



NATIONAL COUNCIL OF ETHICS FOR THE LIFE SCIENCES
Prime Minister's Office

REPORT AND OPINION ON THE ETHICAL IMPLICATIONS OF GENOMICS

(40/CNECV/01)

REPORT

INTRODUCTION

The genome became public news on the last week of June 2000, through an official announcement, which at once spread worldwide, that the full sequencing of the human genome was close to completion, with all the important consequences expected therefrom to the advancement of medical genetics, to the pharmaceutical industry, to public health and to better knowledge of human life.

Roughly two weeks after that announcement, the National Council of Ethics for the Life Sciences (CNECV) approved a work document on the matter¹, which summed up the scientific significance of the full sequencing of the human genome, as well as the ethical perplexities arising from it, and at its close manifested the intention of presenting at a later stage a Report and Opinion in which the themes broached therein would be taken further and completed. The present document aims at fulfilling that intention.

I- SCIENTIFIC SIGNIFICANCE

Scientific advances over the last year have confirmed the expectations mentioned in document 31/CNECV/2000 regarding the genetic characterisation of more diseases, the possibility of pre-symptomatic testing of late-manifestation monogenic diseases or predispositions to common diseases, the search for new approaches to their therapy and the possibility of producing personalised custom medication through pharmacogenetics.

Notwithstanding this, new data emerged to correct or complete the initial picture, which will be briefly noted here before their ethical implications are studied.

1. The sequencing of the human genome is still far from completion. The Director of the French National Sequencing Centre, Jean Weissenbach, declared to *Le Monde* on February 13, 2001, that about 150,000 DNA fragments of different sizes were yet to be decoded, and that about one third of the genes were not yet entirely known. In his opinion, two or three years of work are still needed before we reach the historic moment when we achieve integral knowledge of our genome.

2. The number of human genes, initially estimated at approximately 100,000 or more, is apparently much lower, perhaps somewhere between 26,000 and 38,000, which corresponds to no more than roughly double the genes of the vinegar fly. Hence, it does not seem that the number of genes reflects the complexity of the human being.

3. Although work is still in progress, the results of the comparison between the genome of our species with that of other species (including micro-organisms) reveal a degree of similarity much higher than might be expected from the morphological and physiological diversity. Particularly surprising is the recent discovery of the existence of

¹ CONSELHO NACIONAL DE ÉTICA PARA AS CIÊNCIAS DA VIDA, "Documento Preliminar de Trabalho sobre o Genoma Humano (31/CNECV/2000)", *Documentação VII (2000)*, Lisboa, Presidência do Conselho de Ministros, 2001, pp. 30-36. An English translation exists.



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dozens of human genes that apparently have been transferred horizontally from bacteria to animals. Such results are not to be dismissed with regard to the image Man forms of his place on the planet and of how he must relate to it.

4. As for differences within our species, the data currently available point to a variation figure of only 0.1 %, which apparently indicates that, in terms of our genome, we are all more similar to each other than we might have supposed.

It is also clear now that genetic differences among human beings are found within all human races. Moreover, the variations in genetic sequences within each race are also found in all other races. For now, it seems, the distinction among human races has no genetic support.

5. Many more situations have been found in which the very same human gene is processed in different manner in various organs of the same individual, originating several differing proteins. These are polysemous genes, in which the same significant has several meanings. The cause of this "alternative RNA splicing" is still unknown, but it might reside in the cytoplasmic context of each cell, that is, in the micro-milieu that surrounds the nucleus, and there are recent indications pointing in that direction. If that is so, it will be yet another example of how the environment conditions the expression of the genes. The cloning of mammals has also shown that the same nucleus can produce very different realities depending on whether it is placed in the cytoplasm of a differentiated cell or in an oocyte. Likewise, the *in vitro* differentiation of stem cells in various tissues appears to take place without any genetic alteration of those cells.

6. Such results tend to switch the focus of scientific interest from the constitution of genes to the mechanisms of their expression, and this is reflected in the growing interest in proteomics² as well as in the therapies applied. For instance, in parallel with advances in gene therapy, "therapies of protein repair" have been developed recently, which use specific drugs to restore normal functionality to the mutated protein.

7. It has become increasingly clear that genetic tests for susceptibilities to common diseases do not possess, in the vast majority of cases, the reliability and predicting ability that is sometimes advertised to the public. High reliability is offered indeed by pre-symptomatic tests of late-onset monogenic diseases, which are, however, very rare.

II – ETHICAL IMPLICATIONS

Since the publication of the already mentioned document 31/CNECV/2000, there is apparently greater concern in Portuguese society to adopt ethical and legal norms that make it possible for advances in Genetics to contribute to the full benefit of the human person and its dignity.

Indeed, in January 2001, the Portuguese State ratified the *Convention on Human Rights and Biomedicine*³ (hereinafter referred to as the Convention), which, in many of its articles, defines the appropriate use of the applications of knowledge of the human genome. More recently, the CNECV published Report-Opinion 37/CNECV/01 on Bill no. 455/VIII

² See the Document referred to in note 1.

³ For the text of the Convention, see CONSELHO NACIONAL DE ÉTICA PARA AS CIÊNCIAS DA VIDA, *Documentação VII (2000)*, Lisboa, Presidência do Conselho de Ministros, 2001, pp. 12-25.



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'Personal Genetic Information', proposed by the Parliamentary Representatives of the *Bloco de Esquerda* Party ⁴, partly concerning the same issues.

The present Report highlights some of the more relevant or less explicit ethical implications ensuing from those documents.

1. Genetic determinism and freedom

In the second half of the twentieth century, some reductionist positions in molecular genetics as well as some trends in socio-biology led part of the public to imagine that the analysis of the human genome would find DNA sequences that could explain every characteristic of the human spirit and hence reduce concepts such as freedom, self-determination and guilt to hardly more than delusions of the pre-genomics era. This would have devastating consequences to many structures of our society. The data gathered thus far have not favoured that position.

What has been mentioned in points I.5 and I.6 already shows that the genes represent but capacities, which might be expressed or not and produce one reality or another depending on the environment. To this accrue factors of stochastic mutation and the complex cascades of interactions between the several genes, as well as between the genes, their products and the environment. Today, it is acknowledged that the indeterminism of physical processes is great, and even greater the unpredictability of genetic expression.

It is certain that almost everything in life needs some genetic basis and environmental factors. The difference, from case to case, depends only on the relative proportion of the conjugation of those two determinant elements. Moreover, with the emergence of conscious mind and the consequent capacity for innovation, the environment acquired much greater intervention, enriched now with elements of a different kind such as psychological motivations, cultural values, the historical context of each life story, education, first experiences and acquired habits, etc.

Furthermore, it has been verified that the human subject may have the initiative in decisive events, which run counter to its genes and environment. The genome and its circumstances appear to be necessary conditions but not sufficient conditions for human options.

In philosophy, the problem of self-determination and of freedom in general *versus* determinism is obviously more complex. For our purposes, however, we need only show that genomics does not seem to be of much to the deterministic thesis.

Moreover, these considerations also make it evident how illusory are the expectations that we might be able to manipulate, through the genes, the behavioural and spiritual characteristics of the human being.

2. Global solidarity

The data summarised in point I.3 suggest that the human genome tells our origins and says where we came from. It speaks of the 5,000 million years of our pre-history, since life first sprang on the planet until today. It still bears the marks of the long evolving process that generated us. It reveals the evolutionary stages of historical breakthroughs that became

⁴ CONSELHO NACIONAL DE ÉTICA PARA AS CIÊNCIAS DA VIDA, *Relatório Parecer 37/CNECV/01 acerca do Projecto de Lei nº 455/VIII "Informação Genética Pessoal" proposto pelos Deputados do Bloco de Esquerda*. This Report-Opinion is available at www.cnecv.gov.pt. An English version exists.



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sedimented and gradually restructured themselves during the evolutionary process that led to our species. It keeps the memory of our evolutionary past and it is the family album of our ancestors and the autobiography of our species in twenty-three chapters (the 23 pairs of chromosomes)⁵.

The human genome shows the full extent to which we are kin of the other species now in existence and the many more that foundered. It summarises, in a four-letter enigma, the entire ancestral heritage that Man carries. We carry in our genome the mandate of all the species that preceded us and left upon it their imprint or memory, urging our ontological solidarity with our brethren – animals, plants and microorganisms. We are closer to and more dependent on them than our pride might wish. To protect and respect the bio-environment, therefore, is to protect and respect our own genes. This perspective corroborates the concern of Bioethics to include an ethics of the environment and of global solidarity.

3. Human dignity and genomic science.

The applications of the recent advances of genomics must be implemented with respect for the dignity and rights of the human person, as set down in the *Universal Declaration of the Human Genome and Human Rights* (adopted by the General Conference of UNESCO, on the 11th of November, 1997) and in the *Convention on Human Rights and Biomedicine*.

The Convention considers at great length the principle of informed consent (chap. II), privacy and the right to information (chap. III), as well as non-discrimination (Art. 11) as it applies to predictive genetic tests (Art. 12), to interventions on the human genome (Art. 13), to scientific research on human subjects (Articles 16 and 17) and to research using embryos (Art. 18).

The CNECV, whose opinion was that the Convention ought to be ratified⁶ (as it was indeed) by the Portuguese State, subscribes the ethical principles that underlie it and hopes they will be amply divulged and debated in Portuguese society; the mechanisms leading to its full implementation must be set in motion.

It is particularly important to find new, effective ways to protect confidentiality, especially where sensitive genetic data are concerned, in step with the growing technical capability to store in computer systems the results of genetic tests. Any breach of confidentiality for non-medical purposes could lead to serious social discrimination and stigmatisation. The ethical conditions applying to genetic tests in the work place were laid out in document 31/CNECV/2000, already mentioned. Many of the arguments adduced therein are equally valid concerning the illegitimacy of access to pre-symptomatic genetic tests by insurance companies.

4. Selecting the traits of future generations.

Although the Convention prohibits intentional modifications of the genome of our descendents (Art. 13), it says nothing about the selection of the physical traits of newborns, except for sex determination (Art. 14).

⁵ MATT RIDLEY, *Genome: The Autobiography of a Species in 23 Chapters*, New York, Harper Collins, 2000.

⁶ CONSELHO NACIONAL DE ÉTICA PARA AS CIÊNCIAS DA VIDA, "Parecer 30/CNECV/2000," in *Documentação VII (2000)*, Lisboa, Presidência do Conselho de Ministros, 2001, pp. 9-28. An English version exists.



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Now, by combining *in vitro* fertilisation with pre-implantation genetic diagnosis (which is greatly facilitated with *gene chips*) – and given the more detailed knowledge we shall have in future of the human genome – soon it will be possible to select, out of a few dozen embryos generated by the couple, one or more with the genetic makeup favoured by the progenitors, discarding the rest. It is not a matter of modifying the descendant's genes, but of selecting one or another among the various natural programs.

It is also possible in medically assisted procreation to select the gamete donors in order to obtain, for non-medical reasons, certain physical traits of one's offspring, despite the limited efficacy of that method.

Such practices raise ethical perplexities relating to the principles of non-discrimination and non-instrumentalisation of the human being, and in terms of respect for human freedom.

It is interesting to note that the Explanation of Reasons of the Additional Protocol to the Convention prohibiting the cloning of human beings ⁷ expresses the ultimate reason of that prohibition thus:

"Considering that natural genetic recombination tends to originate greater freedom for the human being than that given to it by a pre-determined genetic makeup, it is in every person's interest to maintain the essentially random nature of the composition of their own genes." ⁸

In our view, it seems obvious that this argument applies just as well to the selection of our children's physical traits.

5. Commercialisation

From the very start of the sequencing program of the human genome, and through the forecasting of its applications, the largest pharmaceutical companies showed their interest in this field, and they invested huge sums in the development of new genetic tests, expecting as their due fast, substantial profits from their application.

Without this investment by the large companies and multinationals, in no way genomics would be at the advanced stage in which it is in fact today, with all the benefits already mentioned. And for that industrial investment to be profitable, patents and a vast commercialisation of genetic tests are necessary.

On the other hand, economic power must not be damaging either to the person's legitimate interests or to the just freedom of research. The latter would be affected if every kind of DNA sequence were the object of patents. With the intent of finding a compromise, The European Parliament and the Commission approved, on the 6th of July 1998, Directive no. 98/44/CE regarding the *Juridical Protection of Biotechnological Inventions* ⁹. Despite the strong controversy raised by that Directive, the CNECV considers that it must be the object of appropriate national legislation¹⁰.

⁷ The text of this Protocol has been published in CONSELHO NACIONAL DE ÉTICA PARA AS CIÊNCIAS DA VIDA, *Documentação VII (2000)*, Lisboa, Presidência do Conselho de Ministros, 2001, pp. 26-28.

⁸ COUNCIL OF EUROPE, *Additional Protocol (to the Convention on Human Rights and Biomedicine) on the Prohibition of Cloning Human Beings*. Available at: <http://conventions.coe.int>. The translation and highlighting of the text are ours.

⁹ *EU Official Journal*, L-213 (30 July 98), p. 13.

¹⁰ CONSELHO NACIONAL DE ÉTICA PARA AS CIÊNCIAS DA VIDA, *Relatório Parecer 37/CNECV/01 acerca do Projecto de Lei nº 455/VIII "Informação Genética Pessoal" proposto pelos Deputados do Bloco de Esquerda*. This Report-Opinion is available at www.cnecv.gov.pt. An English version exists.



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Moreover, it is also important that economic interests do not prevail over the person's legitimate interests. Since the indiscriminate commercialisation of largely affordable pre-symptomatic tests, without appropriate medical indication or specialised psychosocial counselling, may cause the test subject extremely serious problems, either psychological or of social stigmatisation, the performance of such tests is ethically unacceptable.

CONCLUSION

The human genome, adorned with sensational scientific applications, has acquired the public image of a mythical celebrity, with a profile offering different angles of interest to diverse areas of culture and society.

To the unwary public, the genome is the soul or "Book of Life", while the chemist's eye sees only a molecule. To evolution enthusiasts, it is the family album of our ancestry, while biochemists regard it as the instructions manual of our organism. For linguists, it is the biological model of the semantic phenomenon of polysemy, and it is of interest to philosophers in their discussion of freedom versus determinism. For physicians, knowledge of the genome means better prevention, diagnoses and therapies, including custom drugs, while the pharmaceutical industry sees fantastic business opportunities. For environmentalists, it is an argument in favour of a global ethics of the environment, while for jurists it is a potential threat to fundamental rights that must be protected. For many patients, it means a light at the end of the tunnel, while for some healthy individuals it represents an obsessive nightmare. For some employers or insurance companies, it is a mirage of high profits, while for social welfare and pension funds it may represent unbearable expenditure. For sociologists, it is an argument against racial discrimination, while for geneticists it is but a basic working tool. For Stock Exchange investors, it is a pointer to shares that might shoot sky-high, while for the Third World it may represent yet another unfair distancing handicap.

Finally, for bioethicists, knowledge of the human genome and of its applications represents the challenge of finding, among all those various perspectives and vested interests, genuine good for the human person and society.

Lisbon, the 6th of November 2001

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OPINION ON THE ETHICAL IMPLICATIONS OF GENOMICS

(40/CNECV/01)

1. Considering that:

- a) Research on the genome and its applications are of great scientific and social interest,
- b) The results already achieved carry important consequences to the knowledge and the image that human beings gradually construct about themselves, especially regarding their origin, their necessary solidarity with the rest of the biosphere, their margin of freedom vis-à-vis the action of genes and racial non-discrimination,
- c) the protection of the rights and dignity of human beings in view of the applications of the new genetic technologies has been assured by the *Universal Declaration on the Human Genome and Human Rights* and by the *Convention on Human Rights and Biomedicine* – the latter has been ratified by the Portuguese State, and prior to that this Council manifested its agreement to the ethical principles underlying it,
- d) the breach of confidentiality concerning genetic data may give rise to grievous problems of social discrimination and stigmatisation,
- e) pre-symptomatic genetic tests, when performed without appropriate psycho-social counselling, may cause serious psychological disturbances in the subject, as well as social discrimination,
- f) the selection of physical traits of future children represents discrimination that limits their freedom from the start,
- g) the juridical framework of the new technologies is highly desirable, as well as the clarification of the requisites for patenting DNA sequences,
- h) the possibilities of medical applications of the knowledge of the genome in the field of health are important, but their efficacy has technical limitations that are not generally known to the public,

2. The National Council of Ethics for the Life Sciences is of the opinion that:

- a) research on the genome and its applications must be promoted,
- b) the consequences of such research to the knowledge and image that human beings gradually construct about themselves must be widely divulged and be included in educational syllabuses, chiefly with regard to the evolutionary origin of our species, to our solidarity with the other species, to the margin of human freedom human vis-à-vis the action of our genes, and to the fight against racism,
- c) there must be ample promotion of the knowledge of the ethical options underlying the provisions of *Convention on Human Rights and Biomedicine* and of the *Universal*



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Declaration on the Human Genome and Human Rights, along with activation of the mechanisms leading to the implementation thereof,

- d) the mechanisms that assure protection of the confidentiality of genetic data must be reviewed,
- e) pre-symptomatic genetic tests must be done only after the consent of the subject, on the indication of a geneticist physician, following appropriate psycho-social counselling, which must be continued with follow-up and support,
- f) the selection of physical traits of newborns is ethically unacceptable,
- g) the juridical provisions that protect persons against inappropriate applications of the knowledge of the human genome must be completed,
- h) the possibilities and technical limitations of medical applications of the knowledge of the genome must be correctly and widely divulged and debated, generally in Portuguese society and, especially, in education syllabuses.

Lisbon, the 6th of November 2001.

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