingly, populations in Africa, Europe and Southwest Asia looked simi-

lar to one another in terms of frequency of common polymorphisms; Oceania and the indigenous Americas had much more variation. Fresh diversification arose, Mack theorizes, as these smaller, isolated populations confronted new pathogens.

Diddahally Govindaraju, director of the Framingham Heart Study Genetics Laboratory in Boston, says a simple equation that attempts to trace high disease risk to susceptibility genes in a population grouped by ancestry will often fail. Without evolution as a framework, he contends, “the questions are off, the interpretations are off.” Gene action must be understood in the context of adaptive and sometimes haphazard trade-offs as well as developmental stages, the history of human colonization and the pace of environmental change.

Population movement indeed seems to have accelerated changes in human DNA.



PATIENT CHANGES: To get beyond race, a new movement wants physicians to see patients as products of evolution.

A study in the *Proceedings of the National Academy of Sciences USA* found that genes have changed more in the past few thousand years than in the past few million because of altered living conditions. Govindaraju emphasizes that this change is ongoing and does not limit itself to historical populations. A gene that powerfully influences someone’s asthma in India, say, might be irrelevant when that person is living in the U.S. “A population is only a population,” he explains, “in that environment.”

Govindaraju has helped convene a working group funded by the National Evolutionary Synthesis Center in Durham, N.C., that brings together specialists from evolutionary biology, human genetics, anthropology, public health and medicine. The team will start by analyzing data collected in the Framingham Heart Study to document microevolutionary changes over three generations.

Typing people by race or even ancestry, Govindaraju adds, locks clinicians into a static understanding of genes and health. Instead he hopes they will begin to see an individual and the network of genes within the body as an integrated product of family, generation, location and history—and as an organism that is still evolving.

Sally Lehrman is based in the San Francisco Bay Area.

PAUL SAKUMA/AP Photo

DEFENSE

Proactive Prototypes

For new tech systems, a return to competitive prototyping **BY DANIEL G. DUPONT**

Last March a group of Alabama lawmakers met with the Pentagon’s top acquisition official to discuss a new program, the Joint Air-to-Ground Missile (JAGM). The lawmakers—looking out for the city of Huntsville, a legendary missile development hub—wanted to know what came next. The official told them the usual pro-

cess was at work: the military would run a competition for JAGM and pick one contractor to develop it.

A few months later, though, those same lawmakers demanded to know why the usual process would no longer be followed—they had just learned a new plan called for the Pentagon to pick at least two

teams to compete against each other, and they weren’t happy about it.

What had happened was that a new sheriff had come to town—or rather a new top acquisition official, John Young. Last September, Young issued a policy that went beyond competitive bidding and resurrected an old idea: competitive proto-