

Carl was not a geneticist by training or at heart, and although cognizant of horizontal gene transfer, saw it as a creative force at the beginning of cellular evolution (the 'progenote' stage), not as a challenge to defining the 'true' relationships between living things now. Most of the phylogenetic community still holds Carl's belief as foundational. Nor was he, as Mayr complained, a card-carrying taxonomist. So he was free to invent simple intuitive treeing methods that sidestepped the cladist wars already raging at the time he started to present his startling results. Still today at big evolution meetings it is almost as if the rRNA phylogeneticists working on microbes and those who study the evolution of organisms one can see are different tribes, though some now can bridge the gap.

Carl was styled by the *Science* writer Virginia Morell [4] as "microbiology's scarred revolutionary", and the heroic story around his struggle has been told many times over, indeed now has engaged a professional historian of science as well as his colleagues. But extraordinary claims rightly demand extraordinary proofs, and Carl did in the fullness of time win many prizes — the Swedish Academy's Crafoord Prize (the real biologist's equivalent of the Nobel), a MacArthur Foundation Fellowship, the Waksman Award of the US National Academy of Sciences, the National Medal of Science, and the Leeuwenhoek Medal. And he is survived by his army, a legion of researchers owing allegiance not just to his methods but to the intellectual framework he almost singlehandedly imposed on the microbial world. None of us could hope for more.

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Department of Biochemistry and Molecular Biology, Dalhousie University, Halifax, Nova Scotia B3H 1X5, Canada.
E-mail: ford@dal.ca

Quick guides

Human races

Guido Barbujani¹
and Massimo Pigliucci²

What is a race? Ernst Mayr (1904–2005) distinguishes between species in which biological change is continuous in space, and species in which groups of populations with different character combinations are separated by borders. In the latter species, the entities separated by borders are geographic races or subspecies. Many anthropology textbooks describe human races as discrete (or nearly discrete) clusters of individuals, geographically localized, each of which shares a set of ancestors, and hence can be distinguished from other races by their common gene pool or by different alleles fixed in each.

Isn't that concept elusive?

Somewhat. Ever since Lamarck and Darwin, species are no longer regarded as fixed entities; in time, some of them split and evolve into different species. Accordingly, races are often conceptualized as populations of the same species on their way to speciation, but not quite there yet, a rather difficult category to place individuals in. Also, whether geographic variation is continuous or discontinuous may not be obvious. That said, philosophers of science recognize that concepts without sharp boundaries may still be useful in everyday as much as in scientific practice.

So, maybe the concept is elusive in principle, but it works in practice?

Yes, in some species, such as some snails or the gorilla, not to mention a number of plant species. Conversely, highly mobile species, including many birds and marine fishes, do not tend to show geographic clusters of individuals which can be distinguished morphologically or genetically.

What about humans, then? As you may have guessed, opinions differ among experts. Some believe not only that humans are subdivided in biological races, but also that inherited differences between races

result in a range of different abilities (including cognitive abilities). By contrast, others regard human races as entirely cultural constructs unrelated with biological diversity. There are intermediate possibilities too.

Why then is the concept of race so widespread? The idea that races are a natural feature of human diversity has long been the standard for anthropological research. However, scientists trying to list the human races never reached an agreement, and catalogs proposed since the 18th century contain anything between 2 and 200 races. In time, this led to questioning the meaningfulness of racial classification, so that in 1963 Frank Livingstone (1928–2005) wrote: "There are no races, there are only clines" (i.e., geographical gradients). Others disagreed. While stating that universal human rights do not derive from our being identical, but from being all humans, Theodosius Dobzhansky (1900–1975) admitted that human races are poorly defined, but maintained that they exist and predicted they would be better described in the future. The good news is that now Dobzhansky's future has arrived.

So, what do we know now? With a population size exceeding seven billion, humans would be expected to display a large amount of genetic variation. This is not the case, however, suggesting that population sizes were small throughout much of human history. Genetic diversity is highest in Africa and decreases as one moves away from there, probably reflecting repeated founder effects that occurred as anatomically modern humans dispersed into other continents. As a result, most human alleles have a cosmopolitan distribution, that is, they are present in all continents, at different frequencies. Combinations of alleles along the same chromosome, or haplotypes, have a clearer geographical distribution, but still only a minority of them is continent-specific. Some regions of the genome show evidence of local adaptation. Studies of ancient DNA suggest that perhaps there may have also been limited admixture with archaic humans, such as Neanderthals.



Figure 1. The 'folk' concept of races.

While concepts of human races seem all too familiar, here a six-year old offers yet another view, in which biological and cultural differences lead to a very personal description of human diversity. Drawing: Rakel Stensmyr.

What does this imply for the existence of human races? Basically, that people with similar genetic features can be found in distant places, and that each local population contains a vast array of genotypes. Among the first genomes completely typed were those of James Watson and Craig Venter, two U.S. geneticists of European origin; they share more alleles with Seong-Jin Kim, a Korean scientist (1,824,482 and 1,736,340, respectively) than with each other (1,715,851). This does not mean that two random Europeans are expected to be genetically closer to Koreans than to each other, but certainly highlights the coarseness of racial categorizations. On average, nearby populations tend to resemble each other more than distant ones, but individual members of the same population, Watson and Venter in this case, can be very different. In short, if races are defined as subspecies, there is no such thing in humans. The best way to know what is in a person's DNA is to study that person's DNA.

So, my dog has a race and I don't? Human populations are also less diversified than dog or horse breeds, but the comparison is misleading, because stocks in these species were selected by human breeding programs.

Are we all equal, then? No, we all differ genetically from one another, with the exception of identical twins. Tens of millions of the 3 billion nucleotides of our (haploid) genome have been shown to vary, and this

number is increasing, as more and more genomes are being typed. Still, in comparison with other primates, we are very homogeneous, with two random members of our species differing, on average, in 1 nucleotide out of 1,000.

But isn't it possible to classify people just based on their skin color? Hardly. With at least 70 genes involved, skin color is a complex trait and a poor indicator of shared ancestry. Because pigmentation evolved under selective pressure, people of sub-Saharan Africa, Southern India, Australia and Melanesia have all dark skins, despite these populations occurring in distant branches of evolutionary trees based on genetic distances.

What about 'folk' or 'common' concepts of race? The level of disagreement is the same as in scientific studies. In U.S. census forms, for instance, the number of races changed almost every decade (12 in 1960, 6 in 2000, 15 in 2010), and people from different cultures classify people in different ways. Just as an example, in apartheid South Africa, Japanese were regarded as white and Chinese as colored, even though both populations include people with light and rather dark skin.

Can we not just say that races are populations between which there are genetic differences? This definition has actually been proposed, but it has a disadvantage. Any two human populations differ

genetically to some extent, and so each of them would be labeled as a race, in contrast with current taxonomic practice. But there is more; any pair of human groups, even when defined socially (say, dentists vs. plumbers), or arbitrarily (say, those who wore black shoes vs. those who wore shoes of other colors on June 8th, 2010) will differ in the average of many biological properties, say body weight, speed in running, ability to digest milk or sensitivity to bitter flavors. However, this does not mean that a person's weight or ability to digest milk has anything to do with that person choosing plumbing or dentistry. The crucial question is not whether we are identical (we are not) but whether humans are like cell phones, which can be Nokia, Samsung or Motorola, but hardly anything in between, in which case the different human brands could legitimately be called races. The answer is no.

Isn't all this a problem of terminology and good manners, rather than a scientific one? No, assuming that humans come in neat racial packages leads to poor scientific inference. Consider pharmacogenomics: genetic differences determine individual tendencies to metabolize various classes of drugs rapidly, normally or slowly. This often results in slow metabolizers suffering from side effects due to the prolonged interaction between the drug and its biological target, and in fast metabolizers having little or no benefit from treatment. Huge amounts of money have been invested to develop drug dosages specific for, say, the Chinese or the Swedish market. However, here, market really means race; these projects might have worked only if most Chinese had the same metabolizing phenotype, and most Swedes a different phenotype. On the contrary, it has been shown that Chinese and Swedes differ in their average metabolizing rate for debrisoquine and codeine, but both populations comprise the full range of fast, normal, and slow metabolizers. Racial pharmacology appears to be a blind scientific alley, whereas in time we may be able to develop personalized pharmaceutical treatment.

Is it wrong if I use the word race?

Under freedom of speech, anybody is free to use any words. Even if they do not correspond to scientifically identifiable entities, races are a component of our psychological and social world (Figure 1), and as such their importance should not be dismissed. But mutual understanding requires some agreement between speakers and receivers, and so it is better to avoid terms of ambiguous or unclear meaning, especially in science.

Where can I find out more?

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¹Department of Life Sciences and Biotechnology, University of Ferrara, Via Borsari 46, 44121 Ferrara, Italy. ²Philosophy Program, The Graduate Center, City University of New York, 365 Fifth Avenue, New York NY 10036, USA.

*E-mail: g.barbujani@unife.it

Aspergillus

Antonis Rokas

What is Aspergillus? *Aspergillus* is a widely distributed genus of more than 250 species of largely saprophytic filamentous fungi belonging to the phylum Ascomycota. Originally described in 1729 by the botanist and priest Antonio Micheli, the genus got its name from the resemblance of its asexual spore-forming structure to the aspergillum, an instrument for sprinkling holy water, although some modern taxonomists profess that it more closely resembles a toilet bowl brush (Figure 1). To the dismay of amateur and professional systematists alike, *Aspergillus* species are morphologically very similar and hard to distinguish; however, their genomic diversity is on par with that of our own phylum, the Vertebrates.

How does Aspergillus reproduce?

It's complicated! The *Aspergillus* life cycle comprises asexual, parasexual, and sexual stages. Upon germination, haploid asexual spores grow into branched filaments or hyphae of interconnected cells, thus forming a web known as the mycelium. As the mycelium expands, hyphae from the same or from different spores intersect and occasionally fuse, a decision governed by a network of genes based on whether the hyphae are part of the same self or not. The onset of fusion marks the beginning of the parasexual stage — the haploid nuclei of the two mother hyphae will now be part of the same cell, continuing to divide mitotically and experience crossing over events between homologous chromosomes, until random chromosome loss eventually restores the haploid chromosome number. Alternatively, *Aspergillus* hyphae can enter the sexual stage. The specifics of entry to the sexual stage, which are determined by two mating types, differ between species that are obligate outcrossers (also known as heterothallic; individuals possess only one of the two mating types and can only mate with individuals of the opposite type) and species that also are capable of self-fertilization (homothallic; possess both mating types). Generally, the process begins with multiple divisions of a cell that contains two nuclei derived either from the same organism (in homothallic species) or

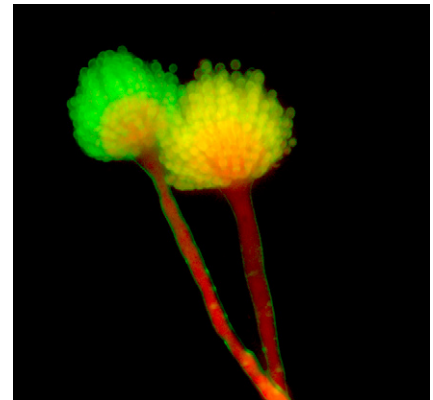


Figure 1. *Aspergillus*.

Two asexual fruiting bodies of the filamentous fungus *Aspergillus oryzae* after 3 days of growth on potato dextrose agar stained with Vybrant-DiO and Lysotracker Red dyes. The round cells at the tips are the asexual spores of the fungus (courtesy of Jonas King and John G. Gibbons).

from different ones (in homothallic and heterothallic species). These divisions eventually give rise to the ascus, the sexual spore-forming structure, in which the two nuclei in each cell fuse to form a diploid cell that undergoes meiosis and produces haploid ascospores. Although most *Aspergillus* species lack a known sexual stage, its recent discovery in a few species, coupled with the presence of intact mating and meiosis-related genes in several additional ones, suggest that many asexual species have cryptic sexual stages yet to be discovered.

What have we discovered from studying Aspergillus in the lab?

Research on *Aspergillus* has greatly contributed to our understanding of eukaryotic primary and secondary (or specialized) metabolism, the control of gene regulation by external environmental factors, the cell cycle, and fungal asexual and sexual development. The birth of *Aspergillus* as a model system dates back to Guido Pontecorvo's pioneering genetic work in the early 1950s on the nature of the gene, whose experiments laid the foundation of the concept of the gene as a unit of function rather than as one of mutation or recombination. One of the most beautiful recent examples of the importance and great value of *Aspergillus* concerns the identification of the genetic basis of the gene responsible for the human metabolic disease alkaptonuria — one of Garrod's classic "inborn errors of metabolism" — which results from