way, and applying the findings will be central to the success of DTC genome tests and credibility of the field[20].

Carry out prospective studies. Agreement on risk predictions by DTC companies does not necessarily imply that the predictions are accurate or meaningful, and at this point in time, we cannot determine who has the 'best' predictions. To effectively assess the clinical validity of these genetic tests the community needs more prospective studies with tens or hundreds of thousands of individuals that measure the predictive value of known markers[21–23]. Such studies are useful because they consider risk markers simultaneously, measure the interaction between different markers and do not assume a risk model. It may be practical to prioritize common diseases with significant health impact because of the large numbers of individuals and the expense associated with prospective studies.

Replicate associated markers in other ethnicities. Genome-wide association studies have been conducted primarily on populations with European ancestry[1]. Disease-associated markers may not transfer from one population to another — allele frequencies or linkage disequilibrium patterns may differ[1,24]. Therefore, we strongly recommend the validation of these markers and the surrounding pattern of genetic variation in other ethnicities.

Sequence rather than genotype. Eventually, sequencing an individual's genome will become economically feasible. Sequencing has an advantage over genotyping because it captures the full spectrum of an individual's variation and determines, rather than infers, a higher resolution of variants. However, identification of variants should not be confused with their interpretation, and pinpointing the causative disease variant will still be challenging[25]. Our ability to identify variants from comprehensive sequence data will far outstrip our ability to characterize their biological effect. However, accurate and complete reporting is a necessary predecessor to a precise functional understanding of genomic data for the consumer. ■

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See Editorial page 697, and online at http://go.nature.com/VqPUE2.

Let's celebrate human genetic diversity

Science is finding evidence of genetic diversity among groups of people as well as among individuals. This discovery should be embraced, not feared, say **Bruce T. Lahn** and **Lanny Ebenstein**.

A growing body of data is revealing the nature of human genetic diversity at increasingly finer resolution[1,2]. It is now recognized that despite the high degree of genetic similarities that bind humanity together as a species, considerable diversity exists at both individual and group levels (see box, page 728). The biological significance of these variations remains to be explored fully. But enough evidence has come to the fore to warrant the question: what if scientific data ultimately demonstrate that genetically based biological variation exists at non-trivial levels not only among individuals but also among groups? In our view, the scientific community and society at large are ill-prepared for such a possibility. We need a moral response to this question that is robust irrespective of what research uncovers about human diversity. Here, we argue for the moral position that genetic diversity, from within or among groups, should be embraced and celebrated as one of humanity's chief assets.

The current moral position is a sort of 'biological egalitarianism'. This dominant position emerged in recent decades largely to correct grave historical injustices, including genocide, that were committed with the support of pseudoscientific understandings of group diversity. The racial-hygiene theory promoted by German geneticists Fritz Lenz, Eugene Fischer and others during the Nazi era is one notorious example of such pseudoscience. Biological egalitarianism is the view that no or almost no meaningful genetically based biological differences exist among human groups, with the exception of a few superficial traits such as skin colour[3]. Proponents of this view seem to hope that, by promoting biological sameness, discrimination against groups or individuals will become groundless.

We believe that this position, although well-intentioned, is illogical and even dangerous, as it implies that if significant group diversity were established, discrimination might thereby be justified. We reject this position. Equality of opportunity and respect for human dignity should be humankind's common aspirations, notwithstanding human differences no matter how big or small. We also think that biological egalitarianism may not remain viable in light of the growing body of empirical data (see box).

ATLANTIDE PHOTOTRAVEL/CORBIS

Will we soon cherish genetic diversity as we now do cultural diversity?

Many people may acknowledge the possibility of genetic diversity at the group level, but see it as a threat to social cohesion. Some scholars have even called for a halt to research into the topic or sensitive aspects of it, because of potential misuse of the information[4]. Others will ask: if information on group diversity can be misused, why not just focus on individual differences and ignore any group variation?

We strongly affirm that society must guard vigilantly against any misuse of genetic information, but we also believe that the best defence is to take a positive attitude towards diversity, including that at the group level. We argue for our position from two perspectives: first, that the understanding of group diversity can benefit research and medicine, and second, that human genetic diversity as a whole, including group diversity, greatly enriches our species.

For scientists to understand human genetic diversity in its totality, group diversity cannot be shunned. It is an integral and meaningful component of overall human diversity. For example, the International HapMap Project, which examines genetic diversity in several hundred individuals, has revealed clear genetic differentiation among the geographic groups represented by those individuals. More importantly, studies increasingly indicate that understanding genetic diversity at the group level can shed light on human evolution, the nature and acquisition of many human traits, including disease conditions, and how genetic and environmental factors interact to produce biological outcomes[1,2,5,6]. Thus, to ignore group diversity is to do poor science.

Neither can many medical applications of genetics safely ignore group diversity. It can facilitate the mapping of disease genes and lead to improved treatments[7,8]. For instance, groups can differ markedly in their ability to metabolize certain anticancer drugs[8]. Examining the potential genetic contributions to these differences may illuminate how genes regulate drug metabolism and allow for more effective treatment. The ultimate goal of medical intervention may be personalized medicine (see page 724), whereby treatment is tailored to the genetic make-up of each individual, but this will remain a distant ideal for years to come. For now, to intentionally overlook the influence of group diversity on disease susceptibilities and treatment outcomes is to practise poor medicine.

In addition to the above arguments, there is a much larger reason to embrace human diversity in all its forms, in our view. Humanity's genetic diversity — small or large, within or among groups — is a resource for, rather than a detriment to, creating a more fulfilling and prosperous society. Just as people have come over time to cherish cultural diversity, so we hope that attitudes will warm towards genetic diversity.

In the natural world, genetic diversity is a source of evolutionary resilience and adaptability. It buffers against changing environments and allows species to occupy broader and more fluid ecological niches. Even for a single individual, differences between its two copies of the genome can often lead to higher fitness. Indeed, sexual reproduction is thought to have evolved as a way for species to take advantage of genetic diversity. Consequently, the loss of a species' diversity often threatens its long-term survival. The susceptibility of agro-monoculture to sudden disease outbreaks or climate changes is just one example.

In humans, genetic diversity may be particularly beneficial at a social or cultural level. Humans are uniquely complex in the social structures they form. Although genetic diversity may not be a prerequisite for social complexity, the former can foster the latter by allowing individuals with different tastes and abilities to make professional and personal choices that they enjoy and in which they are productive, thereby leading to personal fulfilment and contributing to a more prosperous society. Arguably, the United States is one of the most innovative, successful and culturally vibrant countries in the world. It excels in numerous and wide-ranging areas, such as art, sport, business, science and political and economic thought. We believe that this is due in part to the nation's diversity, both cultural and genetic, and to a liberal environment that allows individuals to pursue their unique and varied potentials.

Group differentiation, by furthering this

SUMMARY

- Promoting biological sameness in humans is illogical, even dangerous
- To ignore the possibility of group diversity is to do poor science and poor medicine
- A robust moral position is one that embraces this diversity as among humanity's great assets

diversity, adds to the total depth and breadth of human potential. In our view, the 2008 Olympic Games was a beautiful showcase of human diversity. Diversity at the individual level was evident from the wide-ranging physical attributes associated with different sports. Often athletes from different geographic areas also seem to excel at certain sports. Many of these differences may of course be explained by cultural and environmental influences, but should genetic variation contribute in any way to regional athletic ability, it would be hard not to see group diversity as a great asset of our species.

Discussions of human genetic diversity inevitably touch on many sensitive issues. We therefore provide the following caveats to minimize misinterpretations of our position. First, the recognition that genetic diversity can contribute to variation in biological traits by no means diminishes the role of the environment in influencing many of these traits. Arguments for improving the well-being of individuals and groups through environmental approaches such as better nutrition, education, career opportunities and medical treatment lose none of their strength when embracing genetic diversity. Second, acknowledging differentiation among groups does not reduce the importance of diversity within groups, in which most human diversity seems to lie. Third, although we firmly believe that diversity is beneficial overall, we acknowledge that it might not always be so. For example, genetic diversity can lead to higher disease susceptibilities in some individuals or groups. We nevertheless believe that any downside of genetic diversity, including at the group level, does not detract from its overall benefit to our species.

It is also important to recognize that humanity is diverse in its diversity — which is to say that genetic diversity contributes to variation across numerous physical, physiological and cognitive domains. How individuals or groups fare in one domain can be largely independent of how they fare in others. For example, although IQ is a useful metric of some aspects of intelligence and it is partly heritable, it is far from a complete measure of total mental capacity. Therefore, acceptance of human genetic diversity in its totality necessarily leads to the rejection of unidimensional rankings of the capacity of human individuals or groups. If anything, the study of genetics is taking us towards an ever greater appreciation of the multidimensional nature of human potential.

"Geographic group identify can be assigned on DNA alone."

Genetic diversity is a strength not a weakness of humanity. It is time to acknowledge, embrace and celebrate this strength. There is nothing scientifically improbable or morally reprehensible in the position that people, including groups of people, can be genetically diverse. Those who deny or even condemn human diversity adopt a stance that is both factually doubtful and morally precarious. On the whole, humanity has been and will be stronger, not despite our differences, but because of them. ■

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Emerging understanding of human genetic diversity

Genetic diversity is the differences in DNA sequence among members of a species. It is present in all species owing to the interplay of mutation, genetic drift, selection and population structure. When a species is reproductively isolated into multiple groups by geography or other means, the groups differentiate over time in their average genetic make-up.

Anatomically modern humans first appeared in eastern Africa about 200,000 years ago. Some members migrated out of Africa by 50,000 years ago to populate Asia, Australia, Europe and eventually the Americas[9]. During this period, geographic barriers separated humanity into several major groups, largely along continental lines, which greatly reduced gene flow among them. Geographic and cultural barriers also existed within major groups, although to lesser degrees.

This history of human demography, along with selection, has resulted in complex patterns of genetic diversity. The basic unit of this diversity is polymorphisms — specific sites in the genome that exist in multiple variant forms (or alleles). Many polymorphisms involve just one or a few nucleotides, but some may involve large segments of genetic material[2]. The presence of polymorphisms leads to genetic diversity at the individual level such that no two people's DNA is the same, except identical twins. The alleles of some polymorphisms are also found in significantly different frequencies among geographic groups[1,5]. An extreme example is the pigmentation gene *SLC24A5*. An allele of *SLC24A5* that contributes to light pigmentation is present in almost all Europeans but is nearly absent in east Asians and Africans[10].

Given these geographically differentiated polymorphisms, it is possible to group humans on the basis of their genetic make-up. Such grouping largely confirms historical separation of global populations by geography[5]. Indeed, a person's major geographic group identity can be assigned with near certainty on the basis of his or her DNA alone (now an accepted practice in forensics). There is growing evidence that some of the geographically differentiated polymorphisms are functional, meaning that they can lead to different biological outcomes (just how many is the subject of ongoing research). These polymorphisms can affect traits such as pigmentation, dietary adaptation and pathogen resistance (where evidence is rather convincing)[10–12], and metabolism, physical development and brain biology (where evidence is more preliminary)[6,8,13,14].

For most biological traits, genetically based differentiation among groups is probably negligible compared with the variation within the group. For other traits, such as pigmentation and lactose intolerance, differences among groups are so substantial that the trait displays an inter-group difference that is non-trivial compared with the variance within groups, and the extreme end of a trait may be significantly over-represented in a group.

Several studies have shown that many genes in the human genome may have undergone recent episodes of positive selection — that is, selection for advantageous biological traits[6]. This is contrary to the position advocated by some scholars that humans effectively stopped evolving 50,000–40,000 years ago[15]. In general, positive selection can increase the prevalence of functional polymorphisms and create geographic differentiation of allele frequencies. **B.T.L. & L.E.**