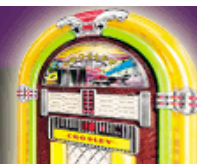


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LETTERS

Examining Priorities for a Primate Genome Project

We agree with the premise of Edwin H. McConkey, Agit Varki, and cosignatories that "[a] primate genome project deserves high priority" in the U.S. biomedical research enterprise (Letters, 25 Aug., p. 1295), but we disagree with their selection of the chimpanzee as the focus for these efforts, and with the recommendation to commit resources to genome sequencing at this time.

The choice of which primate to select for this \$100 million project should be driven by the goals of the National Institutes of Health's (NIH) mission to promote human health through research. Although chimpanzees have been vital for many advances in biomedical research and continue to serve critical research needs, they are not a commonly used model. With fewer than 1000 federally supported chimpanzees in U.S. research colonies and a moratorium on breeding, the chimpanzee is unlikely to become a widely used animal model. Because it is not practical to use chimpanzees for most research purposes, a focus on chimpanzee genomics would have little impact on future opportunities and progress in biomedical research.

The initial plan to sequence the human genome was deferred until a detailed gene map was constructed, and we contend that constructing gene maps of nonhuman primates deserves priority over sequencing, for the same scientific and cost-benefit reasons. Furthermore, the resources should be devoted to those species that are most widely used as primate models for genetic research on human diseases and for which extensive physiological data are available--namely, baboons and rhesus macaques.

Another high priority for a primate genome project would be research on gene expression. To the extent that this research is supported by the NIH, the driving force behind it should be to develop a better understanding of biological mechanisms that differentiate healthy from disease states. In that regard, those nonhuman primate species that are used extensively as models in biomedical research offer many more opportunities for scientific advancement through gene expression studies than do chimpanzees.

Regarding the goal of defining the genetic changes that underlie human uniqueness, it is not only peripheral to the NIH mission but also is not well served by a sequencing-first approach. Most sequence differences between humans and chimpanzees will be functionally neutral, and simple comparison of sequences will not identify the few functional changes among the large number of neutral substitutions.

We urge the National Human Genome Research Institute (NHGRI) and the National Center for Research Resources to consider carefully the scientific value of sequencing the chimpanzee genome by comparison with investing equal resources in supporting gene expression research and developing detailed gene maps of nonhuman primates that are extensively used in biomedical research. The potential health benefits of these research activities in well-characterized, widely-used Old World monkey models will be much greater than those obtained from sequencing the chimpanzee genome.

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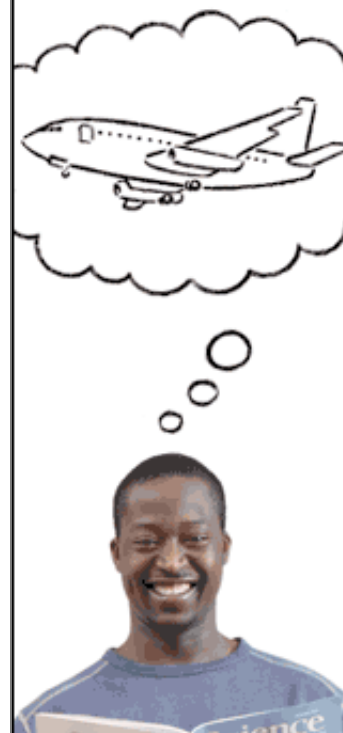
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Response

In our original letter we presented the arguments in favor of a primate genome project and suggested that the project should focus both on the chimpanzee, because it is our closest evolutionary relative, and on one of the well-studied Old World monkeys, which would be more suitable for experimental purposes and for studies of gene expression. Thus, we have a substantial area of agreement with VandeBerg and colleagues. However, we disagree with their statement that "a focus on chimpanzee genomics would have little impact on future opportunities and progress in biomedical research." The potential relevance of chimpanzee genome data for understanding such diseases as AIDS, Alzheimer's, malaria, and others has been presented elsewhere ([1](#)).

VandeBerg and colleagues also say that "the goal of defining the genetic changes that underlie human uniqueness [is] peripheral to the NIH mission." This implies that the genes involved in human uniqueness are never involved with human disease, a highly unlikely assumption. For example, genes that underlie bipedal locomotion may be involved in many malfunctions of the musculoskeletal system, and genes that mediate specific aspects of human cognition are likely to be involved in mental illness. In general, it will not be possible to separate genomic information relevant to human evolution from that relevant to human disease. The close similarity of the chimpanzee and human genomes also increases the likelihood of finding disease-related differences quickly. Furthermore, any genomic differences found between Old World monkeys and humans will be easier to interpret if the corresponding regions of the chimpanzee genome are also available.

We did not mean to imply that a primate genome project should begin with or be limited to total sequencing of the chimpanzee genome. Our hope is that NHGRI (and other funding agencies in the United States and elsewhere) will consider a variety of approaches to primate genomics that may advance our understanding of human genetic function in health and disease. Suggestions such as those made by VandeBerg and colleagues will contribute to the decisions that must be made by the administrators of the funding agencies. The main purpose of our letter was to emphasize the need to give high priority to genomic studies on primates, rather than limiting comparative genomics to nonprimate mammals in the immediate future.

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A Primate Genome Project Deserves High Priority

Edwin H. McConkey and Ajit Varki

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