Ethics assessment in different fields

Genetics

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Annex 2.c.6
Ethical Assessment of Research and Innovation: A Comparative Analysis of Practices and Institutions in the EU and selected other countries
Deliverable 1.1

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Contents

1 Genetics

1.1 Basic description[1]

Genetics or molecular biology is the branch of biology that deals with the principles and mechanisms of heredity and with the genetic contribution to similarities and differences among related organisms. It is a common topic of modern medical and biological research (Different of genomic, see below).

1.2 Sub-specialties and tools

1.2.1 Clinical genetics

Clinical genetics is the practice of clinical medicine with particular attention to hereditary disorders.

Metabolic (or biochemical) genetics involves the diagnosis and management of inborn errors of metabolism in which patients have enzymatic deficiencies that perturb biochemical pathways involved in metabolism of carbohydrates, amino acids, and lipids.

Cytogenetic is the study of chromosomes and chromosome abnormalities. Nowadays, molecular technologies are becoming widely used for this purpose.

Molecular genetics in medicine is the science of the biological characteristics of the human genome that are of relevance for the etiology, diagnosis, treatment, and prevention of disease. (3). Molecular genetics involves the discovery of and laboratory testing for DNA mutations that underlie many single gene disorders and epigenetic abnormalities.

Mitochondrial genetics concerns the diagnosis and management of mitochondrial disorders, which have a molecular basis but often result in biochemical abnormalities due to deficient energy production.

Genomics is a discipline in genetics that applies recombinant DNA, DNA sequencing methods (exome and genome-wide sequencing (WES/WGS,)), and bioinformatics to sequence, assemble, and analyse the function and structure of genomes (the *complete* set of DNA within a single cell of an organism)[2,3]. Genome medicine and synthetic biology are two new applications of genomics.

Human genetics is the study of inheritance as it occurs in human beings.

Medical genetics/Genetic medicine[4] is the specialty of medicine that involves the diagnosis and management of hereditary disorders. Medical genetics refers to the application of genetics to medical care and differs from Human genetics. Human genetics is a field of scientific research that may or may not apply to medicine. For example, research on the causes and

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[1] http://en.wikipedia.org/wiki/Genomics

[2] National Human Genome Research Institute, “A Brief Guide to Genomics", Genome.gov. http://www.genome.gov/18016863

[3] Klug, William S, Michael R. Cummings, Charlotte A. Spencer, Michael A. Palladino, *Concepts of Genetics* (10th ed.), San Francisco, Pearson Education, 2012.

[4] http://en.wikipedia.org/wiki/Medical_genetics. Medical genetics

inheritance of genetic disorders would be considered within both human genetics and medical genetics, while the diagnosis, management, and counselling of individuals with genetic disorders would be considered part of medical genetics.

Genetic medicine is a newer term for medical genetics and incorporates areas such as gene therapy, personalised medicine, and the rapidly emerging new medical specialty, predictive medicine.

1.2.2 Diagnostic

Genetic testing is a type of medical test that identifies changes in chromosomes, genes, or proteins.

1.2.3 Treatment

Gene therapy is the genetic engineering of humans by replacing defective human genes with functional copies. This can occur in somatic tissue or germline tissue. If the gene is inserted into the germline tissue it can be passed down to that person's descendants.[5]

1.2.4 Research

DNA databanks are databases of DNA data. A DNA database can be used in the analysis of genetic diseases, genetic fingerprinting for criminology, or genetic genealogy

Genome/Exome -wide sequencing: Whole genome sequencing is a laboratory process that determines the complete DNA sequence of an organism's genome at a single time. This entails sequencing all of an organism's chromosomal DNA as well as DNA contained in the mitochondria. Exome sequencing is an efficient strategy to selectively sequence the coding regions of the genome as a cheaper but still effective alternative to whole genome sequencing. Exons are short, functionally important sequences of DNA which represent the regions in genes that are translated into protein. [6]

Genome-wide association study: A genome-wide association study is an approach that involves rapidly scanning markers across the complete sets of DNA, or genomes, of many people to find genetic variations associated with a particular disease.[7]

1.2.5 New frontiers

Reproductive technology encompasses all current and anticipated uses of technology in human and animal reproduction, including assisted reproductive technology, contraception, prognostics and others.

Genetic enhancement: In general, genetic enhancement refers to the transfer of genetic material intended to modify non-pathological human traits. The term commonly is used to describe efforts to optimise attributes or capabilities -- perhaps by raising an individual from standard to peak levels of performance[8].

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[5] http://en.wikipedia.org/wiki/Genetic_engineering

[6] http://en.wikipedia.org/wiki/Whole_genome_sequencing

[7] https://www.genome.gov/20019523. Genome-wide association studies

[8] http://www.genome.gov/10004767.

"The term "human enhancement" encompasses a range of approaches that may be used to improve aspects of human function (e.g. memory, hearing, mobility). This may either be for the purpose of restoring an impaired function to previous or average levels, or to raise function to a level considered to be "beyond the norm" for humans."[9] To define what is meant by normal or when a genetic intervention is "enhancing" or "therapeutic" or how the benefit from a genetic enhancement should be calculated in comparing its risks and benefits are some of challenges of Genetic enhancement.

1.3 Genetics and life science

1.3.1 Genetic engineering/transgenic[10]

Genetic engineering, also called genetic modification, is the direct manipulation of an organism's genome using biotechnology. Genetic engineering alters the genetic makeup of an organism using techniques that remove heritable material or that introduce DNA prepared outside the organism either directly into the host or into a cell that is then fused or hybridised with the host. This involves using recombinant nucleic acid (DNA or RNA) techniques, cloning and stem cell research (although not considered genetic engineering, are closely related and genetic engineering can be used within them), synthetic biology is an emerging discipline that takes genetic engineering a step further by introducing artificially synthesised genetic material from raw materials into an organism[11].

In Europe genetic modification is synonymous with genetic engineering. Within the scientific community, the term *genetic engineering* is not commonly used; more specific terms such as *transgenic* are preferred.

In medicine genetic engineering has been used to mass-produce insulin, human growth hormones, follistim (for treating infertility), human albumin, monoclonal antibodies, ant haemophilic factors, vaccines and many other drugs.

Genetic engineering is used to create animal models of human diseases and test potential cures[12].

1.3.2 Green genetics and plant breeding

Plant breeding is the science of improving the heredity of plants for the benefit of humankind. The transition from wild types of plants to cultivated ones started in the early history of man. Wild and cultivated plants differ in yield, content, maturation, resistance to pathogens, insect pests, heath and drought, soil stress and many other traits.

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[9] The Academy of Medical Sciences, "Human enhancement and the future of work", Report from a joint workshop hosted by the Academy of Medical Sciences, the British Academy, the Royal Academy of Engineering and the Royal Society, November 2012. https://royalsociety.org/uploadedFiles/Royal_Society_Content/policy/projects/human-enhancement/2012-11-06-Human-enhancement.pdf

[10] http://en.wikipedia.org/wiki/Genetic_engineering

[11] Andrianantoandro Ernesto, S. Basu, D.K. Karig, R. Weiss, "Synthetic biology: new engineering rules for an emerging discipline", *Mol Syst Biol,* Vol.2, May 2006.

[12] http://en.wikipedia.org/wiki/Genetic_engineering - cite_note-76

As Acquaah describes in Principles of Plant Genetics and Breeding: "Plant breeding is a deliberate effort by humans to nudge nature, with respect to the heredity of plants, to an advantage. The changes made in plants are permanent and heritable. This effort at adjusting the status quo is instigated by a desire of humans to improve certain aspects of plants to perform new roles or enhance existing ones."[13] He stresses that terms plant breeding and plant improvement are often used alternately and the whole process aims to make plants "more useful to humans".

A basic type of plant breeding is selection and crossing – breeders select plants with desirable traits and reproduce them. Some examples of modern breeding methods are: breeding of polypolids, mutation breeding and generation of haploids.

"Modern plant breeding is a discipline that is firmly rooted in the science of genetics. Plant breeding as a human endeavour has its origins in antiquity, starting off simply as discrimination among plant types to select and retain plants with the most desirable features. Remarkably, the practice of selection remains the primary strategy for crop improvement, even though many technologically advanced techniques have been added to the arsenal of the modern plant breeder. Plant breeding differs from evolution in that the former is planned and purposeful."[14]

The biggest challenges of plant breeding are:

- Finding and fixing novel allele combinations (QTL – quantitative trait loci)
- Finding and fixing desirable combinations for market release
- Monitoring and controlling possible gene flow that might occur

The crucial step in this process is exploring, exploiting and enhancing genetic variation which can only be conducted with new technologies derived from disciplines such as: molecular biology, genetics, molecular genetics, genomics, recombinant DNA etc. For example, for random and targeted mutagenesis researchers may use TILLING (targeted induced local lesions in the genome). This may lead to creating new alleles by site-specific mutations in targeted genes (chlorosolfuron resistance in rice and tobacco, imidazolinone resistance in maize).

A large number of science disciplines directly impact plant breeding, and several are closely associated with it, like "plant breeding, genetics, agronomy, cytogenetics, molecular genetics, botany, plant physiology, biochemistry, plant pathology, entomology, statistics, and tissue culture. Knowledge of the first three disciplines is applied in all breeding programs." [15]

Genetically engineered plants are generated in a laboratory by altering their genetic makeup. Adding one or more genes to a plant's genome using genetic engineering techniques usually does this. GM technology is still developing, with plastid transformation as promising tool for the eco-friendly production of bioactive proteins.

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[13] Acquaah, G., *Principles of Plant Genetics and Breeding,* Blackwell Publishing Ltd, 2007.
[14] Ibid.
[15] Ibid.

1.4 Values and principles

The basic principles of autonomy, dignity, integrity and vulnerability imply a universal protection of the human person with intrinsic value as an end-in-itself. The legal protection of the human body is carried out in the European Commission, the European Parliament and in the Council of Europe, which has developed a Convention on Human Rights and Biomedicine to be ratified by the various European Countries. The concept of human dignity is central to international bio law.

- Dignity[16] is the state or quality of being worthy of honour or respect and moral status. There are several contested conceptions of dignity in European culture. Dignity is identified with the capacity for autonomous action, the capacity for experiencing pain or pleasure, being human (in the biological sense) or being a living organism or system. Acknowledging various definitions, our view is that it is possible to argue successfully that human beings have duties towards the nonhuman part of living nature.
- Autonomy and the Right to Self-Determination. Respect for persons – the duty to respect the autonomy of research participants and protect those with reduced capacity. Respecting autonomy entails the provision of sufficient information to research participants so as to obtain their free, informed, and ongoing consent.
- Informed consent. Manifestation of the free and conscious volition that is validly emitted by a capable person or through an authorised representative, after adequate information has been provided
- The Obligation Not To Do Harm. Non-maleficence – the duty to minimise and prevent harm to research participants.
- Beneficence. The duty to maximise net benefits for research participants and for society as a whole, while advancing knowledge.
- Privacy/confidentiality. Data and Privacy Protection
- Integrity[17]. The idea of integrity expresses the untouchable core, the basic condition of dignified life, both physical and mental, that must not be subjected to external intervention. Therefore, respect for integrity is respect for privacy and in particular for the patient's understanding of their own life and illness. Integrity refers to the coherence of life of beings with dignity that should not be touched and destroyed.
- Equity[18]. The value of equity requires equal respect for the entitlements, interests and preferences of others, including in questions of fair and just distribution of expected benefits and costs.
- Solidarity.[19] The value of solidarity requires the avoidance of social divisiveness and exploitation, and the active promotion of the welfare of those

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[16] http://www.oxforddictionaries.com/definition/english/dignity

[17] Rendtorff, Jacob Dahl, and Peter Kemp, *Basic Ethical Principles in European Bioethics and Biolaw, Autonomy, dignity, integrity and vulnerability (Vol I),* Centre for Ethics and Law, 2000. ISBN-10: 849235254X.

[18] Nuffield Council on Bioethics, "Emerging biotechnologies: technology, choice and the public good", Chapter 4, London, 2012.
http://www.nuffieldbioethics.org/sites/default/files/files/Emerging_biotechnologies_Chapter4.pdf

who are less advantaged, including bearing costs of research and knowledge gathering on behalf of others.

- Distributive Justice implies the distribution of risk and burden on the one hand and benefit on the other be fair.
- Vulnerability[20] expresses two basic ideas. It expresses the finitude and fragility of life which, in those capable of autonomy, grounds the possibility and necessity for all morality. Vulnerability is the object of a moral principle requiring care for the vulnerable. The vulnerable are those whose autonomy or dignity or integrity are capable of being threatened. As such all beings who have dignity are protected by this principle. But the principle also specifically requires not merely non-interference with the autonomy, dignity or integrity of beings, but also that they receive assistance to enable them to realise their potential.
- Principle of non-commercialisation of the human body and its elements, that is: prohibition of the sale of human organs, embryos and genes.
- Reciprocity – the duty to promote trust between researchers and research participants.
- Responsibility. A duty, obligation or liability for which someone is held accountable.
- Right not to know[21]. Individuals may have a legitimate interest in not knowing their genetic make up to avoid serious psychological consequences; this interest, far from being contrary to autonomy, may constitute an enhancement of autonomy; the right not to know cannot be presumed, but must be "activated" by the individual's explicit choice, and , that this is not an absolute right, in the sense that it may be restricted when disclosure to the patient is necessary in order to avoid a risk of serious harm to third persons.
- Sustainability - avoiding significant or irreversible depletion of non-renewable natural resources or damage to ecosystems or the environment
- Respect for reproductive autonomy.
- Responsible Research and Innovation[22]. The term is new, so definitions are evolving. The debate is currently centred on science and technology-based research and innovation, in particular on emerging technologies - notably nanotechnologies, genomics, synthetic biology and geo-engineering. However, the use of the term "innovation" is commonly used to describe the application of any type of invention which significantly improves products, systems or services. Ethical assessment - ethical assessments may be considered as part of

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[19] Nuffield Council on Bioethics, "Emerging biotechnologies: technology, choice and the public good", London 2012. http://nuffieldbioethics.org/emerging-biotechnologies/emerging-biotechnologies-chapter-downloads

[20] Rendtorff, Jacob Dahl, and Peter Kemp, *Basic Ethical Principles in European Bioethics and Biolaw, Autonomy, dignity, integrity and vulnerability (Vol I),* Centre for Ethics and Law, 2000. ISBN-10: 849235254X.

[21] Andorno, R., "The right not to know: an autonomy based approach", *J Med Ethics.* Vol.30, 2004, pp. 435–440.

[22] European Commission, "Options for Strengthening. Responsible Research and Innovation", Report of the Expert Group on the State of Art in Europe on Responsible Research and Innovation, 2013.
http://ec.europa.eu/research/science-society/document_library/pdf_06/options-for-strengthening_en.pdf.

technology assessment or separately. This process explores ethical implications of pathways and trajectories.

- Caution. The virtue of caution means that the greater the degree of exposure to uncertainty and ambiguity, the greater the responsibility deliberately to gather deeper and more extensive knowledge prior to making policy commitments.

1.5 Values and principles for Green genetics

Plant genetics, Green genetics and Plant Breeding are used denoting plants modifications both using the traditional crops modifications and modern biotechnology methods including genetic engineering that allows the transfer of genes from one plant, or even animal organism, to the other plant. Ethical values and principles could be seen from at least two different dimensions – one addressing the impact on the biodiversity and ethics of the plant modifications that could not happen naturally outside the lab, and the other looking at the effects on humans and the whole ecosystem that food containing GM plants is introducing. The former can be evaluated through the principle of sustainability and the potential impact on the whole ecosystem, as well the potential disturbance of the environmental balance. Regarding the later, we can discuss the principle of the general welfare and interest of citizens, as well the people's rights, especially their freedom of choice as consumers. The principle of distributive justice can address the fair share of the consequences to the whole community.

Most often posed questions are: effects of GM crops on health and environment, the role of GM crops in feeding the world population and solving the problem of "world hunger", whether GM food should be labelled, what should be the role of government regulations in the process of GM food production and market (regulations vary in a given country on the intended use of the products of the genetic engineering), effects on pesticide resistance. All the above addresses the values of "transitional" Non-maleficence of GM plants that could transfer modifications to the conventional crops and wild plants and also impacting the food chain of humans and animals. Also, the value of Solidarity could be referenced in connection to the welfare of less privileged ones in terms of producing the sufficient food amounts at one hand, and indirectly forcing people with low income to buy more affordable GM products before all side effects are known and the policy commitments made (Caution principle).

As Acquaah argues: "It is often said that these modern technologies for plant genetic manipulation benefit the developing countries the most since they are in dire need of food, both in quantity and nutritional value. On the other hand, the intellectual property that covers these technologies is owned by the giant multinational corporations. Efforts will continue to be made to negotiate fair use of these technologies. Appropriate technology transfer and support to the poor third world nations will continue, to enable them to develop capacity for the exploitation of these modern technologies."[23]

2 Ethical issues

Genetics and genomics applications have been considered carefully, with special attention to the release of information about the test and test results, the confidentiality of genetic

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[23] Acquaah, G., *Principles of Plant Genetics and Breeding,* Blackwell Publishing Ltd, 2007.

information, the voluntariness of the test request , the express, free and informed consent, the responsibility towards blood relatives and the psychological impact of the test and counselling. Results may cause stigmatisation, discrimination, family discord and psychological distress, thus the test provider should supply easily understood, accurate, appropriate and adequate information, which is also available in accessible formats, to consumers before obtaining consent for a genetic test[24].

Ethical issues most often discussed in the literature for the particular field of genetics/ major ethical issues have to do with:

- Biotechnology, new developments in genetics, genomics
- Human genetic, databases and related issues, e.g. management of data collection, bio banks, and health registers,
- Share information,
- Research and clinical practice, and
- Use of the biotechnology in green genetics.

2.1 Data Protection. Registers. Bio banks.

- Potential identification of personal data. Genetics and genomics data (genotyping will become routine) will be integrated as electronic health records (EHRs) and other databases, thereby increasing the potential identification of personal data.
- Discrimination. Predictive genetic tests should not be carried out for insurance purposes. Measures to ensure respect for the fundamental rights of persons without discrimination in the context of the insurance contracts should be implemented.
- Cession data/ biological sample a third party. Access, governance, data enclaves, safe harbours ("havens") and international data transfer should be considered.
- Limits of autonomy and right not to know. One of the reasons why new genetics challenge individualistic principlism is that genetic material reveals information not just about the individual but also about consanguineous relations and continues to be potentially identifying when compared with database information, thereby challenging the traditional mainstays of medical ethics – those of informed consent and confidentiality upheld by autonomy and beneficence.
- Return of research results and incidental findings. When, how, by who, should disclosure these results, especially in the context of new genetic technologies and genetic testing involving minors.
- Data Protection in internet-based genetic testing is often insufficient. Genetic tests via the Internet pose ethical problems pertaining to patient self-determination, counselling, and data protection.

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[24] Human Genetics Commission (UK), "A Common Framework of Principles for direct-to-consumer genetic testing services", London, 2010. http://www.sashg.org/documents/HGC-UK-Policy-on-DTC-testing.pdf

2.2 Biotechnology, new developments in human genetics

2.2.1 Novel neurotechnologies[25]

Principles: beneficence and caution. These encompass not only protection against the potential safety risks of interventions, but also those interests associated with unintended impacts on privacy and the promotion of autonomy both in treatment-specific decisions and in the wider context of patients' lives. There are also important public interests in equity of access to the products of innovation, the preventing of stigma and protecting and promoting public understanding and trust in novel neurotechnologies.

The special status of the brain therefore provides both a reason to exercise beneficence by finding ways to intervene when injury or illness causes brain disorders, and a reason for caution when we are uncertain what the effects of this will be

Five key interests must be considered in relation to novel neurotechnologies:

- Protection of safety, taking into account risks alongside expected benefits.
- Promotion of autonomy (both in the sense of supporting people's capacity to make their own decisions and in the sense of protecting their sense of who they are).
- Protection of people's privacy, bearing in mind that some devices may collect sensitive personal data.
- Promotion of equity both in terms of access to innovative products, and in addressing social stigma and discrimination.
- Promoting public understanding of and trust in novel neurotechnologies.

2.2.2 Genetic testing.

Principles: autonomy, Non-maleficence. Recent developments in genetics have created expanding possibilities for genetic testing. The exome/genome-wide sequencing and the use of non-invasive prenatal test (NIPT) for genetic screening represent new ethical challenges increased by the provision of genetic testing services directly to the consume (tests such as direct to consumer/foetal sex determination/ discrimination).[26]

Genetic testing in minors: Special attention has raised performing TG in children. The opinion of the minor shall be taken into consideration as an increasingly determining factor in proportion to his or her age and degree of maturity. The parents (or legal guardians) should participate as much as possible in the decision-making process regarding the health care of their children. If the decision of the minor's parents or legal guardians is not in the direct benefit of the minor, health care professionals have the responsibility to defend the interests of the minor.

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[25] Nuffield Council on Bioethics, "Novel neurotechnologies: intervening in the brain a guide to the report", June 2013.ISBN:978-1-904384-29-8.
http://nuffieldbioethics.org/sites/default/files/Novel_neurotechnologies_report_PDF_web_0.pdf

[26] Deans, Zuzana, Melissa Hill, Lyn S. Chitty and Celine Lewis. "Non-invasive prenatal testing for single gene disorders: Exploring the ethics", *European Journal of Human Genetics,* Vol.21, 2013, pp. 713–718.

Predictive genetic testing in minors: Major discussions with regard to predictive genetic testing in minors, incidental and intentional carrier testing, particularly predictive genetic testing for adult-onset disorders, for preventable or treatable childhood-onset disorders, for unpreventable or untreatable childhood-onset disorders and carrier testing have been raised.

Genetic counselling (GC): GC is always required (and it should be ensured) when considering genetic testing and the counselling sessions should be oriented to empower individuals and families to make their own decisions. Practitioners and policymakers should continue to strive for consistent service provision, and high-quality information giving and counselling by genetic counsellors or other appropriately trained healthcare professionals who are uniquely placed to promote informed choice.

2.2.3 Genetic therapies

Principles: beneficence, caution, justice, uncertainty, ambiguity. There are also ethical concerns should the technology be used not just for treatment, but for enhancement, modification or alteration of a human beings' appearance, adaptability, intelligence, character or behaviour. The distinction between cure and enhancement can also be difficult to establish.

Economics - Cost of new genetic therapies should be discussed and considered from the point of view of justice.

In the context of recent developments in the germline gene therapy (it is also referred to as germline genetic engineering) of mitochondrial disease, there are a number of ethical and policy questions to consider:[27]

- Is mitochondrial DNA part of the germline? How does germline modification by nuclear DNA or mitochondrial DNA differ, and are those differences of ethical significance?
- Is mitochondrial DNA associated with identity? If so, what is the nature of the connection and how might it affect ethical assessment of mitochondrial DNA alteration?
- Which is at issue when considering key ethical distinctions: the principle of germline modification, or the degree of germline modification? How should we characterise a degree of germline change?
- Should mitochondrial donation be thought of as a type of "transplant," or as a "systemic therapy"?
- What ethical concerns are raised by the possible use of mitochondrial donation for non-medical purposes?
- If mitochondrial donation is approved for medical purposes, what government policies or professional guidelines should be in place to promote ethically sound practices?

2.2.4 Genetics and human behaviour

Principles: auto-determination, human dignity, dignity of humanity, stigmatisation.

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[27] Frankel, M.S. and B.T. Hagen, "Germline Therapies", *Nuffield Council on Bioethics,* London, 2011. http://www.nuffieldbioethics.org/sites/default/files/files/Germline_therapies_background_paper.pdf

Two general categories of neuroethical issue can be discerned: those emerging from what we can do and those emerging from what we know.

In the first category are the ethical problems raised by advances in functional neuroimaging, psychopharmacology, brain implants and brain-machine interfaces. In the second category are the ethical problems raised by our growing understanding of the neural bases of behaviour, neural mechanisms of decision making, free will, moral and legal responsibility, and moral judgement.

However, some authors there is no reason for adherents of behavioural genetics, or critics, to regard it as offering a radically new way of understanding human life which threatens to undermine the dignity of humanity. It complements, and does not displace, the familiar social sciences, the humanities and indeed our ordinary understanding of behaviour.[28]

2.2.5 Reproductive technology

Principles: autonomy, human dignity, caution, responsibility.

Many issues of reproductive technology have given rise to bioethical issues, since technology often alters the assumptions that lie behind existing systems of sexual and reproductive morality.

Also, ethical issues of human enhancement arise when reproductive technology has evolved to be a potential technology for not only reproductively inhibited people but even for otherwise reproductively healthy people.

Prenatal sex selection for non-medical reasons, Ethics and Policies for Human Cloning, Ethical Dilemmas in Stem Cell Therapy, Gene Therapy, germline therapies and specific issues with regard to mitochondrial donation and clinical practice and about if the Genetic Engineering of Humans should be allow are some of the relevant ethical issues regarding Reproductive technology and new embryology.[29,30]

Mitochondrial DNA (mtDNA) donation procedures evoke further concern with respect to informed consent because they involve not only to patient or subject at hand, but also future generations and to extend proxy consent across multiple generations tit may be a stretch. Similarly, the intergenerational nature of hereditable genetic modification suggests a higher threshold of safety because treatment may impact all succeeding generations.

2.3 Limits/challenges of human genetics

It is necessary to work for making a clear distinction between genetic enhancement and genetic therapy and to pay attention to issues of justice in debates about the ethical, legal and social implications of genomic technologies. Specifically,

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[28] Nuffield Council on Bioethics, “Genetics and human behaviour. The ethical context”, October 2002. http://www.nuffieldbioethics.org/sites/default/files/Genetics%20and%20human%20behaviour.pdf

[29] Dondorp W., G. De Wert, G. Pennings, F. Shenfield, P. Devroey, B. Tarlatzis, P. Barri, K. Diedrich. “ESHRE Task Force on ethics and Law 20: sex selection for non-medical reasons”, *Human Reproduction*, Vol. 6, 2013, pp.1448-54.

[30] Gilbert, Anna Tyler, Emily Zackin, F. Scott, *Bioethics and the New Embryology: Springboards for Debate,* Sinauer, 2005.

- What are the “eugenic” implications of the new genetics? genetic perfectionism can lead to eugenics respect for the difference and freedom of the individual
- Germline therapy that makes possible the active genetic manipulation of future human generations.
- Quimeras. Would it be acceptable to generate chimeras in the future? Would it be acceptable manipulation of the genome of human embryos for research purposes?

2.3.1 The ethics of patenting DNA

Classical exclusion from patentability by contradiction to public order and morality has been broadened his field absolute limits (e.g. human cloning procedures or modifying genetic identity of human or animal).

Concerns have been articulated relating to the effects of awarding exclusive rights, albeit time-limited, in this field. Conversely, it has been argued that patents on DNA are necessary to stimulate investment in research and development on new healthcare products and processes, to assure protection in the market for new products and to facilitate the disclosure of scientific information.

Four potential problems that may arise as a result of patents that assert rights over DNA sequences being granted are:

- Preventing or hindering development of new or improved medicines and treatments;
- Limiting access to healthcare by increasing the cost of diagnostic [tests] and treatment for certain diseases;
- Exploiting information and materials and inhibiting their free exchange between researchers;
- Involving parties in extensive and costly legal battles.

Therefore, on one hand the patentability of genes may have adverse consequences for the future of medical research; on the other, the appropriation of the gene is contrary to the equitable sharing of benefits arising from research.[31]

2.3.2 The ethics of animal use in research[32]

Principles: Refinement, Reduction and Replacement. Researchers from Europe has created a Basel Declaration in which is stressed that research should adhere to the 3 R's (Refinement of scientific techniques, Reduction in numbers of animal used, and Replacement of animal procedures with non-animal procedures) and is called for more trust, transparency and communication on animal research.

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[31] Nuffield Council on Bioethics, “The ethics of patenting DNA. A discussion paper”, London, 2000. http://www.nuffieldbioethics.org/sites/default/files/The%20ethics%20of%20patenting%20DNA%20a%20discussion%20paper.pdf

[32] Nuffield Council on Bioethics, “The ethics of research involving animals”, May 2005. http://nuffieldbioethics.org/sites/default/files/The%20ethics%20of%20research%20involving%20animals%20-%20full%20report.pdf

Transgenic animals. The techniques used in animal transgenesis should be improved, are not fully controlled. In addition to the direct effects of the techniques (superovulation, surgery, microinjection ...), the process of transgenics has a significant impact on mortality and genetic modifications in animals can have severe adverse effects on the health of animals are obtained.

Risks to environmental safety and health of humans or other animal species bound to the current problems of transgenesis techniques require a detailed assessment of the risk / benefit ratio case by case. The assessment must take in to account the difficulty to establish a priori all potential risks of transgenics process, especially those who may have an effect on the environment or on human health in the medium and long term.

2.3.3 Ethical issues in green genetics

There are many concerns regarding ethical issues in, for example, the food industry, as the introduction of genetically modified (GM) plants has become one of the most controversial disputes of the modern age.

GM plants are often seen as unnatural. Some scientists and a large part of the public argue that it is unethical to treat nature and living beings in a way that it will bring some benefits to the industry regardless the consequences this treatment may have on the natural equilibrium.

> After examining all the scientific evidence in the light of these ethical considerations, one can take the view that the genetic modification of crop plants, as so far developed, does not differ to such an extent from conventional plant breeding or other human interventions with the natural world as to make the process morally objectionable in itself. GM technology is a new tool which plant breeders are using to achieve their breeding goals more accurately and rapidly.[33]

Many questions have been raised. What are the dangers and what are the benefits of applying new biotechnologies in agriculture? Some argue that embracing new technologies will solve the rapidly growing problem of world hunger. On the other hand, researchers examining a negative or harmful influence of such techniques on living beings reported contradictory results.

The possible harm of GMO food intake to humans is the subject of numerous scientific papers in the last decade. Food produced from genetically modified organisms remains the subject of controversy, which makes it the most prominent topic among researchers, stakeholders, farmers, consumers and non-governmental organisations and biotechnology companies. Maybe the main concern for stakeholders in the process in the GMO production is that a small number of companies will create monopoly in the market.

No one can deny that a potential risk to the environment is present. We can’t consider crops to be self-contained organisms because their pollen is spread by the wind, insects and other plants leading to a possibility that a gene, which has been inserted into one plant, may enter another. Aside from the danger of super-weeds, the potential danger of GMOs for other creatures in the ecosystem is most common ethical issue.

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[33] Nuffield Council on Bioethics, “Genetically Modified Crops: the ethical and social issues”. http://www.nuffieldbioethics.org/sites/default/files/GM%20crops%20-%20full%20report.pdf

3 Institutionalisation: EU and International

3.1 Organisations dealing with ethics of genetics

- Committee on Bioethics (DH-BIO) of the Council of Europe
  http://www.coe.int/t/dg3/healthbioethic/default_en.asp
- European Society of Human Genetics – ESHG
  https://www.eshg.org/58.0.html
- Eurogentest "Network of Excellence" funded by the European Commission's 6th framework Programme
  http://www.eurogentest.org
- Austrian Bioethics Commission
  http://www.bka.gv.at/site/4070/default.aspx
- Nuffield Council on Bioethics
  http://nuffieldbioethics.org/about
- European Commission. International dialogue on bioethics
  http://ec.europa.eu/bepa/european-group-ethics/publications/opinions/index_en.htm
- World Medical Association
  http://www.wma.net/en/10home/index.html
- Human Genome Organisation (HUGO)
  http://www.hugo-international.org/educationalresource.php
- American Society of Human Genetics (ASHG)
  http://www.ashg.org/pages/policy_statements.shtml
- BioethicsWeb
  http://www.intute.ac.uk/bioethicsweb/
- American Society for Bioethics and Humanities (ASBH)
  http://www.asbh.org/publications/exchange.html
- Kennedy Institute of Ethics
  https://bioethics.georgetown.edu/
- The Hastings Center - Bioethics and Public Policy
  http://www.thehastingscenter.org/Default.aspx
- National Core for Neuroethics, (The University of British Columbia)
  http://neuroethicscanada.ca/National_Core_for_Neuroethics/Home.html
- Neuroethics Society
  http://www.neuroethicssociety.org/
- Stanford Center for Biomedical Ethics, (Stanford University). Program in Neuroethics
  http://neuroethics.stanford.edu/
- Society for Neuroscience
  http://www.sfn.org/
- The Wellcome Centre for Neuroethics, (University of Oxford)
  http://www.neuroethics.ox.ac.uk/

3.2 Global organisations dealing with ethics of genetics

- World Health Organisation - Ethical, Legal and Social Implications (ELSI) of Human Genomics
  http://www.who.int/genomics/elsi/en/

- Ichan School of Medicine at Mount Sinai
  http://www.bioethics.nih.gov/home/index.shtml
- National Institutes of Health - The Department of Bioethics
  http://icahn.mssm.edu/education/bioethics
- Miami Dade College - Earth Ethics Institute
  http://www.earthethicsinstitute.org/index.asp
- European Institute of Bioethics
  http://www.ieb-eib.org/en/
- Stanford University Center for Biomedical Ethics
  http://bioethics.stanford.edu/
- The Danish Council of Ethics
  http://www.etiskraad.dk/en.aspx
- Council of Europe - The Department of Bioethics
  http://www.coe.int/t/dg3/healthbioethic/default_en.asp
- Bioethics Committee, UNESCO
  http://www.unesco.org/new/en/social-and-human-sciences/themes/bioethics/
- Kennedy Institute of Ethics, Georgetown University
  http://kennedyinstitute.georgetown.edu/
- Center for Ethics - Institute of Biomedical Ethics, University of Zurich
  http://www.ethik.uzh.ch/ibme_en.html
- Ethics Institute, University of Utrecht
  http://www.uu.nl/faculty/humanities/EN/organisation/departments/department-of-philosophy-and-religious-studies/EthicsInstitute/Pages/default.aspx
- Croatian Unit of the International Network of the UNESCO Chair in Bioethics, Zagreb, Croatia
  http://www.unesco-chair-bioethics.org/UI/C02.aspx?uid=C8CC5381B89AB7D2

3.3 International frameworks and protocols

- Council of Europe, Convention for the Protection of Human Rights and Dignity of the Human Being with Regard to the Application of Biology and Medicine: Convention on Human Rights and Biomedicine. ETS No: 164, 1997.
  http://conventions.coe.int/Treaty/en/Treaties/Html/164.htm
- Council of Europe, Additional Protocol to the Convention on Human Rights and Biomedicine concerning Biomedical Research. ETS No: 195, 2005.
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- Council of Europe, Explanatory Report to the Convention on Human Rights and Biomedicine. Strasbourg: Council of Europe, 1997.
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- Council of Europe, Committee of Ministers, Recommendation on Prenatal Genetic Screening, Prenatal Genetic Diagnosis and Associated Genetic Counselling. (Rec NºR (90) 13. June 21 1990.
- Council of Europe, Steering Committee on Bioethics (CDBI/INF), Additional Protocol to the Convention on Human Rights and Biomedicine, concerning Genetic Testing for Health Purposes. Strasbourg, 27.XI.2008
  http://conventions.coe.int/Treaty/EN/Treaties/Html/203.htm

- Council of Europe, Additional Protocol to the Convention for the Protection of Human Rights and Dignity of the Human Being with regard to the Application of Biology and Medicine, on the Prohibition of Cloning Human Beings. ETS No. 168. http://conventions.coe.int/Treaty/en/Treaties/Html/168.htm
- Council of Europe, Committee of Ministers, Recommendation R (97) 5 of 13.02.1997 on the Protection of medical Data. https://wcd.coe.int/ViewDoc.jsp?id=571075&Site=CM&BackColorInternet=C3C3C3&BackColorIntranet=EDB021&BackColorLogged=F5D383
- European Parliament and of the Council, Directive 98/44/EC of the 06.07.1998 on the legal protection of biotechnological inventions. http://eur-lex.europa.eu/smartapi/cgi/sga_doc?smartapi!celexapi!prod!CELEXnumdoc&numdoc=31998L0044&model=guichett&lg=en
- European Commission, Commission Decision of 7.11.2012 on setting up a Commission expert group on development and implications of patent law in the field of biotechnology and genetic engineering. http://ec.europa.eu/internal_market/indprop/docs/invent/dec_121107_biotechinventexpertgroup_en.pdf
- European Commission, Recommendation of 07.02.2008 on a Code of Conduct for Responsible Nanosciences and Nanotechnologies Research. http://ec.europa.eu/nanotechnology/pdf/nanocode-rec_pe0894c_en.pdf
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- United Nations Organisation for Education, Science and Culture (UNESCO), Ethics and politics in
- Nanotechnology. Ethics of Science and Technology at UNESCO. Division of Ethics of Science and Technology, Paris, 2006. http://unesdoc.unesco.org/images/0014/001459/145951e.pdf
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- Kyoto Protocol https://unfccc.int/kyoto_protocol/items/2830.php
- Nagoya Protocol http://www.cbd.int/abs/about/
- Cites Convention http://www.cites.org
- The Convention on Biological Diversity: Changing Ethical and Legal Frameworks for Biodiversity Research and Prospecting http://www.fao.org/docrep/003/y1237e/y1237e05.htm
- Cartagena Bio Safety Protocol http://bch.cbd.int/protocol/
- Universal Declaration on Bioethics and Human Rights, UNESCO http://unesdoc.unesco.org/images/0014/001461/146180e.pdf

4 Institutionalisation: national

4.1 Organisations dealing with ethics of genetics in Serbia

- Centre for the Study of Bioethics
  http://www.instifdt.bg.ac.rs/cbs/index_en.html
- Central and Eastern European Network of the UNESCO Chair in Bioethics
- Serbian Unit of the UNESCO Chair in Bioethics
  http://www.unesco-chair-bioethics.org/UI/C02.aspx?uid=C8CE71D81DDE096A
- Cambridge Working Group for Bioethics Education in Serbia
  http://www.instifdt.bg.ac.rs/cbs/Cambr_RG_en.html
  http://journals.cambridge.org/action/displaySpecialPage?pageId=4988
- National Committee for Bioethics
  http://www.sanu.ac.rs/English/Bioethics/Izdavastvo.aspx
- Bioethics Society of Serbia
  http://www.med.bg.ac.rs/

4.2 Scholars with publications in high impact factor international journals or by reputed publishers:

- Vojin Rakic (Journal of Medical Ethics, American Journal of Bioethics, Cambridge Quarterly of Health Care Ethics (2))
- Milan Cirkovic (Publication by Oxford University Press and publication by Cambridge University Press)
- Violeta Besirevic (Bioethics)

4.3 Other scholars with bioethics publications or in relevant positions:

- Aleksandar Damjanovic
- Dragoslav Marinkovic
- Zvonko Magic
- Veselin Mitrovic
- Hajrija Mujovic Zornic
- Dusanka Krajnovic
- Jovan Babic

4.4 Government Ministries and other organisations

- Ministry of Education, Science and Technological Development
  http://www.mpn.gov.rs/?lang=sr-YU
- Parliament of Serbia, Board of Education
  http://www.parlament.gov.rs/national-assembly.467.html
- Faculty of Agriculture, University of Belgrade
  http://www.agrif.bg.ac.rs
- Ministry of Energy, Development and Environmental Protection
  http://www.merz.gov.rs/en
- Consumer Association of Serbia
  http://www.apos.org.rs/cms/index.php
- Astra Zeneca

http://www.astrazeneca.com/About-Us/Worldwide-locations/Country/Serbia-and-Montenegro
- Hemofarm
  http://www.hemofarm.com/Default.aspx?Lang=en&Layout=Products
- Roche
  http://www.rochesrbija.rs/portal/serbia-nct
- Victoria Group
  http://www.victoriagroup.rs/

5 Evaluation

Global bioethics: is it necessary to state a global bioethics to address bioethical issues in the global context? For instance:

- To resolve question of whether genetic material is personal property, common property, intellectual property, or a part of a person or an extension of a person – or of peoples or global bioethics is international research ethics
- To resolve the inconsistency of the existing rules and regulations across the world when we consider the effects of patenting regimes (also on developing countries), "medical trafficking" of goods, services and people (as well as human material in general), and "reproductive tourism", which for instance includes patients travelling to different countries to benefit from procedures forbidden or nor provide in their home country[34].

Regarding other issues that are related to the green genetics we would like to raise the following:

- There is a possibility to patent the technology but the patenting of a living organism provokes very controversial reactions. There is a point of view that this is not innovation but a discovery because the genes and the recipient plants already exist as products of the evolution and that they are not *de novo* created.
- There is a possible conflict of interest in cases when the expert, who is member of the National Committee of Biological Safety, would have to consider a case that is the result of the work of his own laboratory or institute.

6 Journal and conference series

- OMICS-ETHICS Research Group. http://www.omics-ethics.org/en/what-is-human-enhancement
- Agriculture Systems
  http://www.journals.elsevier.com/agricultural-systems/
- Achievements in the Life Sciences

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[34] Hellsten, Sirkku K., " Global Bioethics: Utopia or Reality?", *Developing World Bioethics* Vol.8, 2008, pp. 70–81.

http://www.elsevier.com/journals/achievements-in-the-life-sciences/2078-1520
- Environmental Ethics, USA
  http://www.cep.unt.edu/enethics.html
- White, Lynn, “The Historical Roots of our Ecologic Crisis" (March 1967)
- "The Tragedy of the Commons" (December 1968) by Garret Hardin
- The Trumpeter: Journal of Ecosophy, Canada http://umpeter.athabascau.ca/index.php/trumpet
- Environmental Values Journal.
  umpeter.athabascau.ca/index.php/trumpet
- Journal of Agricultural and Environmental Ethics http://link.springer.com/journal/10806
- Food Fray: Inside the Controversy Over the Genetically Modified Food http://www.amazon.com/Food-Fray-Controversy-Genetically-Modified/dp/0814401643
- Ethics and the Environment

6.1 Journals and conference papers in Serbian

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- Environmental and Agronomic Impact of the Herbicide Tolerant GM Rapeseed, Zdjelar G., Nikolic Z., Marijanovic Joromela A, *et. al.*
- Ethics in Scientific Results Application: Gene and Life Forms Patenting, Kostantinov K, Mladenovic Drinic S, Andjelkovic V & Babic M, 2010, Genetika Journal
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7 Key publications

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Gilbert, Scott F., Anna Tyler and Emily Zackin, *Bioethics and the New Embryology: Springboards for Debate*, Sinauer, 2005.

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Roskies, Adina L., "Neuroethics for the new millennium", *Neuron*, Vol. 35, No.1, Jul 2002, pp.21-23

Aggarwal, Neil Krishan and Elizabeth Ford, "The Neuroethics and Neurolaw of Brain Injury", *Behavioural Sciences & the Law*, Vol. 31, No. 6, Nov. 2013, pp.789-802.

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Rantanen, E., H Hietala, U Kristoffersson, I Nippert, J Schmitke, J Sequeiros, H Kääriäinen, "Regulations and practices of genetic counselling in 38 European countries: The perspective of national representatives", *European Journal of Human Genetics,* Vol. 16, No. 10, Oct 2008, pp.1208-16.

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