THE NEW BIOLOGY AND ITS IMPACT IN BIOMEDICAL STRATEGIES AGAINST HIV/AIDS

by Gayle E. Woloschak

Abstract. The sequencing of the human genome and the initiation of the structural genomics projects have ushered in a new age of biology that involves multi-lab, high-cost projects with broad task-oriented goals rather than the more conventional hypothesis-driven approach of the past. The new biology has led to the development of new sets of tools for the scientist to use in the quest to solve mysteries of human disease, biomolecular structure-function relationships, and other burning biological questions. Nevertheless, the impact of the new biology on the field of AIDS investigation has been minimal, predominantly because many of the tools in the HIV field of study were developed before the full advance of the new biology was felt in the biomedical community. Many of the high-cost megaprojects that involve large technological advances and are marketed as projects of promise to the biomedical community are not likely to significantly impact the field of HIV/AIDS research and cannot serve as a substitute for direct funding to the HIV/AIDS scientists working for vaccine development, an understanding of mechanisms of disease causation, and new tools for therapeutic intervention.

Keywords: Acquired Immune Deficiency Syndrome (AIDS); AIDS and ethics; AIDS and scientific inquiry; ethics and decision making in AIDS patients; Human Immunodeficiency Virus (HIV).

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THE NEW BIOLOGY

High-cost projects that involve many different interdisciplinary laboratories have been important in space biology, high-energy physics, and other fields requiring specialized expensive equipment. The dedicated commitment of a group of scientists devoted to a particular project is perhaps best shown in the efforts of the United States and the National Aeronautics and Space Administration (NASA) to place a person on the moon during the 1960s. Large teams of investigators from all over the world were employed at a great expense in manpower and hardware to accomplish this single goal; determination and ingenuity both were required for the final accomplishment. The landing of a man on the moon cannot be attributed to the accomplishments of any single individual but rather is the collective accomplishment of a large team effort. Such accomplishment has generally been a result of a "big science" initiative that was developed as a package and marketed to the government based on the promise of the final goal.

Biology has not usually been driven by big-science initiatives but rather has been the realm of individual investigators working in their laboratories and with their lab groups to chip away at a problem of significance to the community of biologists in a relatively narrow field of investigation. This changed with the onset of the Human Genome Initiative in the 1980s, a project that was marketed to the government as changing the way we treat disease and even challenging our views of who humans are and where we come from. This field of genomics evolved into the sequencing of multiple genomes including those of bacteria and viruses, yeasts, the nematode worm *Caenorhabditis elegans,* fruit flies, humans, mice, rats, and more. Certainly this work has led to great advances in our understanding of each of the organisms sequenced. For humans, we learned more about genes important in repairing damage to our genetic material, genes important in specific diseases were more easily compared with their evolutionary counterparts, and sequence information told us about relationships between genes and gene families.

The field of genomics—sequencing genomes—led to the development of a structural genomics initiative, which aims at determining the three-dimensional structure of every protein encoded for by every gene. While the initiative is only partially completed, the information gained from this work has already had significant impact on the area of drug design, in which molecules that mimic three-dimensional structures of abnormal proteins can be used therapeutically to intervene in abnormal processes such as tumor progression, inflammation, and infection.

More recent efforts have gone into functional genomics—megaprojects designed to determine the function of every gene in the body of an organism. These studies have been initiated for small organisms such as the nematode worm *C. elegans* that can be genetically manipulated, but for humans such studies are not possible with current approaches. The general methods that have been employed include the functional knocking out or inactivation of every gene, one by one, in a single organism to determine what impact this has on the function of the whole organism. Recent work with *C. elegans* has attributed functions to several genes that, up to that point, had unknown functions (Kamath et al. 2003).

By-products of these new biology initiatives have led to major biomedical developments in recent years. Most areas of medical treatment and diagnosis are likely to be impacted, including discovery of genetic causes of some hereditary diseases, genetic screening for disease susceptibility, molecular profiling of tumors to ascertain genetic alterations, improved preventive and therapeutic modalities based on molecular profiling, and early diagnosis of disease.

In general, the new biology is expensive, requires special laboratory equipment and software, and can best be accomplished in large groups that have teams of bioinformatics specialists, molecular biologists, engineers, biochemists, and others. In addition, it has been predicted that because of the high costs some of the new technology will be made available only to those who can afford it. The cost of sequencing human genomes in a few years has been estimated at $500,000 per person, and the cost of expression profiling and analysis is estimated at $20,000. There are general concerns that the actual benefits of these technologies, while felt to a limited extent by all people, will mostly benefit the wealthy who can afford the new tests that will result from the technology. Furthermore, some fear that inexpensive mini-tests for disease susceptibilities will enable health insurance companies to segregate insured people into different cost categories based on their projected risk estimates for disease.

While these new big-science biology initiatives have contributed significant new information to the broad community, they still have not replaced the smaller-scale studies done by individual investigators working with a small team of scientists perhaps collaboratively on a focused hypothesis-driven project.

Impact of the New Biology on HIV/AIDS Investigations

While the new biology has been marketed to the government as holding great promise for biomedical tools against HIV/AIDS, most of the important discoveries relevant to new treatment and diagnostic tools against HIV/AIDS have not been significantly affected by the new biology discoveries. HIV strains had been sequenced before the new biology genomics era, and structures of HIV proteins had been solved and placed on government Web sites before the onset of the structural genomics initiative. Drug design in the field has progressed predominantly by conventional methods, and, while gene expression chips have yielded useful information about

HIV-infected cells, breakthrough discoveries have not been forthcoming as they have been, for example, in tumor-cell classification, in which new categories of tumors have emerged from these gene-chip studies.

One area of HIV/AIDS investigation that might be impacted by the new technology in the coming years is the use of gene chips for determining HIV strains and sequences of individual viral isolates. This could be important if particular isolates are associated with an effective therapeutic advance or a particularly good or bad prognosis. Such HIV-sequencing chips have been developed and depend upon new technology that came about as a result of the Human Genome Initiative.

In general, most fields of biomedical research, including cancer biology, genetic medicine, and neurobiology, have benefited more from the new biology than the field of HIV/AIDS research has (Woloschak 2003). Some spillover to the HIV field is inevitable, but AIDS is not likely to be the direct beneficiary of the science of technology of the new biology.

Responsibility and the New Biology

Responsibility has not yet been (and is not likely to be) found to be encoded for in the human genome, but responsibility is one of the hallmarks that distinguishes humanity from other creatures on Earth. From an evolutionary perspective we can observe expressions of humanlike responsibility in other animals: reptiles and birds build nests and protect their young, and mammals feed and protect their young until they can fend for themselves. In human beings, though, this expression of responsibility carries beyond care for our young and for the members of our clan into a responsibility for all things—fellow humans, all creatures on Earth, the planet itself, even the cosmos. The importance of this responsibility is seen in our stories. In Genesis, God gives humanity dominion over the earth and responsibility for all things, and Cain as a murderer rejects responsibility when he says “Am I my brother’s keeper?” (Genesis 4:9 RSV) Christian teachings emphasize responsibility for others—those who hunger, those in prison, those in need.

How can human beings show responsibility in the way we develop tools and strategies to combat HIV/AIDS? To date, humanity has not had an outstanding performance in equalizing treatment and therapies around the world. Most of the therapies that have been developed to counter HIV infection have benefited developed nations (Ammann 2003). Africa, the Caribbean countries, and Asia are losing large portions of their young populations to this horrible disease, and strategies to eradicate it have not even slightly impacted those nations. Examples of irresponsibility in the HIV/AIDS front abound. In the United States, there has been little effect on the deaf population of education about how HIV is transmitted, because educators have relied on verbal presentations and not on signing. In some

African nations, funding exists to punish with death those who have AIDS and commit rape, but none exists to protect the unborn from HIV transmission when the mother has HIV, even if such a child is a result of a rape that might be punished by a death sentence. Like the new biology, treatment for HIV/AIDS is available only to the few who can afford it, both in the United States and elsewhere. Many drugs, such as some of the protease inhibitors, are cost-prohibitive for development and/or therapy. Yet, unsafe new drugs (such as HAART, highly active antiretroviral therapy, which has caused liver damage and led to death in some cases) are released without sufficient testing, again showing a lack of responsibility.

The Nuffield Council on Bioethics was convened to discuss the problem of HIV/AIDS in developing nations, and their discussions resulted in a list of duties crucial for evaluating actions and policies for research in developing countries. Among the duties listed as most important for HIV/AIDS research are the alleviation of suffering, showing respect for all persons, being sensitive to cultural differences, and taking great care to not exploit the vulnerable. It is especially noted that care should be taken to address health problems of developing nations hand in hand with addressing the health problems of the developed world (*www.nuffieldbioethics.org*).

As in all things, humans must act responsibly in the development of tools and approaches to treating HIV/AIDS. Options to consider as approaches to counter this disease include the following:

1. Research that applies to developing nations must be supported.
2. Poverty is a source of ignorance about HIV/AIDS worldwide, and battling AIDS requires battling poverty as well.
3. Educational programs that reach out to the disabled, to underdeveloped nations, and all people must be developed.
4. Humanity must not depend exclusively on new biology for a cure; individual efforts in vaccine development and therapeutic intervention must continue through government-funded programs.
5. We all must work to change attitudes about materialism, to establish responsible actions, and to engender compassion in the world.

Saint Isaac the Syrian offered the following advice on compassion: “Brother, this is what I recommend: to let the weight of compassion within you tip the scale to the point that you might feel within your heart God’s own compassion for the world” (The Ascetical Homilies of St. Isaac the Syrian, Holy Transfiguration Monastery, 1984).

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