

GENETIC DETERMINISM, REDUCTIONISM AND DISCRIMINATION: TIGHTENING THE CHAINS BECAUSE OF THE HUMAN GENOME SEQUENCE

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SUMARIO: I. *The human genome project and the ELSI program*. II. *Genetic determinism and reductionism and the human genome sequence*. III. *Where do we go from here?* IV. *Conclusion*. V. *Additional notes*.

The simultaneous publication of two separate versions of the human genome sequence in February, has been acclaimed as “humanity’s great gift”, a “landmark”, “unparalleled in the history of biology”, and a “stunning” an “awesome” “scientific accomplishment”. The two versions, one published in *Science* by J. Craig Venter and colleagues of Celera Genomics, the other in *Nature* by the International Human genome Sequencing Consortium, headed by Francis Collins, director of the National Human Genome Research Institute, are the results of hard work by thousands scientists across the globe who contributed to the almost complete nucleotide sequence of human DNA, often called the book of life. The Editorial that precedes the lengthy human genome report in *Science* underlines this accomplishment:

The inspired vision to launch the genome project, 10 years ago, now rewards the confidence of those who believe that the pursuit of large-scale fundamental problems in the life sciences is in the *national interest*“ (emphasis added). Knowledge of such importance and magnitude gives humanity a powerful tool for unlocking the secrets of our genetic heritage and for finding our place among the other participants in the adventure of life. Not only will the human genome sequencing provide new approach to biology, it also “revolutionizes the way we look at human disease”. Scientists will acquire

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“new power to analyze the effects of individual genes and examine a more integrated view of the whole ensembles of genes as they form a living human being”.

These hyperbolic statements are reminiscent of others made 10 years ago, when at the launching the Human Genome Project, leaders consistently described the human genome as the “book of Life”, and the human genome project as a search for the “ultimate answers to the chemical underpinnings of human existence”. These statements support the view that genetic knowledge is the ultimate in determinism, reductionism and hereditarianism, and that “knowing the human genome we will know what it is to be human”. The conceit has been that “once the structure and function of the genome is understood, it may seem possible to have a gene-based explanation of most phenotypic characteristics, including most aspects of human health, disease and even behavior”.

To address the ethical, legal and social implications of the human genome project (ELSI), including its deterministic and reductionistic tendencies, 5% of its total budget was set aside by US Congress under the initiative of James Watson, then, head of the HGP.

Ten years ago I was invited at the first ELSI-funded workshop to speak on genetic determinism and reductionism. *Genetic determinism* is the belief that genes determine who we are, including behavioral characteristics. *Genetic reductionism* is the belief that by understanding humans at the molecular level we will know what it is to be humans.

This past January, at the occasion of the 10th anniversary of the ELSI Program, I was invited to return to NHI to speak again on the same issues. This is what I said. This was not a cause of celebration. We have done almost nothing to protect people against genetic discrimination, or to avoid the fallacies of genetic determinism and reductionism. In fact we have become even more reductionistic than we have ever been. To illustrate this point I used a few examples, including human cloning.

In this presentation, I would like to briefly revisit the ELSI program and then briefly explore how discussion of genetic reductionism and determinism has affected the way geneticists see their work. I will conclude with what I think we need to do.

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I. THE HUMAN GENOME PROJECT AND THE ELSI PROGRAM

Presumably, the ELSI program was established to address the ethical, social, and legal implication of the human genome project. At the first ELSI-funded workshop, participants identified 4 items with the goal of developing a prioritized research agenda for ELSI: 1) when and how genetic tests should be introduced into medical practice; 2) how confidentiality and privacy of genetic information could be preserved; 3) how genetic discrimination could be prevented, and 4) how the HGP would affect our concept of disease, normalcy and humanness. At the heart of the last item is reductionism and determinism, and these concepts also govern item 3, *i.e.* genetic discrimination. My own contribution to this workshop and later book entitled *Gene Mapping. Using law and Ethics as Guides*, edited by George Annas and Sherman Elias, was a chapter on Genetic Reductionism and Determinism. In this chapter I explain that a general perception that human genetics is fundamentally deterministic and reductionistic could lead to the misapplication of genetic information and foster socially dangerous ideologies. Just as the Nazi physicians enthusiastically misused genetics to promote and implement their racial hygiene program in the 1930's and 1940's, so too others could misuse the fruits of the Human Genome Project to justify the destruction of all embryos less than perfect, the *de facto* creation of a new biological underclass (GeneRich vs. the Naturals, and the Defectives) and the systematic ostracism of the "genetically unfit". Society could have a powerful genetic tool for controlling individuals through an entire series of labeling and interventions: a bio-politics of the *population*. Problems of criminality, behavioral deviation, individual capability, even differences between gender, race and general intelligence could be viewed as exclusively genetics and thus as deterministic. If this perception prevails, the beneficent application of genetics could be at best problematic in preventive and curative medicine, and public health, and dangerously destructive of human rights, and human dignity.

After this first of its kind workshop, the ELSI program produced more than 285 research and educational projects and more than 25 workshops, conferences, and public educational events. Nonetheless, as central as these issues were to the human genome project, it seems fair to conclude that they have been inadequately addressed, and that the ELSI program

has had little, or no impact on genetic scientists and their research agenda (almost 200 citations, not one ELSI citation). Both Venter in *Science*, and Collins in *Nature* ended their human genome sequence reports as if there have been no ELSI program. For example, Venter stated:

There are two fallacies to be avoided: determinism, the idea that all characteristics of the person are “hard wired” by the genome; and reductionism, the view that with complete knowledge of the human genome sequence, it is only a matter of time before our understanding of gene functions and interactions will provide a complete causal description of human variability.

And Francis Collins wrote: “The ethical, legal and social issues are of comparable importance [to the human genome sequence] and could appropriately fill a paper of equal length”.

The failure of ELSI was to be expected. The program was conceived and viewed as parallel to the work of geneticists, never as an integral part of it. Also, ELSI sidesteps the fundamental question as to whether the HGP should be done at all. This was understandable, and perhaps necessary if ELSI had to exist at all. Nevertheless, by sidestepping this fundamental question, ELSI created two problems. *First*, it allowed the philosophical, ethical, legal and social discussion to proceed as if this question has been resolved, which was simply not the case. *Second*, it gave the impression that the ethical, legal and social implications of the HGP were unrelated to the fundamental question as to whether the genome project should be done at all. This may be true in some cases, but it is not true in all cases. Ultimately, almost no scientists, including Watson, himself, who initiated ELSI, took the ELSI group seriously: “I wanted a group that would talk and talk and talk and never get anything done”. This permitted genetic scientists to proceed without safeguards and restraints.

II. GENETIC DETERMINISM AND REDUCTIONISM AND THE HUMAN GENOME SEQUENCE

It is today even clearer than it was a decade ago that knowledge of the human genome affects the way we think about ourselves, our concepts of normal, and pathological, health disease and even self-identity.

In the world of genomics or proteomics, if we continue to speak of the living being, we do so at such a high level of abstraction that we can easily lose all human perspectives, and reduce humans to their genes, proteins interactions, proteins alterations, and reactions, and ultimately to their disorders. The continuing hunt for genetic predisposition to diseases, and so-called disease genes is an example. We speak of genetic predisposition to breast cancer, colon cancer, Alzheimer's, and colon cancer gene, skin cancer genes etc... but as philosopher Matt Ridley has rightly noted in his book *Genome*: “to define genes by the disease they cause, is about as absurd as defining organs of the body by the diseases they get. Livers are not there to cause cirrhosis, heart to cause heart attacks, and brains to cause strokes”.

Health has become de facto genetic. To be sick is to have been made fundamentally flawed, to be inherently defective. And this eliminates a person's responsibilities, excesses and imprudence. Genes threatens to become the measure of all humans. The human genome sequence reinforces this threat. It is as if humans live their lives at the genetic level. Craig Venter even acknowledged, although mildly:

At the protein level, minor alterations can have dramatic effects on cellular physiology. The dynamic system that forms an organism has many ways to modulate, which suggests that definition of complex systems by analysis of single genes is unlikely to be entirely successful... The modest number of human genes (26 to 38,000) means that we must look elsewhere for the mechanisms that generate the complexities inherent in human development and the sophisticated signaling systems that maintain homeostasis.

French philosopher, George Canguilhem, perceptively noted decades ago that it is a fundamental mistake to think that by understanding life at the molecular level we can understand anything about the living. In his words: “one does not scientifically dictate norms to life”. Likewise, his start student, Michel Foucault, warned that the geneticization of diseases would create a new biological underclass and could lead to the systematic ostracism of those labeled genetically unfit. Genetic reductionism and determinism thus combine to promote genetic discrimination, and threaten to subvert a beneficent medicine by converting it into a tool of oppression. By labeling people as “genetically defective” or at risks for genetic disorders, we, effectively, limit their lives' choices. James Watson provided an example of this type of oppression when two months ago at the Uni-

versity of California at Berkeley, he told a group of students that “skin color is biologically linked to sexual activity and that thin people make for better worker than fat people”. In his words: “whenever you interview fat people, you feel bad because you know you are not going to hire them”.

It must also be emphasized that we go out of our way to deny that we are reductionistic by describing our actions as necessary to meet lofty beneficent goals. Let’s take human cloning, for example, which since *Dolly*’s birth, has almost overshadowed all other genetic issues. Proponents of human cloning have described it, not as genetic replication (which is just that) but as a new form of human reproduction that would give infertile couples another reproductive choice. But cloning techniques that combine the genetic material of a single individual with an egg whose nucleus has been removed to produce a child, are inherently reductionistic, since the intent and content of cloning is only to make genetic duplicate. The child produced can only inherit the exact genetic copy of that person’s nuclear genetic material. In cloning only genes matter. Reproductive cloning thus would reduce humans to their genetic essentials: simple DNA replication, genes multiplying exactly the very structure of DNA. But, people reproduce, not genes. People are not and should not be viewed as vehicles for genetic replication. This violates universal human rights principles, human dignity and respect for persons.

The language of beneficence also helps disguise problems of stigmatization and discrimination. For instance, in the case of behavioral genomics we go out of our way to suggest that geneticization of mental disorders is a good thing for the mentally ill since it would decrease the stigma attached to these disorders. In *Toward Behavioral Genomics*, McGuffin et al., at the Social, Genetic and Developmental Psychiatry Research Center of Kings College London, wrote:

It has sometimes been suggested that geneticization is likely to increase the stigma of mental disorders. To the contrary, far from increasing the stigma, advances in genetics have the opposite effect. As a case in point, it is now perfectly acceptable for an ex President of the United States and his family to acknowledge that he has Alzheimer’s disease, a disorder for which much progress has been made in understanding its basis at a molecular level. We predict that this is the start of a trend and that identifying genes involved in behavioral disorders will do much to improve public perception and tolerance of behavioral disorders.

Obviously, the authors have not consulted disability groups who face constant discrimination because of their disorders, and fear that genetic screening of embryos and fetuses will reinforce discrimination against mental disabilities (1249)

The language of beneficence is perhaps even more dangerous when it helps disguise that which is probably the ultimate goal of the human genome project: the abolition of all diseases and the quest for immortality. To want to live forever, and be spared the infirmities of age is not a new dream. But it is only a dream. It is nonsense to believe with William Hazeltine, the CEO of Human Genome Sciences, that “Death is a series of preventable diseases”. Death is not a disease and it is not preventable. To expect the eradication of all diseases once we understand the human genome is a dangerous dream. And as G. Canguilhem emphasized: “to dream of absolute treatment is often to dream of treatment that is worse than the disease”.

Knowing the working human machine at its molecular level without considering the context in which we live our lives is useless. But as G. Annas stated: “we have lost all perspectives. We will never be able to understand life or how it should be lived, or what it means to be humans by exploring or understanding our lives, or bodies at the molecular, atomic or even sub atomic level”.

III. WHERE DO WE GO FROM HERE?

To resist imputing meaning to life from the human genome, we must articulate our health goals clearly and develop strategies to meet these goals. These goals cannot (or at least not only) be to eradicate all diseases, or even to live a longer (“healthier”) life in a youthful body, even though these goals appear today attractive to those who seek to fulfill them. Life is not indifferent to the conditions in which it is possible, and thus life, not science, establishes norms. Scientists may claim humans as their new frontiers in human genetic exploration, but they cannot and should not tell us how we should live our lives, reducing humans to their genes. We must also integrate a meaningful definition of humans goals into our definition of medical or genetic progress, and refuse the genetic imperative to accept reductionistic and deterministic thinking as a necessary price

for progress toward the mirage of absolute remedies and virtual immortality.

Practically, this means that we must think globally and at the species level about genetic interventions, which like cloning will profoundly affect the inherent characteristics of what it means to be humans. There has been enough public outcry at the prospect of human reproductive cloning. Together we should support the view enunciated by *UNESCO Universal Declaration on the Human Genome and Human Rights and in the Additional Protocol on the Prohibition of Cloning Human Beings* (1999) that says:

Our first imperative is the protection of the human species (preamble) and Any intervention seeking to modify the human genome may only be undertaken for preventive, diagnostic or therapeutic purposes, and only if its aims are not to introduce modifications in the genome of any descendants (article 13).

Article 10. (protocol): Any intervention seeking to create a human being genetically identical to another human being whether living or dead is prohibited.

We must work together through worldwide assemblies or forum under the aegis of the United Nations to debunk a beneficent language that has helped disguise the harmful and dangerous effects of reproductive cloning and its likely consequences of germline genetic modifications. Democratic and public debates will heighten and sharpen our understanding of genetic interventions and developments that has been thus far limited, fragmented, profit-oriented and less than morally and socially responsible. Such debates will help prevent misguided legislative actions based on misguided and inappropriate conceptions, and bring human rights perspectives in reproductive genetics to the forefront of public consciousness.

We must work together toward a global treaty on the genetic future of the human species. This treaty would need to be ratified by all member countries of the United Nations and strict sanctions must be imposed on those who violate the treaty. It must be emphasize that to the extend that human cloning techniques are necessary to make genetic engineering efficient and useful, outlawing human reproductive cloning research will in effect outlaw human genetic enhancement as well.

We must also forbid genetic interventions like screening of embryos or fetuses and children for genetic predisposition and risks of diseases that they may never get. These interventions reduces humans to their disorders, their disease genes, and are unacceptable and harmful effects of increasing stigmatization and discrimination.

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In the US funding for big science must be towards interventions that seek to improve the lives of people (like stem cell research) and only if the aims are not to introduce genomic modification of our children.

We need strong genetic privacy legislation as we begin to collect and maintain genetic information in many different forms, such as pathology specimens, blood bank donations, newborn screening samples and research collections. In the US, armed forces require all members to donate a sample of their DNA for future casualty identification. Many countries, including the US, maintain forensic DNA banks for criminal identification, and DNA banks for commercial use. In Iceland, the parliament passed a bill allowing a private biotechnological company, *Decode Genetics* to combine all Icelanders' genetic medical and generational information into one database to be sold to researchers. Estonian scientists are trying to create a similar genetic databank.

IV. CONCLUSION

In conclusion, let me say this. To combat genetic reductionism and determinism and protect individuals against violation of their privacy and rights will not be easy. The strong beneficence language of science is contagious and pervasive as this passage in *Science* illustrates.

The sequencing of the human genome heralds a new age of medicine with enormous benefits for the general public. For example, it will allow scientists to identify all of the genes contributing to a giving disease state, leading to a more accurate diagnosis and precise classification of disease severity. In addition, healthy patients can know the diseases, for which they are at risk, giving them the opportunity to make beneficial lifestyle changes or to take preventive medications to protect their health. Understanding the genetic bases of heritable diseases also will allow researchers to develop therapeutics at the molecular level, resulting in better treatments with fewer side effects.

One of the greatest difficulties will be for legislators, policy-makers and global organizations (as well as professional organizations) to strike a balance between "timely promotion and use of the best genetic research and interventions, and careful protection of people from genetic stigmatization and discrimination.

We must also remind ourselves of the UNESCO *Universal Declaration on the Human Genome and Human Rights* which state:

Article 1o.: The Human Genome underlies the fundamental unity of all members of the human family, as well as the recognition of their inherent dignity and diversity.

Article 2o. a) Everyone has a right to respect for their dignity and for their rights regardless of their genetic characteristics.

b) That dignity makes it imperative not to reduce individuals to their genetic characteristics and to respect their uniqueness and diversity.

We must finally expand our perspectives rather than continue to narrow it. The human genome sequence may provide the framework upon which all the genetics, biochemistry, physiology, and ultimately phenotype depends, and the boundaries for scientific inquiry. And genetic scientists may use reductionistic research techniques and strategies to advance scientific knowledge, but they must always be thinking about the whole human person, avoiding sweeping statements that lead to misconceptions and misguided interventions. And for those of us concerned with the reductionistic tendency of genetic science, we must move from the level of the doctor-patient relationship and a close-up focus on biomedical ethics to the level of the human species and human rights perspective.

V. ADDITIONAL NOTES

After 10 years of hard work and fierce competition between key genetic players, Venter and Collins, the two reports on the human genome sequence point to the complexity of organisms, recognizing that there is no meaningful correlation between the number of genes, neurons or cell types on the one hand, and the structural or behavioral complexity of organisms, on the other hand. The genome sequence may provide “the framework upon which all the genetics, biochemistry, physiology, and ultimately phenotype depends, and the boundaries for scientific inquiry, but this knowledge tells us nothing about humans qua humans, and should not lend itself to genetic determinism and reductionism”. Essentially, “genetics is the realm of nonlinearities and epigenesis”. To simply examine the number of neurons, cell types or genes or of the genome size, alone, will not account for the differences in complexity that we observe.