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Screens for Life: In DNA We Trust

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1. Introduction

Health is today genetic. To be sick is to have been made “defective,” a bad “terroir” which produces defective products, made up of genetic errors, DNA misspelling, and so called “disease genes.” Prevention, not treatment, is the only option. But it is not that simple. The correlation between “terroir” and products, i.e. between genes and diseases, genotype and phenotype is often not a straightforward causation. Most conditions are linked to multiple gene variations, difficult to interpret. To decipher the human genome is a complicated task, and one that has increasingly become the “stuff” of everyday life of modern adults in the twenty first century.

Scientists have helped the process of “geneticizing” human existence, by announcing, in fanfare, and five years ahead of schedule, the completion in 2000 of the Human Genome Project – the mapping and the sequencing of the human genome. Shortly after, James Watson, the co-discoverer of the DNA structure, and J. Craig Venter, the inventor of the ‘shotgun’ sequencing strategy used to decode the genome, have their own DNA sequenced, published and publicized in the media. Observers wonder whether the “1,000- Dollar Genome” would be next and genome mapping a “must have” for the not so rich and famous. The Socratic moral imperative “Know Thyself,” gains a new meaning, “Know Thy Genes;” unravel who you are at a sub-molecular level.

For-profit genomic companies such as 23&me and Navigenics, have already offered DNA screening to their paying members, and successfully convinced them that there is a near 100% causative effect between gene variations and diseases: genomic screens can help detect and prevent health risks. These direct-to-consumer companies have used a new technology, so called “gene chip” to screen thousands of genes simultaneously and identify mutations that are known to correlate to diseases. A gene variation, for example, may correlate to a marker for a heart condition, and it is argued that the person has a higher chance of developing heart disease and ought to do something to prevent it. The question is, of course, what? Disease causation is complicated, and meaningful prediction based on genomics is at best tentative. For example, 20 genes may correlate to a person height, these genes only explain 3% of height variation between people, or about 1/3 of an inch of the variation in height.

Nowhere in medicine has genetic science been more pervasive than in fertility clinics and prenatal care services. Whereas, in a not so distant past, pregnant patients could only be “screened” for conditions such as Down’s syndrome or trisomies, today, they may choose among a variety of genetic conditions that may affect the health of the child-to be. DNA microarray or “gene chips” currently being explored in research settings may allow screening for thousands of genes at once, and once introduced in clinical practice may be requested by prospective parents concerned about the health of their future child. The next step would be to make the whole fetal genome sequencing (WGS) available to the pregnant patient, once free fetal DNA can be easily extracted from maternal blood. The whole fetal genome sequencing could introduce a difference in kind, compared to more traditional screening methods because of the amount of information it produces at once.

Prospective parents want their babies to be healthy and are willing to submit to all kinds of screening tests, inconveniences and burdens for it. Prenatal screening gives them comfort and reassurance that the pregnancy is going well. But a “normal” fetal screen may be inaccurate (false negative) and thus misleading, and an “abnormal” screen may be misleading (false positive), and even harmful, i.e. putting the pregnancy at harm’s way through additional genetic tests. How to manage and use prenatal screens and the amount of genetic information they generate are critical if the goal is to promote rather than prevent the birth of healthy babies. Can a reasonable argument be made in favor of using these new screens in routine prenatal care, to ensure that the benefits outweigh the harm?

One of the most memorable moments in my professional life was when I took issue on these very questions with Israel Nisand, a celebrated and enormously influential French obstetrician-gynecologist. The question was: Are physicians obligated to disclose to their pregnant patients all they know about their fetuses despite serious concerns that patients may use this information to unnecessarily terminate the pregnancy? The debate took place in Monaco, in April 2000, during the International Symposium on *Procreation and the Rights of the Child*, sponsored by AMADE (*Association Mondiale des Amis de l’Enfance*, or *World Association of Children’s Friends*), and UNESCO (*United Nations Educational, Scientific and Cultural Organization*), two internationally known organizations whose mission is to undertake, support and promote all initiatives relevant to the interests and protection of children around the world - UNESCO since its creation in 1949, and AMADE since 1963 when Princess Grace of Monaco founded the organization “whose purpose is to ensure or make ensure the physical, moral and spiritual welfare of children throughout the world without any distinction as to race, sex, nationality or religion and in a spirit of complete independence.”

More than 500 people representing about 25 nations were in attendance at the opening session at the Auditorium-Rainier III, which faces the sumptuous palace of Prince Rainier and Princess Grace bordering the vividly colorful, sunny harbor. My intervention at the Plenary Session on *Human Cloning* caused little public debate. The prospect of human cloning is viewed around the world with such repulsion and moral condemnation (as a violation of the right of a child to be born with an “open future,” and an assault to human dignity) that the nations of the world seemed to have reached a tacit agreement against its being attempted or carried out. And the UNESCO *Universal Declaration on the Human Genome and Human Rights*, has made it clear in its recommendation, Article 11 that “Practices which are contrary to human dignity, such as reproductive cloning of human beings, shall not be permitted.” (The difficulties in enforcing the prohibition against human

“reproductive” cloning resided elsewhere, in the linkage of human replication cloning -the making of human clones- and research cloning -also called therapeutic cloning- or the making cloned embryos for stem cell research. Most countries have found it scientifically beneficial to do nuclear transfer cloning for research purposes but not reproduction cloning to make a clone child. They wanted to prohibit replication cloning or the making of human clones, and not research cloning.) At any rate, the ensuing round table discussion drifted away from human replication cloning and towards prenatal genetic screening – a practice that has become increasingly more sophisticated and is today being challenged by the deployment of new technological screens, such as the advent of the whole genome sequencing. To many in the audience, prenatal genetic screening has been associated with eugenics (or selected breeding) of past years. The growth of genetic knowledge has spurred a massive explosion in new screening technologies and the fear has been that this could provide eugenicists the tools they have been looking for to further their program, i.e., to weed out all “defective” or undesirable embryos or those unfit to belong to the “human race.”

In the USA, there has been no overarching principle to help decide whether an existing or a new prenatal screen should be routinely offered to patients. Prenatal screening policy has been hampered by ongoing abortion controversy, with the right-to-life position opposing any fetal screening on the basis that it could be used to justify prevention of a birth, and the pro-choice position affirming parental autonomy and favoring parental right to almost any fetal intervention, including unlimited access to information about fetuses. Because of the abortion controversy and to avoid charges of eugenics, prenatal counseling has been, by and large, non-directive, and respectful of parental decisions.

Citing his own practice, Israel Nisand publically defended his decision *not* to inform his pregnant patients of finding he considered inconsequential or inconclusive because of fear that patients may use it to terminate a wanted pregnancy.¹ Findings that indicate, for example, “minor” conditions, such as polydactyly, cleft-palate or lip, short limbs, and conditions that could be corrected at (or soon after) birth, or treatable in time of the screen; findings that reveal anomalous conditions of unknown origin or clinical significance may, for Nisand, be justifiably kept undisclosed to the pregnant patient. According to Nisand, disclosure of such findings may cause more harm than good to the pregnant patient (and her physician), and therefore be irresponsible. It would put physicians in an undesirable position of terminating (unnecessarily) a wanted pregnancy at the request of the pregnant patient who may fear that her fetus may have additional (and more severe) medical problems and physicians cannot guarantee her that it doesn’t. Nisand also explained, that “Out of 750, 000 pregnant women, 550, 000 undergo prenatal screening using maternal blood sample - a non invasive medical procedure which entails almost no risk. Ten percent of these women (or 55,000) may show an increased risk in Trisomy and will undergo an invasive procedure such as amniocentesis or chorionic villus sampling (CVS) to confirm or refute screening results. These procedures impose small but potentially significant risks (about 1 to 2%) to both the fetus and the mother. (Noninvasive screening of fetal aneuploidy are also available, such as ultrasound but have limited reliability). This means that, at the very least, a total of 550 fetuses will be aborted, 280 of which will be “true trisomy” and 270 fetuses will be healthy.... (in other words), for one “trisomy” identified, two healthy fetuses are aborted. This is unacceptable to physicians and tragic to patients who want so desperately a baby....(in all), These situations are tragic for those who want a child and of

serious concerns to physicians who find no satisfactory pleasure in aborting “healthy” fetuses. Unchecked disclosure of fetal findings undermines the original prenatal screening purpose which is to promote rather than prevent the birth of healthy babies.”^{1,2}

French philosopher-physician, Georges Canguilhem perceptively noted decades ago, that health, disease, and normality are not properties of the molecules or genes, and thus may not be inferred from molecular or genetic readings.³ These are the result of the interaction between the entire organism and its environment. And thus, at the molecular or sub-molecular level health, disease, and normalcy have no meaning. This observation may highlight the difficulties in determining the health of a fetus at the genetic (microscopic) level, and to articulate prenatal screening practice and policy on the basis of such a determination.

Though this might explain the reluctance to disclose all that is known about a fetus’ genetic make-up, it remains that I couldn’t disagree more with Nisand’s decision not to disclose to his pregnant patients what he knew about their fetuses. This struck me (and I recall, the entire audience in Monaco, as well) as utterly patronizing to women and ethically unacceptable. To withhold information because of doctors’ concerns that their patients may use it to make a decision they do not approve of, is, I was convinced, a violation of a woman’s right to autonomy and informed consent. It was, as I argued then, to favor beneficence, i.e. doing good based on the physician’s assessment of harm/benefit of information disclosure, at the expense of respect for persons and their rights to make an informed choice and self-determination.

I did not expect Nisand and colleagues to agree, and they didn’t. But I stood firm on my position, convinced that patients have the right to be informed of all we know about their fetuses. I vehemently argued that an ethical physician is responsible for carefully explaining risks and benefits of screening and the meaning of the findings, and when satisfied that the patient understood the information provided, the physician should respect the patient’s decision, even if in disagreement with it. I made it clear that non disclosure (or withholding) of prenatal information for any reason is ethically unacceptable. It violates the human rights of women, and undermines the fundamental tenets of medical ethics - respect for persons, autonomy and beneficence. Little did I know that Nisand’s proposition would deserve serious attention in light of new genetic screens.

2. DNA microarray prenatal screening: Challenges to informed consent

An opportunity to revisit this issue presented itself at the occasion of the 2003 international symposium on *Prenatal Diagnosis*, in Buenos Aires, sponsored by the *American College of Obstetricians and Gynecologists*. The question raised was whether the use of DNA microarray to screen fetuses could undermine the informed consent requirement in the doctor-patient relationships. My position in Monaco was clear: there is no finding, the insignificance of which is such that it warrants non-disclosure: Pregnant patients must be informed of what physicians know about their fetuses. But is this still feasible, practical or meaningful in light of new fetal genetic screens? This was the question I began to raise in Buenos Aires. What goes on here? The question belongs in the present tense because it is by no means settled. This is why⁴.

Historically, in the United States, screening practice has been conducted one condition at a time, beginning with the detection of Down syndrome. Women aged 35 years or older were

offered amniocentesis to screen for this syndrome. Selection of this cut-off age for screening was an attempt to balance the risk that a baby would be affected by a chromosomal disorder with the risk that spontaneous fetal loss would result from amniocentesis. Presently, prenatal screening includes use of maternal blood to test for α -fetoprotein, human chorionic gonadotropin, and β -unconjugated oestriol. Quad screening also tests for dimeric inhibin A.

The use of a maternal blood sample rather than amniotic fluid led to the recommendation that all pregnant women should be screened for Down's syndrome and neural-tube defects, such as anencephaly and spina bifida. Cost-benefit analysis, together with counseling of patients and informed consent, has been used to decide whether any additional disorders should be screened for. Every decision has been made—one disorder at a time—after a systematic examination of its implications by professional associations (such as the American College of Obstetricians and Gynecologists and the American College of Medical Genetics) that make recommendations for clinical application. These recommendations have been informed by the severity of the disorder and the accuracy of the screening interventions. In 2007, the American College of Obstetricians and Gynecologists recommended that *all* women who present for prenatal care before 20 weeks of gestation be offered screening and invasive diagnostic testing for aneuploidy, irrespective of age, and be counseled about the differences between screening and invasive diagnostic testing.

The introduction of DNA microarray technologies makes individual decisions about screening for each disorder impracticable and attempt at differentiating screening (i.e., interventions used to detect any anomaly or disorder in a population) and diagnostic testing (i.e. detection of a specific disorder in an individual patient) ineffectual. Massive amount of information of unknown importance will be generated, making information disclosure unrealistic, if not harmful. While genetic screening of adults allows time to rescreen to confirm findings and to interpret or ignore screening results, in prenatal care it might allow only weeks or even days for a critical decision on the viability of a pregnancy.

All screening methods produce both false positive and false negative results as above noted.⁵ Furthermore, anomalies that would have remained hidden during a lifetime “as non-activated tendencies in the absence of environmental challenges, and thus could have been ignored,”³ are now exposed, and examined. The search may be so extensive that no fetuses may be found to be “worthy of life.” But even with a 100% accuracy this would not help because there is no such a thing as “perfect” genome since all humans are programmed for death. Such quest for a “healthy” fetus, and therefore a healthy baby may result in having none. The more detailed the search for defects, the less likely it is to produce information that translates into useful knowledge about the health of a fetus, and thus the future health of the child. There are anomalies that should not be revealed and findings that are to be left silent for the benefit of the pregnant patient and her future child.

These considerations led me to conclude in 2003 that “unless physicians take a firm position against the use of these new genomic technologies in the contested terrain of prenatal screening they will probably have to surrender to parental requests for screening and disclosure either because they incorrectly assume that consumer choice is equivalent to autonomy or because of unjustified concern over being sued for wrongful birth, (i.e., not having disclosed enough information to make an informed choice about whether to continue a pregnancy).”⁴ This was, in essence, if not completely, the position adopted by Dr. Nisand, my colleague in Monaco, and against which I had argued, though in a different context. I came to realize that it was less about non-disclosure of genetic information than

the manner in which non-disclosure was achieved that fueled my arguments. Physicians should not have the authority to decide unilaterally what and whether to disclose based on what they think is a “minor” or a “serious” fetal condition. This decision belongs to the patient informed by her physician. Judging a condition as minor or serious is highly subjective, i.e., it rests on the subject, or the person who makes a judgment; that which is minor to one person may be serious to another. The difficulty is to give these concepts an objective (i.e. scientific) content.

3. Fetal DNA sequencing

The completion of the human genome project, a decade ago, failed to bring about the therapeutic breakthroughs it promised. Except for a small number of genetic conditions, the predictive power of gene sequencing as been low and detailed catalog of gene expressions has been so far of little interest. Misha Angrist, (a pioneer in *Personal Genome Project* , who had his genome sequenced) noted: “Time and again, the paucity of genomic information was striking: I would find mutations in genes that coded for proteins but the proteins’ ascribed functions would be so general and/or tentative as to be meaningless. In some cases, the proteins didn’t even have names, let alone functions assigned to them.”⁵

Regardless of paucity of success in assigning functions to proteins coded genes , research has intensified on successfully extracting cell free fetal DNA from maternal plasma samples in early gestation. Extracting cell free fetal DNA is difficult because these cells constitute less than 10% of total DNA in maternal plasma, and intact fetal cells are even less. The hope is that once fetal DNA can be easily (i.e. noninvasively), dependably and inexpensively obtained from maternal blood, it may be sequenced and would provide the genetic blueprint of a fetus, with actual and predictive power to reveal all that which may affect the health of the future child. George Annas has used the metaphor of “future diary” to illustrate it.

A close analogy to fetal DNA sequencing would be the “whole body scan,” or the computerized tomography (CT) body screen, also called computerized axial tomography (CAT) screening. This CT Body screen has been marketed as a preventive or proactive health measures for asymptomatic (“healthy”) individuals, to assist in detecting that which could potentially be harmful medical conditions. Theoretically, the whole body (CT) scan would permit a transparent view of the entire body and help detect harmful and deadly conditions in early stages, and therefore save lives. However, in practice, the risks outweigh the benefits. For example, risks may include a low rate of finding meaningful markers for actual diseases; confounding results because of “incidentomas” or pseudo anomalies, i.e. anomalies that are often not related to any disease and which may be benign^{6,7}; high costs of the procedure itself and the relatively high level of radiation exposure associated with it which may cause cancer later in life. No data have been presented to the FDA to demonstrate that the whole body CT scan is effective for screening or testing individuals without symptoms. FDA has not approved CT screen for whole body screening use. Nonetheless, physicians may decide that a asymptomatic patient may benefit from CT screening (“off-label” use of the medical device).

A similar scenario may unfold with regard to fetal DNA sequencing. This may create problems analogous to, but much more damaging than other methods of screenings, including DNA microarrays. Fetal DNA screens would combine questions similar to routine

screening methods, but the complexity of the results will add new elements that make disclosure of fetal information and subsequent parental decision about the pregnancy much more complicated. Users of these screens may either (incorrectly) think that there is nothing more important to know about their fetuses than their genomes if it is for health preservation and avoidance of diseases or may (unjustifiably) oversimplify gene expression and the predictive power of DNA sequencing.

Deploying the whole fetal genome in prenatal practice is controversial and difficult to interpret.⁸ It is controversial because it could be damaging to the future child since it does constitute the child's permanent medical record and may be used to discriminate against the child, once born. It may be misleading and falsely reassuring because of false positive and false negative findings. Moreover, patients are notoriously ignorant about genetics, and nonetheless, may request direct access to the fetus' genomic data, just as they may have direct access to their own genome. And geneticists, themselves are divided on what conditions should be considered serious, and have conflicted views on genomic findings, which limit their capability to reasonably inform and counsel their patients. Genomic data are difficult to interpret, and the time spent to sift out and interpret these data in way that could be meaningful to patients may be so enormous as to be impractical.

Direct- access to fetal genomic data may exacerbate these problems. Direct-to-Consumers genetic testing companies have used different strategies to minimize the difficulties inherent to the practice and help adults navigate their genetic screens. For example *23&me* and *Navigenics* have provided customers with inexpensive and easy to understand genetic information, including a basic understanding of the meaning of predisposition to specific disorders and ethnic ancestry, but have offered little scientific explanation. *Sciona* genetic firm has chosen to link genetic information to a customer's lifestyle, and *DNA Direct* supplies customers with access to qualified doctors to help interpret genetic test results. In all, profit rather than scientific knowledge has been the immediate driving force.

Genes operate through a series of instructions that may be spelled out, but cannot be fully predicted and explained. The deeper we delve into our genome, the more opaque it becomes. It may be possible to retrospectively determine what might have predisposed a person to actual disorders. But no model exists that may help to comprehensively predict how genes respond to challenges, interact with the environment and restructure themselves to ensure health and survival.⁹ Genetic markers commonly associated with a specific disease say little about a future child's health or the seriousness of future diseases.

Nonetheless, prospective parents may request the whole genome sequencing of their fetuses, once it is feasible and affordable (or even if they must pay the extra cost) because they believe it will give them all the information they need about their babies' future health. Just as Bill Clinton, then president, believed it was a good idea to give parents at the birth of their newborn, a CD with the sequencing of the child's entire genome, we too believe that it is a good idea to give prospective parents a CD of fetal cell DNA sequencing that they may explore as the same time the fetus develops *in utero*. But, of course, there is a major difference between information that relates to a child having full legal and moral rights, including a right to privacy, and genomic information of a not- yet- born child having interests in life and health, but no right to be born. One may be seriously concerned at the prospect that prospective parents might select their future children by genetically auditioning them via fetal DNA sequencing, before permitting them to be born. And there are also questions about parents' rights to know and the child's right to privacy. What

should physicians do to reasonably assist and counsel their pregnant patients? Should they respond positively to request by prospective parents and adopt a market-based genomic model or consumer choice? Should they remain neutral or should they take action to help ensure that fetal genomic information, if and when it is part of routine prenatal care, constitutes knowledge that is reasonably understandable and meaningful, and when put in a realistic context reflects the actual concerns of their pregnant patients? Of course there is always the option of not offering prospective parents whole genome screens of their fetuses because of the many confounding variants of uncertain or unknown clinical utility, validity, or significance. Results of these screens, if reported to the pregnant patient may caused a level of stress and anxiety that may put the pregnant patient and the entire pregnancy in jeopardy. However, this option strikes me as untenable, in a culture of “laissez faire” in assisted reproduction.

Other alternatives include offering routine genome screening of fetuses and let physicians decide what findings to disclose, based on professional standards developed by relevant medical practice standards committees – the *Professional Standards Model*, or letting the pregnant patient decide about whether to be screened and what information to have access to – the *Consumer Model*.

Professional Standards Model, gives physicians the authority to decide on disclosure of findings they believe may cause more harm than good, based on their medical judgment. This Model, in effect prioritizes harm-benefit assessment of genomic screens over the parental right to informed consent, and is based on the ethical concept of beneficence, Doing good. , i.e., a procedural mechanism that evaluates the overall benefit of the genetic intervention over harm. This Model substitutes the question of right to informed consent with a welfare question, i.e. what should be done to promote the best interest of patients. The first question is relevant to the pregnant patient; the second question is relevant to physicians who decide what should be done to protect the interest of patients. information and genetic findings are worth disclosing to the pregnant patients. It marginalizes (even displaces) the rights of prospective parents in favor of the welfare question and is mostly procedural rather than substantive. It conflates the concepts of autonomy (individual rights) and beneficence (doing good, maximizing benefits, minimizing harm).

The *Consumer Model* alternative leaves the decision about whether to be screened, and what information to have access to, to the pregnant patient. It is probably a model that is most consistent with American values since it favors individual right to autonomy and consumer choice, permits the pregnant woman to manage her pregnancy, decides whether or not to be screened, the amount of information she needs and whether and when to access this information. A genetic counselor is necessary before allowing access to genomic data and afterwards for interpreting these data. Because genomic information is inherently information overload, and the majority of genomic findings is not clinically useful or meaningful and readily applicable, patients will need to know in advance how deeply they want to delve into their fetuses' genome. This is an extremely difficult task, and virtually every geneticist - physician as well as expert commentator has insisted that anyone who wants to access genomic data must be accompanied by serious genetic counseling services. This makes sense.

One way to accomplish this task (which should be discussed, but currently strikes me as the most reasonable) would be to routinely offer fetal genomic screening and disclose information about the specific conditions which prospective parents themselves are most

concerned about (e.g., Down syndrome, neural tube defect), including conditions that have caused pain, disability and suffering to previous children in the family. Other conditions may be disclosed such as those that have been qualified as “serious” by prospective parents, by a regulatory agency in terms of the disability, pain and suffering they cause (as in Britain) or by law because they are fatal at an early age, and incurable at the time of the screen (as in France). Exception to disclosure, could include, for example, conditions considered “serious” but predictably may develop in adulthood or late in life, such as breast cancer, Alzheimer’s, Parkinson’s etc... This is because, any documentation on these conditions may become part of an individual’s medical record and could be used to stigmatize or even discriminate against the individual patient. This also raises the question of privacy protection right, or to put it another way, limits of parental rights to know.

Parents would have access to the remaining genomic data in the fetal genome (if they so desire), or could be provided with information attached, (e.g., via a website or flash drive), but only after they had undergone some education/counseling by a qualified genetic counselor. The counselor will assist patients after they have reviewed the genetic data themselves, and continue to assist them afterwards.

I favor this third model because it leaves the decision about whether to be screened, and what information to have access to, to the pregnant patient. This model recognizes the fundamental ethical principle of respect for persons, their rights to autonomy and self-determination within the doctor- patient relationship, but also taking into account the physician’s assessment of the patient’s welfare and wellbeing. But this assessment does not trump the fundamental rights of the individual patient. This model is not the exact equivalent to consumer choice, nor is it paternalistic but should be viewed as a crucial part of informed consent.

Genome sequencing makes enormous amount of information available to pregnant patients who want it and are willing to responsibly undertake genetic education and counseling. Genomic data, put in context, can help pregnant patients make an informed choice about their pregnancies in accordance with their values and preferences.

There is a caveat, however. Because fetal genomic screens gives us access to information contained in the entire fetal genome, it may be less costly than using DNA chips or microarray technology. To then decide on the conditions we may want to screen for may be, therefore, counterproductive and counterintuitive. So, if choosing those specific conditions that should be disclosed is the recommendation, we may want to explore the reasons why, in the first place, we give legitimacy to genomic screens in prenatal care. These reasons may weaken as we discover that there are actually very few genetic conditions prospective parents may want to know about when they look at genetic screens of their fetuses, and these conditions do not require the sequencing of the entire genome; they may simply require good family history practice.

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Two new factor have been added to the ideological change in the second half of the past century: the “ecological impact” of humankind on the environment due to the population increase; and the “ innovative impact of science, first with atomic physics, which introduced the scission of the fundamental unit of matter, the atom, and then witch molecular biology, which led to the decoding of genetic information and intervention of biological engineering that annihilate our concepts of individual and species as fundamental units in biology. This stage of fundamental rethinking is however overshadowed by the threat of ecological disaster and catastrophic population increase, which not only impose limits to development, but undermine the very survival of Humankind. The future survival our species in fact depends on the interaction between its reproductive characteristics and the productivity of the territory, which, even if increased by the intellectual capability of the human brain, has intrinsically limits. The adaptive choices (which are also biotechnological and biomedical) of the interaction between human population and the natural ambience is the conceptual basis of the new discipline “Global Bioethics”.

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