

The New Genomics: Global Views of Biology

The Human Genome Project is well along—by some accounts, ahead of schedule—making it highly likely that the entire human genome will be sequenced by the year 2005. This has led many in the genetics community to ask: "What will be done after this goal is attained?" In the recent *Genome* issue of *Science*, one of the leaders in this field, Eric Lander, has addressed the question by putting forth several specific goals for what he calls "the new genomics."

First and importantly, Lander views the genome project as the biologist's equivalent of the periodic table. Just as the periodic table gave chemists and physicists building blocks to understand their 19th-century world, the genome project will provide scientists of the next century the building blocks to understand biology. Accordingly, he proposes 10 goals for the next phase of genomics, which he sees as a transition from structural to functional genomics.

1. Routine resequencing of large regions of the human and mouse genome. The rationale is that this will be needed to fully define the extent of variation, eg, polymorphism, in the human genome. Such information will be necessary to understand how genetic variation contributes to the causation of common diseases.
2. Systematic identification of all common variants in human genes. This represents an extension and ordering of the previous goal.
3. Rapid sequencing of other organisms. Lander argues that comparative DNA sequencing will unlock evolutionary relationships not previously appreciated. He notes that sequence conservation will provide a powerful tool to determine functional constraints of genes and their products and a means to identify regulatory regions and important structural features of proteins.
4. Simultaneous monitoring of the expression of all genes. This is needed to generate a complete picture of the state of a cell and a basis for distinguishing among many different cell types. This goal would be achieved through description and cataloging of cell- and tissue-specific gene expression.
5. Develop generic tools for manipulating cell circuitry. Lander reasons that monitoring gene expression is insufficient to understand biologic functions. Rather, he points out that they must be disrupted and manipulated to fully define them; and he urges improvements of tools to accomplish this in model organisms in which functions can be monitored.
6. Monitor the level and modification state of all proteins. This goal focuses on gene products—proteins—rather than genes themselves. Lander argues that many functions of proteins reflect posttranslational modifications, which cannot be determined by analysis of the gene alone.

7. Systematic catalogs of protein interactions. Proteins do not function in a vacuum. Rather, their functions reflect interactions with other molecules; and diseases are due to disturbances in these interactions. This goal would lead to a comprehensive "interaction map" of the genome.
8. Identification and cataloging of basic protein shapes. This represents a more complex level of defining proteins.
9. Increased attention to ethical, legal, and social issues. This goal addresses the need to use the new knowledge in a responsible way.
10. Public education. This is related to goal 9. Lander emphasizes that the new information will provide people with choices regarding how the information will be used. He holds that education is the best safeguard to prevent its misuse.

Lander ES. *Science* 1996;274:536-539.

Editor's comment: *This is a thoughtful and insightful commentary that is useful for both geneticists and nongeneticists alike. It underscores that the Human Genome Project is not an end in itself, but a stepping stone to a more complete understanding of biology and disease.*

William A. Horton, MD

2nd Editor's comment: *Dr. Lander's proposals to study gene aspects are in the broadest perspectives of development, physiology, and microbiology—and are mind-boggling. The analogy that comes to my mind is: "We now have the land, what are we going to build?" The important question to be asked is: "What will all this constructively mean to the human race?" The answers are unknown, but very exciting prospects exist.*

Robert M. Blizzard, MD

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