PUBLICATION OF THE COMMITTEE FOR THE FUTURE 3/2020

DEVELOPMENT OF GENETIC ENGINEERING IN DIFFERENT AREAS OF APPLICATION 2018–2020

DEVELOPMENT OF GENETIC ENGINEERING IN DIFFERENT AREAS OF APPLICATION 2018–2020

Risto Linturi

PUBLICATION OF THE COMMITTEE FOR THE FUTURE 3/2020

Cover: Misucell

Back cover: artwork Tulevaisuus, Väinö Aaltonen (1932),
Photo: Vesa Lindqvist.

Tulevaisuusvaliokunta

Committee for the Future

Parliament of Finland
FI-00102 Eduskunta
Helsinki
Finland

www.parliament.fi

Helsinki 2020

ISBN 978-951-53-3760-3 (paper back)
ISBN 978-951-53-3761-0 (pdf)

Contents

Preface

This report is a prime example of new ways to support knowledge-based decision-making. Its background is the following. The Council of the European Union has requested a report on the status of novel genomic techniques (NGT) under EU legislation from the EU Commission as well as suggestions for actions, if needed, by the end of April 2021. To this end, the EU Commission gathered information of NGTs from the member states. In Finland, the survey was coordinated by the Board for Gene Technology. The Board also approached the Committee for the Future in the Parliament of Finland, asking if the Committee had deliberated on the state of gene technologies since its 2018 report on radical technologies.

The Committee for the Future has been commissioning foresight studies on radical technological developments since 2013. This work has led to the development of a new kind of foresight method, the Radical Technology Inquirer (RTI), and a series of reports. The most recent one came out in 2018 and its English translation in 2019. The method is based on crowdsourcing, meaning that hundreds of volunteers explore various media to spot evidence of advances in radical technologies on an ongoing basis. In order to enable systematic assessment, these developments are divided into 100 radical technology categories. The volunteers constantly scan for new evidence and discuss these documents in a curated social media group, seeking to identify the most comprehensive and credible source for each identified new development. This update report is based on analysing the crowdsourced evidence that has come up since the publication of the 2018 RTI report in technology categories that relate to NGTs.

This update is only half-tailored to the EU Commission's information need, however; it is focused on NGTs, yet it is global rather than country-specific. This is because the RTI method is designed to follow radical technological developments on a global level. Its anticipations are based on knowing what is currently technologically possible rather than on knowing where that capability currently lies. A geographically and technologically broad scope is all the more important, as the RTI method seeks to anticipate not only the development of specific technological fronts but especially the long-term societally transformative impacts of interconnected technological developments.

The Committee for the Future has commissioned the development of the RTI method from Risto Linturi and Osmo Kuusi, who are among the leading technology foresight specialists in Finland. Linturi is also responsible for maintaining and curating the respective crowdsourcing of evidence, i.e. the social media group that currently involves over 3,000 members, half of whom are constantly active. Linturi has written this NGT's update report, except for this preface which represents the joint view of the Committee for the Future. The Committee's view is based on both this report and the Committee's other work regarding the development of gene technologies and the ethics of technological development.

As the reader will find out from the pages below, some truly extraordinary capacities are currently emerging in the field of NGTs. In section 2 of this report, Mr Linturi summarises recent technological developments in DNA reading and writing, genetic editing, cell culture, epigenetics, cell simulations, artificial cells and synthetic biology. In section 3 of this report, he discusses the significance of these developments for food production and nutrition; industrial manufacturing and materials; well-being and health; environment and sustainable development.

Linturi points out a number of examples that show the benefits of NGTs. For instance, gene technologies enable better curing of various types of cancer as well as many hereditary diseases and disorders, lessened environmental impacts of food production and new ways to replace fossil fuels. Linturi also illuminates the risks of NTGs. For instance, a group of students has been able to order separate sequences of the anthrax bacterium and combine these into a functional disease. Also, it is becoming possible to modify the DNA of plants from a distance by spreading genetically modified pollen. All in all, even if there was no malicious intent, the likely spreading of handheld gene sequencing in the 2030s, for example, may make it impossible for individuals to keep their DNA information private. As gene editing becomes easier, Linturi even anticipates that it may eventually become a recreational activity.

These observations underscore Linturi's core message: Many kinds of gene technologies are becoming so easy to purchase and operate that their criminal use is impossible to control. According to Linturi, the only counter-measure is to utilise these technologies for good on a broad scale, so that society would always have sufficient know-how and competence to react to any emerging problems.

In many earlier statements and reports, the Committee for the Future has emphasised various ethical issues that we inevitably encounter as new technological capabilities emerge. In its preface to the report on gene technologies, the Committee emphasised the need to keep the legislation regarding gene technologies updated, as the old regulation does not match the properties of the new inventions. The Committee also pointed out e.g. how reactions to gene technologies highlight the difference in values: What is disgraceful alteration of life for some people may be a useful means to reduce harmful pesticides for others.

To make better sense of the ethical dilemmas of radical technologies, the Committee for the Future has commissioned a separate report. In that report, Professor Ahlqvist raises 20 societal tensions given rise by various knowledge-intensive technologies. In its preface to the report, the Committee summarised these tensions in 20 questions. In light of the present report, the following tensions and questions, among others, are important:

- Opportunities vs. risks: What are the extremes?
- Resilience of nature: How may the technology increase or decrease it?
- Physical space: Does the technology change it, its meaning, or ways to experience it?
- Centralising vs. distributing: How does the technology influence the location, accumulation and access to information, resources, infrastructure and people?

- People's agency: Does the technology change it? For whom?
- Organic vs. artificial life: Does the technology influence life, or our understanding of it?

Some examples of very promising opportunities and risks are mentioned above, and the reader finds concrete examples from the following pages. The other questions on the above list help with understanding the issues at stake, if we want to emphasise the good uses of new technologies. For instance, gene technologies might increase the resilience of nature, if they were used to a significant degree to replace outdoors food production with indoors alternatives and if this enabled the reduction of monoculture cultivation on outdoors agricultural land. This, in turn, would change the meaning of physical space – i.e. traditional fields and pastures, if they acquired stronger significance as places for maintaining biodiversity, for example. Such development would likely also change urban space, as parts of the land could be taken under new kinds of food and materials production with the advance of cell culturing. These developments might not only mean changes in the location of the parts of the food and materials production chain but also re-distribution of its ownership and profits. From a regulatory point of view, there emerges e.g. the issue of whether regulation should be more flexible for gene technologies for genetically modified organisms to be used in closed and controlled environments indoors. In outdoor use, there is the pertinent issue of how to weigh the risk for unintended environmental damage against the possibilities of intended environmental benefits. The spreading of capabilities in synthetic biology and gene editing certainly also forces us to consider not only the risks of artificially altered genes spreading to the environment, but also how we should value, tolerate and regulate living entities in which the distinction between natural and artificial - or even between human and animal - is blurred.

The Committee for the Future has utilised the RTI results in its various statements, and the results have also informed Finnish regulatory planning, the planning of professional education and regional planning processes. Furthermore, the results have raised considerable corporate foresight interest. This report is published in English in the spirit of securing the international availability of the newest RTI results.

The Committee for the Future also wants to stimulate discussion on the status of European technology foresight and the anticipation of broader socio-technical change. The EU Commission has already funded one technology anticipation project (RIBRI) that was inspired by the RTI approach. In the Committee for the Future's view, establishing a permanent capacity to monitor and anticipate socio-technological development on an ongoing basis would be even more important than individual research projects. While the RTI method requires considerable coordination, facilitation and analytical work by dedicated experts, its core features would suit a European facility well: The crowdsourcing of news of technological progress is an affordable, efficient and transparent way to collect data. The systematic tracking of all radical technologies in an undiscriminating manner produces a rich resource of technological change to be used as background material in many types of preparation and planning of regulation and policies. The utilisation of participatory workshops in the interpretation of the data functions to reduce research bias, which is an in-built risk in any kind of foresight effort.

The Committee for the Future welcomes the reader to enjoy the most recent RTI results regarding recent and upcoming developments in new genomic techniques and the respective anticipated societal impacts.

Helsinki 18 September2020

The Committee for the Future

Joakim Strand, Chairperson (Swedish Parliamentary Group)
Pirkka-Pekka Petelius, Vice Chairperson (Green Parliamentary Group)

Members

Marko Asell (Social Democratic Parliamentary Group)
Harry Harkimo (Liike Nyt-Movement's Parliamentary Group)
Hannakaisa Heikkinen (Centre Party Parliamentary Group)
Mari Holopainen (Green Parliamentary Group)
Katja Hänninen (Left Alliance Parliamentary Group)
Ville Kaunisto (Parliamentary Group of the National Coalition Party)
Pasi Kivisaari (Centre Party Parliamentary Group)
Ari Koponen (The Finns Party Parliamentary Group)
Antti Lindtman (Social Democratic Parliamentary Group)
Merja Mäkisalo-Ropponen (Social Democratic Parliamentary Group)
Arto Pirttilahti (Centre Party Parliamentary Group)
Kristiina Salonen (Social Democratic Parliamentary Group)
Sari Tanus (Christian Democratic Parliamentary Group)
Sinuhe Wallinheimo (Parliamentary Group of the National Coalition Party)
Jussi Wihonen (The Finns Party Parliamentary Group)

1 Summary

This report has been prepared for the Finnish Parliament's Committee for the Future. It identifies the key areas of genetic engineering and the areas of application related to it. It also briefly describes recent breakthroughs noted by Tulevaisuusvaliokunnan radikaalit teknologiat -joukkoistus (Radical technologies crowdsourcing group of the Committee for the Future) since the publication of the report 'Societal transformation 2018–2037: 100 anticipated radical technologies, 20 regimes, case Finland'. The report starts with the summary and conclusions, which are explained in more concrete terms in the following chapters, along with their background. First, technological advancement is described separately for each technology, after which the significance of the technologies for key areas of application is examined. The aim of this text is not to replace but to supplement the reports 'Societal transformation 2018–2037: 100 anticipated radical technologies, 20 regimes, case Finland' (1/2018) and 'Geeniteknologia' (Genetic engineering, 2/2018) by the Committee for the Future. However, the text has been written so as to be readable independently of the aforementioned, particularly if the reader is familiar with the subject matter. Developments prior to 2018 will not be examined here; where they are concerned, this report refers to the observations made in the 1/2018 report.

1.1 Technological advancement

In addition to genome editors, this review covers technologies related to DNA sequencing, identification of sought genomes and cell culture as well as the modelling of the function of DNA and cells. Epigenetics, i.e. the study of the structure that regulates actual DNA, is examined in its own section.

Technological advancement has continued to progress rapidly in every respect over the last two years. The rise of epigenetics into an important topic in many ways is particularly worth noting. It is also important to note the expanding role of CRISPR technology in a great number of tasks, ranging from original genetic engineering to diagnostics and gene therapy. As the use of CRISPR technology expands and becomes more diverse, efficient control of the use of the technology is becoming impossible.

1.2 Development of the areas of utilisation

The most promising areas for utilising genetic engineering are food production, health care, material production and energy production. Among these areas, the technology has been developed the most rapidly for health care applications. Genetic engineering is already being applied in many ways, in addition to which significant new diagnostic and treatment methods are constantly being discovered. The causes are being identified for many serious hereditary diseases, including national diseases such as degenerative diseases related to old age and cancers. Blind persons have regained their sight and deaf

people can hear again. In addition to explaining these diseases, genetic engineering also promises to treat them, and many treatment methods for serious diseases that are based on genetic engineering are already undergoing or progressing towards clinical trials.

In other areas, application has progressed more slowly. At present, the development of food production is restricted by outdated legislation. The need for development is increasing due to climate change, plant diseases and environmental toxins as well as population growth. Indoor farming and the biotechnological production of protein offer a closed environment for advancing genetic engineering, which should be made sufficiently simple, at least with regard to the regulations. Material production and the production of raw materials for energy benefit from genetic engineering, but progress primarily remains at the level of basic research for the time being. The promises are great, but development is still at a relatively early stage for commercial operators to embrace it.

1.3 Political recommendations

The most important political recommendations are related to the strengthening of genetic engineering expertise in all areas and applications of genetic engineering. It must be understood that the broad expertise and practical response preparedness required cannot be maintained nationally or even at the EU level if activities are restricted on account of minor risks and by stricter means than in competing countries. Another thing that must be understood is that a lack of broad expertise and narrow practical preparedness cause their own significant risks in a global environment. The most difficult regulatory restrictions in this respect are related to the application of genetic engineering in plant breeding and other food production. There are also problems with the availability of genetic data related to research and personalised health care as well as the undeveloped state of industrial applications, which should be supported with research investments and education policy measures at the national and EU levels.

2 Background and progress of technological advancement

2.1 DNA sequencers

Background: There are several reasons and also several technologies for sequencing DNA. DNA uniquely identifies individuals in criminal investigations, for example, and even helps predict facial features, but it is also used to identify diseases and other characteristics. Counterfeit foods, diagnosis of infectious diseases and numerous other applications focused on well-being benefit from DNA sequencing, which is becoming increasingly affordable.

In addition to DNA, it is possible to sequence the RNA codes of viruses as well as RNA codes related to intracellular function. It is also possible to sequence the epigenetic settings in cell DNA, i.e. methylation, which tells us which genes are active and which ones are deactivated. This information tells us which cell is in question and provides other information about the state of the cell.

Several techniques are used to sequence DNA. Some of them require the DNA to be amplified before sequencing. The most common technique for this purpose is PCR. Some techniques are sensitive in such a way that amplification is not required. Some techniques are able to use biochips or selective amplification to identify whether a sample contains certain genetic sequences, while others decode the DNA or RNA sequences as they are in the sample.

DNA sequencers are examined in chapters 2.1.2 and 2.1.4 of the 1/2018 report.

Recent events: Oxford Nanopore (https://nanoporetech.com/applications/dna-nanopore-sequencing) has served as a pioneer in technology in which, instead of short and chopped sequences that are assembled digitally afterwards, DNA is sequenced as long strands by drawing them through a nanopore. The technology is becoming efficient and more precise, requiring the sequencing to be carried out fewer times. Illumina, which dominates the industry market with more traditional technology, has promised to drive the cost of sequencing the whole human genome down to $100, but the practical production cost related to high-quality sequencing of the human genome has stagnated at $1,000 for a while, a level that Oxford Nanopore is also already capable of providing.

Many companies have started offering DNA sequencing services to their clients at a price substantially lower than the production cost and at a poor quality. Promises have also already been made to provide DNA sequencing free of charge if the customer allows their genetic data to be used for further purposes. The technology that seems to have advanced the most rapidly is the identification of individual DNA sequences for the purpose of identifying both infectious diseases and cancer and even their epigenetic location. The sequencing of epigenetic data has also advanced rapidly. The use of CRISPR technology for affordable identification of DNA sequences is among the most recent breakthroughs.

Foresight: According to theoretical models, nanopore technology will allow DNA sequencing to be carried out at a price several times cheaper than is possible at present. It seems credible that, over the 2020s and 2030s, households will have access to smartphone accessories that will at first allow the occurrence of selected DNA sequences to be tested and later for the whole genome to be sequenced. This will also make it possible to identify infectious diseases, the composition and origin of food and the DNA of people close to us. The protection of privacy will unavoidably crumble in this respect.

New sources since the 1/2018 report:

Ultrasound can reveal gene expression in the body;
https://www.sciencedaily.com/releases/2019/09/190928082737.htm

The cost of sequencing the human genome has decreased to less than $1,000;
https://www.genome.gov/about-genomics/fact-sheets/DNA-Sequencing-Costs-Data

An affordable, portable DNA sequencer delivers 99.9% precision;
https://www.nature.com/articles/s41467-019-09637-5

CRISPR as a diagnostic tool, a prototype for at-home tests;
https://www.theverge.com/2018/4/26/17281724/mammoth-biosciences-crispr-diagnostic-tool-disease-detection

Detection of a target sequence within an uncultured sample with CRISPR-Chip;
https://www.nature.com/articles/s41551-019-0371-x

A test identifies early-stage cancers and their locations, only 1% rate of false positives;
https://www.fiercebiotech.com/medtech/asco-grail-s-blood-test-identifies-a-dozen-cancers-before-they-can-spread-early-results

Free-of-charge DNA sequencing and compensation for the use of the genome;
https://www.npr.org/sections/health-shots/2018/11/15/667946213/startup-offers-to-sequence-your-genome-free-of-charge-then-let-you-profit-from-it

2.2 DNA writing

Background: The writing of DNA sequences does not only serve genetic engineering. DNA sequences can be written both for the purpose of altering the genome controlling a cell's function and by recording data in a DNA sequence. As a method of recording data, DNA writing is, for the time being, only a promising area of research, having not yet reached a practical level. However, the data storage density of DNA exceeds that of all existing data storage devices, but writing and sequencing DNA is, for now, difficult compared to other data storage technologies.

Writing DNA sequences is not necessary for editing a genome if the replacement of individual base pairs is not counted as *DNA-writing*. Furthermore, some genetic engineering is based on genes that occur in other organisms, and DNA writing is not

required in transferring them. When DNA writing is used, the change in the genome occurs when the written DNA sequence is transferred with a genome editor to the desired part of the target organism's genome. The function of genome editors is described in more detail in the following section, 2.3.

DNA writing is examined in chapter 2.1.2 of the 1/2018 report.

Recent events: The production of DNA sequences is becoming increasingly routine. The writing process can be carried out almost flawlessly, and this flawlessness can be verified by sequencing the sequences that are written. DNA writing is simultaneously becoming accessible to everyone in terms of the equipment used and so cheap that it cannot be controlled. There are also services being created at the global level that allow customers to order the DNA sequences they want. A good example of this is a group of students who ordered pieces of Anthrax through several different services and combined these pieces into functional Anthrax for a student project.

Foresight: Writing and amplifying DNA sequences will become increasingly easy. If the market evolves in such a way that DNA writing becomes a common service, it can be controlled at least to some degree, and it will be possible to restrict the writing of parts of the DNA of known infectious diseases, for example. If the activities are based on cheap devices purchased by users for themselves, their use will, in practice, be impossible to control.

New sources since the 1/2018 report:
Writing of whole genomes funded and under development;
https://neo.life/2019/11/the-dawn-of-cheap-and-easy-dna-writing/

DNA writing is becoming easy and cheap, while control is becoming impossible;
https://www.npr.org/sections/health-shots/2019/09/24/762834987/as-made-to-order-dna-gets-cheaper-keeping-it-out-of-the-wrong-hands-gets-harder?t=1583496283229

2.3 Genome editors

Background: The task of genome editors is to take the desired DNA sequence inside the target cell and insert it into a specific part of the target cell's genome. In other words, a genome editor must be able to penetrate a cell, locate the part to be edited and insert the selected sequence into the part in question. The transferred sequence can be separately written or copied from another organism. It is also possible for the genome editor to locate the desired part of a genome and edit the base sequence directly in the desired manner.

Use of CRISPR technology has rapidly become widespread among researchers due to its easy accessibility, efficiency and simplicity. There are several variations of the technology, some of which are able to spread widely in tissue cells. These variations differ from each other in terms of precision and the length of the sequence edited as well as in whether or not they cut the genome, make a change to an individual base or insert

a DNA sequence without cutting the genome. As the editors also locate the selected part of the genome, their use extends beyond genetic engineering to the identification of diseases and hereditary characteristics, among other things.

In addition to the editing of hereditary genetics, genome editors are used in multi-celled organisms to edit the genome of specialised tissue stem cells and other tissue. This is referred to as gene therapy, and its most common goal is related to health care.

Genome editors are examined in chapter 2.7.60 of the 1/2018 report.

Recent events: The most important phenomenon is the rapid spread of CRISPR technology. A great number of CRISPR variations have been created. Some versions of the editor can be distributed into human tissue widely, even curing hereditary diseases in human adults. One event that can be considered to have shocked the science community and the general public is the birth of the first gene-edited children in China. Before this, a baby was born in the UK with mitochondrial DNA inherited from a different individual than the rest of his X and Y chromosomes, i.e. the child biologically has DNA from three different parents. The need for this arose from a genetic defect in the mother's mitochondria. The science community was also bewildered by an experiment in which scientists sought to increase the intelligence of monkeys by transferring human DNA to them. The use of CRISPR technology to treat diseases is rapidly becoming more diverse.

Foresight: It is apparent that genome editors are already easily available and usable with the skills and equipment that are typical for students of cell biology and that can be obtained by amateurs. Gene editing is likely to spread beyond business and research activity to recreational activity. Editors will become increasingly efficient in such a way that they can multiply and spread to tissues and all cells through the bloodstream, even changing the DNA of a human adult. Ease speeds up the realisation of the great promises of genetic engineering, but it also creates new risks, the prevention of which requires broad preparedness from genetic engineering, as many of the expected problems cannot be prevented with traditional methods.

New sources since the 1/2018 report:

CRISPR/Cas9 is precise and predictable when used correctly;
https://phys.org/news/2018-12-scientists-crispr-code-precise-human.html

Gene-edited children, Lulu and Nana;
https://www.technologyreview.com/s/614762/crispr-baby-twins-lulu-and-nana-what-happened/

Increasing the intelligence of monkeys with a human gene;
https://www.discovermagazine.com/mind/scientists-put-a-human-intelligence-gene-into-a-monkey-other-scientists-are

The lifespan of a nematode has been amplified fivefold with genetic engineering;
https://www.sciencedaily.com/releases/2020/01/200108160338.htm

Prime: a precise CRISPR editor that does not sever the DNA strand (the problem is that the vector is not efficient and does not penetrate all cell walls);
https://www.technologyreview.com/s/614599/the-newest-gene-editor-radically-improves-on-crispr/

New CRISPR technique inserts long DNA sequences without cutting the genome;
https://www.nature.com/articles/d41586-019-01824-0

A CRISPR method for fighting viruses inside cells;
https://www.scientificamerican.com/article/scientists-program-crispr-to-fight-viruses-in-human-cells/

Fighting antibiotic resistance with CRISPR technology;
https://phys.org/news/2019-12-crispr-based-amplified-antibiotic-resistant-genes.amp

Switch for organ regeneration found in junk DNA;
https://www.telegraph.co.uk/science/2019/03/14/harvard-university-uncovers-dna-switch-controls-genes-whole/

Reprogramming a broad gene matrix with a new CRISPR technique;
https://ethz.ch/en/news-and-events/eth-news/news/2019/08/revolutionising-the-crispr-method.html

2.4 Cell culture

Background: The purpose of cell culture is to reproduce a cell. The cell in question may be genetically modified. The tissue created with cell culture can be used for many purposes, such as for raw material in biotechnology or as part of a production process. In the food industry, it can be used for food. In medicine, genetically modified cells can be injected into the body for medical purposes, 3D printed into tissue or organs or used for research purposes.

Cell culture is examined in chapter 2.7.63 of the 1/2018 report.

Recent events: When researchers learned to convert specialised cells back into unspecialised stem cells, cell culture became faster, and the number of different types of experiments increased, also producing a great number of successful research outcomes. The specialisation of stem cells and the culturing of cells belonging to the desired tissue type is starting to be a routine activity. Scientists have also learned to print living cells into a tissue structure with the help of support structures that are absorbed into the tissue. This is used to produce organs that are viable for transplantation. Genetically modified and cultured tissue has been injected into tissue and the bloodstream for treatment purposes almost on a routine basis. Cell culture is also being developed for industrial purposes, but it is more difficult to obtain information on development carried out in industrial processes, particularly when the development has progressed to the commercial stage.

Foresight: Cell culture will become routine activity in which the selected cell is converted into a stem cell, its cell type is chosen and the cell is reproduced. This activity will become computer-assisted and it may be combined with genetic engineering. Cultivated tissue can be used as raw material or as a producer of raw material in industry, energy production, food production or medicine. The method will also become available to households, which will make personalised drug manufacturing possible for biohackers, for example. Controlling this type of private activity may become challenging in the same manner as controlling the producers of computer viruses.

New sources since the 1/2018 report:

3D printing of living skin and blood vessels for skin grafts;
https://news.rpi.edu/content/2019/11/01/living-skin-can-now-be-3d-printed-blood-vessels-included

A functional, 3D printed heart cultivated from stem cells;
https://onlinelibrary.wiley.com/doi/full/10.1002/advs.201900344

A functional, 3D printed mini liver cultivated from the patient's reprogrammed cells;
http://agencia.fapesp.br/researchers-create-functional-mini-liver-by-3d-bioprinting/32217/

Vision restored with a transplant engineered from stem cells;
https://www.moorfields.nhs.uk/news/successful-trials-new-treatment-moorfields-fight-against-sight-loss-caused-amd

A- and B-type blood converted into O-type blood;
https://naturemicrobiologycommunity.nature.com/users/261113-peter-rahfeld/posts/49635-an-enzymatic-pathway-in-the-human-gut-microbiome-that-converts-a-to-universal-o-type-blood

2.5 Epigenetics

Background: Epigenetics is a rapidly rising area of research. The most important part of the genome, which distinguishes organisms, is formed by the genes that code proteins. Genes decide the sequence of amino acids in proteins, which in turn affects the shape of the proteins and the ways in which they function in the body. Different proteins are produced in different situations, and the most important thing for the body is the data on the cell type. For example, whether the cell is a root hair cell, nerve cell or blood cell. This data is encoded into the genome of each cell with methylation. All of this together is called epigenetics. In other words, we are talking about data on the status of each cell, but it has been proven that this too might be partly hereditary, even if it is a 'learned characteristic'.

Methylation sequencing identifies which cell type the DNA is from. When cancer destroys cells, DNA sequences that allow the type and location of the cancer to be identified are released into the bloodstream. By editing methylation, it is possible to

change the cell type and edit a skin cell into a gamete or produce stem cells for cell culture, for example. It also seems that the cell ageing mechanism, 'the biological clock', is encoded into methylation and that cells can be rejuvenated. If we want to make cells produce the desired proteins or prevent their production, this can also be realised by means of epigenetics.

Epigenetics is examined in chapter 2.7.62 of the 1/2018 report.

Recent events: Epigenetics has evolved particularly rapidly in the area of diagnostics. It appears that the identification of the cell type and the state of a cell, e.g. reliable identification of the type and location of an early-stage cancer with a blood test, is at the breakthrough stage. The significance of epigenetics for ageing and the rejuvenation and changing of individual cells into stem cells are relatively recent developments, and collecting stem cells from embryos is hardly ever discussed anymore.

Foresight: All the promises of epigenetics are still in the process of being revealed, but it now seems possible and even likely that numerous diseases and types of tissue damage related to ageing can be both diagnosed and repaired with epigenetic reprogramming. With methylation, it is also possible for microbes to be made to produce a variety of material structures, i.e. metamaterials, that are impossible or difficult to produce with traditional methods.

New sources since the 1/2018 report:

Modification of the cells in the immune system to cure allergies;
https://www.sciencedirect.com/science/article/pii/S0142961219305319

In addition to methylation, another mechanism that regulates the function of the genome has been discovered;
https://phys.org/news/2020-01-discovery-gene.html

Methylation holds the key to ageing, stem cells have been rejuvenated;
https://medicalxpress.com/news/2020-02-molecular-reverses-chronic-inflammation-aging.html

Cells can be rejuvenated with epigenetics;
https://www.nature.com/articles/d41586-019-02638-w

A review of rejuvenation treatments with the help of epigenetics;
https://joshmitteldorf.scienceblog.com/2019/07/30/rejuvenation-at-the-cell-level/

2.6 Cell modelling and synthetic biology

Background: The function of cells has been modelled for a very long time. The greatest breakthrough in modelling took place when DNA was discovered, but details have been added at an accelerating pace since then. The prospect is that the function of a cell could be simulated, covering everything from hereditary factors to internal and external cell

signals, protein metabolism and other functions. This data makes it possible to simulate the effect of hereditary factors, methylation, medications and the environment on the function of cells and organs. For the time being, the models are still rough.

Cell modelling also offers an opportunity for synthetic biology. The effect of genetic engineering on the function of a cell can be planned and tested with the help of a simulation model, which makes both the testing and collection of results several times easier than repeating the same tests in real life. This makes it possible to conduct numerous tests and even assign the testing to an AI, after which the successful variations can be verified with real-life testing.

Synthetic biology means creating partly or completely new DNA in an organism. Viruses, yeasts and bacteria are the simplest to experiment with, and their significance in biotechnological production is increasing. One exotic variation of synthetic biology is six- and eight-letter DNA, which have been proven to be stable and capable of self-replication. They make it possible to describe a variety of proteins several times greater than is possible with the four-letter DNA found in biological life. Additionally, the risk of this type of DNA ending up as part of living organisms or being able to spread in nature is completely inexistent.

Cell modelling and synthetic biology are examined in chapter 2.7.61 of the 1/2018 report.

Recent events: Precise modelling of the function of cells is evolving gradually as understanding of intracellular mechanisms and the simulation capacity of information technology increase. There are still unknown principles associated with intracellular mechanisms. Synthetic biology is even evolving in surprising directions after six- and eight-letter DNA proved to be stable. The whole DNA of E. coli and a significant part of the DNA of yeast have been successfully replaced with synthetic DNA.

Foresight: When the internal and external functions of cells are successfully modelled and simulated, starting from the genome, it will become possible to digitally test the response of cells to genetic modifications and external stimuli, such as food and medications. Then it will be possible to conduct tests to the extent allowed by computer capacity, with both humans and AI controlling the tests. A cell simulation model allows digital drug tests to be conducted on tissue type specific cells according to an individual's own DNA but also for the genome's modification to be engineered and tested and for completely new types of synthetic cells to be engineered with an eye to production processes and separation techniques.

New sources since the 1/2018 report:

Building a synthetic cell from the bottom up in 10 years;
https://www.nature.com/articles/d41586-018-07289-x

Human Cell Atlas catalogues every type of cell in the human body;
https://www.npr.org/sections/health-shots/2018/08/13/636938467/ambitious-human-cell-atlas-aims-to-catalog-every-type-of-cell-in-the-body

The genome of E. coli has been fully swapped with an artificial one;
https://www.technologyreview.com/s/613534/researchers-swap-genome-of-gut-germ-e-coli-for-an-artificial-one/

Eight-letter DNA proven to be stable;
https://gizmodo.com/freaky-eight-letter-dna-could-be-the-stuff-aliens-are-m-1832823430

3 Background and development of areas of application

3.1 Food production and nutrition

Background: With the evolution of CRISPR technology, genetic engineering has become precise and efficient compared to traditional breeding. As the climate warms up, environmental toxins spread and the global population increases, many needs for plant breeding have arisen. Examples of the characteristics sought include plants that have a higher yield and require less pesticides, plants that are suited for vertical farming/aquaculture with LED lighting and plants that grow in salt water. Genetic engineering could also enhance the manufacturing of protein grown by fermentation with the help of single-celled microbes as well as the manufacturing of cultured, biotechnologically produced meat and plant-based imitation meats.

Genetic engineering in food production is briefly touched upon in several sections of chapters 1.4 and 2.7 of the 1/2018 report.

Recent events: Indoor farming has rapidly become more common, and there is now active debate about lighter regulation of genetic engineering of plants intended for indoor farming. It has also been proposed that the restrictions on genetic engineering be relaxed with regard to biotechnologically produced protein due to the low risks involved. Because of expected challenges in food production, investments are rapidly increasing, even in radical breeding. Useful discoveries include nitrogen-fixing maize, grain that grows in salt water and grain with more efficient photosynthesis, among other things.

Foresight: Genetically modified plants suited for aquaculture in vertical stacked layers under LED lighting significantly increase the efficiency of indoor farming and the variety of plants. Genetic engineering brings diversity to the biotechnological production of meat and protein. As a result, an increasing number of producers abandon food production that takes up a great amount of space.

New sources since the 1/2018 report:

A rice strain engineered in China grows in salt water;
https://nextshark.com/china-invents-rice-can-grow-salt-water-can-feed-200-million-people/

Solein, which is produced by electricity, can successfully compete against soya;
https://www.bbc.com/news/science-environment-51019798

Nitrogen-fixing maize has been developed;
https://journals.plos.org/plosbiology/article?id=10.1371%2Fjournal.pbio.2006352

The yield of crop plants has been improved by enhancing photosynthesis;
https://www.nature.com/articles/s42003-019-0561-9

Introduction of cultured meat to the market in 2021?
https://wsvn.com/news/us-world/how-close-are-we-to-a-hamburger-grown-in-a-lab/

Dubai will introduce the world's largest LED farm;
https://amp.thisisinsider.com/dubai-emirates-airlines-world-largest-vertical-farm-2018-7

3.2 Industrial production and materials

Background: Many natural materials are bewilderingly sophisticated compared to industrially produced materials. Examples include leather and nacre. Producers seek to harness bacteria and yeasts into factories that are controlled with the help of genetic engineering and methylation to produce the materials desired in any one place and at any one time so that they attach to the surfaces. This allows layered and even complex structures to be produced. At their simplest, microbes are made to produce the desired chemicals for the needs of the pharmaceutical, food, chemical or construction industries.

New materials are increasingly developed digitally instead of in chemists' laboratories. Atoms, the molecules they form and the metamaterials created from them in various forms can be modelled digitally. Simulations and AI make it possible to test various compounds and their behaviour. The materials discovered through this method can be superior in terms of their properties but impossible to manufacture by traditional methods. Genetically modified microbes may be a solution to the efficient production of these types of materials. Biotechnological processes normally occur in room temperature, and they are typically energy-efficient and scalable to industrial levels.

Genetic engineering related to material technology is briefly touched upon in several sections of chapters 1.6 and 2.7 of the 1/2018 report.

Recent events: A new method called LOCKR has been developed. It allows cells to be programmed to function in the desired manner, depending on the situation. LOCKR is a genetic modification made to a cell's genome with e.g. CRISPR technology, after which the cell is able to identify selected situations and, once the conditions are met, activate and deactivate pre-determined genes. There has also been significant development in research into biofuels. By using microbes, sunlight, carbon dioxide and water, researchers are learning to produce raw materials increasingly efficiently.

Foresight: The biotechnological production of many raw materials and other materials will become easy once the adjustment and control of processes becomes automated and once we learn to stimulate the internal processes of microbes and control them based on the genome and epigenetics. In the future, the biotechnological production of materials will prove to be more sustainable than both chemical and traditional biological processes. The production of synthetic fuels with the help of microbes will most likely become an important development trend.

New sources since the 1/2018 report:

General news about material technology under the section 'biotechnology';
https://tulevaisuuspankki.fi/en/articles

Genetically modified chickens lay eggs containing anti-cancer drugs;
https://www.bbc.com/news/science-environment-46993649

LOCKR programming activates the cell in the desired manner in the selected situation;
https://www.bbc.com/news/science-environment-46993649

Microorganisms with a nanosurface produce plastic and fuels from light and carbon dioxide;
https://m.phys.org/news/2019-06-light-powered-nano-organisms-consume-co2-eco-friendly.html

3.3 Well-being and health

Background: The sequencing of the human genome is becoming increasingly affordable and beneficial. The genetic causes of hereditary diseases and exposure to them are being discovered relatively quickly, and scientists have learned to cure many serious diseases with the help of genetic engineering. At the same time, numerous hereditary characteristics have been identified in a manner that allows considerably more effective and precise advice based on unique DNA to be provided instead of demographic guidelines issued for lifestyles and nutrition.

Gene therapy has proven to be a promising and, in narrow areas, already functional method in the treatment of various cancers and hereditary diseases. Epigenetics, together with cell culture, has also yielded results in the treatment of many types of tissue damage and even the symptoms of old age.

Genetic engineering related to health care is briefly touched upon in several sections of chapters 1.12, 2.1.2–2.1.4 and 2.7 of the 1/2018 report.

Recent events: The use of the CRISPR method in diagnostics has advanced rapidly. The role of epigenetics in diagnostics, cell culture, pharmacotherapy and the rejuvenation of tissue has become an important subject of research, and promising trends similar to breakthroughs can be seen in all these areas.

For an increasing number of diseases, treatments developed with the help of stem-cell therapy and cell culture have progressed to clinical trials with promising results. Artificial organs developed with the help of cell culture and 3D printing of cells are already functional for many organs and approaching clinical trials. Organ parts that are the easiest to produce have been grown, and there have been reports of successful human trials.

Foresight: Wellness and health technology are evolving increasingly rapidly. Rising trends include remote and self-diagnostics, personalised medication adjusted to the individual's DNA, lifestyle and metabolism as well as dietary and other lifestyle

guidance. A significant part of this development is tied to genetic engineering. An increasing number of diseases that are considered to be serious will be learned to be diagnosed at an early stage and even cured completely. It is possible that methods to prolong the healthy life expectancy of humans by 20–30% will already be discovered in the 2020s or 2030s.

New sources since the 1/2018 report:

CRISPR diagnosis tool used at home identifies diseases;
https://www.theverge.com/2018/4/26/17281724/mammoth-biosciences-crispr-diagnostic-tool-disease-detection

A prototype identifies 13 cancers from a blood sample at a production cost of €200;
https://www.toshiba.co.jp/rdc/rd/detail_e/e1911_06.html

The immune system provides a new channel for attacking cancer cells;
https://www.hs.fi/tiede/art-2000006380050.html

Using a portable device to print cultivated skin to cover a burn wound;
https://www.sciencedaily.com/releases/2020/02/200204163652.htm

A smartphone accessory analyses several diseases from spit samples;
https://www.eurekalert.org/pub_releases/2020-02/uoc-ply020620.php

Curing blindness with CRISPR therapy;
https://futurism.com/neoscope/scientists-attempt-cure-blindness-crispr

Treating sickle cell disease with a CRISPR-modified cell culture;
https://www.npr.org/sections/health-shots/2019/07/29/744826505/sickle-cell-patient-reveals-why-she-is-volunteering-for-landmark-gene-editing-st

Inhalable mRNA medication under development;
http://news.mit.edu/2019/inhalable-messenger-rna-lung-disease-0104

An mRNA melanoma vaccine that modifies T cells succeeds in human trials;
https://www.labiotech.eu/medical/universal-cancer-vaccine-biontech/

3.4 Living environment and sustainable development

Background: Genetic engineering has been considered to be a risk for the living environment. The growing pressure related to the living environment has increased research in which genetic engineering is used to reduce the burden on the environment. Indoor farming, biotechnologically produced meat, plants that are resistant to pests and plant diseases, production that requires less space and has a higher yield, biofilms that produce fuels, and many other goal-oriented technologies seek success with the help of genetic engineering.

The continuously improving ability to read and process genetic data helps us study and understand the environment and its burdens. The strengthening ability to identify and develop responses to globally spreading plant diseases, viruses that spread to humans and animals as well as viruses and bacteria produced for the purpose of terrorism plays an important role. Genetic engineering has become so easy that its criminal use cannot be controlled. The only efficient method is to harness the technology for beneficial use to such a large degree that the ability to respond to problem situations is strengthened.

Genetic engineering related to the living environment and sustainable development is briefly touched upon in several sections of chapters 2.6.50, 2.7 and 2.8.74 of the 1/2018 report.

Recent events: DNA sequencing has been extensively utilised in the study of the routes of the spread of the coronavirus for the purpose of cutting off the chains of infection and developing a vaccine. Research investments have been directed towards the needs of the environment and sustainable development, which has begun to show in research results. The wide spread of CRISPR technology yields both benefits and risks. Genetic engineering can be carried out with very modest resources. Development cannot be controlled, and malicious or negligent development work cannot be prevented. Additionally, researchers are now able to spread the CRISPR editor with the help of pollen. In practice, this means that pollen that contains a genome editor can be spread into the air, where it travels to plants, pollinates them and simultaneously modifies the DNA of the seeds. This makes it possible to modify naturally occurring plants even over long distances. As this cannot be controlled or prevented in practice, we must develop capabilities to detect and respond to this.

Foresight: Industrial byproducts and household waste will be increasingly promising raw materials for the circular economy once we learn to process them with genetically modified organisms into energy and new raw materials and separate substances from them that could not be separated with previous technology. In the future, bio-based separation and processing methods that are based on genetic engineering also promise to reduce energy consumption by industry and agriculture and the use of chemicals. Observation of the harmful chemicals and microbes in the environment will become an everyday civic activity. On the other hand, environmental risks will also increase due to climate change, chemicalisation and bioterrorism.

New sources since the 1/2018 report:

Genetically modified E. coli uses carbon dioxide as a source of carbon (similarly to plants);
https://www.nature.com/articles/d41586-019-03679-x

DNA sequencing used in identifying the routes of the spread of the coronavirus;
https://www.technologyreview.com/s/615317/gene-sleuths-are-tracking-the-coronavirus-outbreak-as-it-happens/

Transgenic fungi kill malaria mosquitoes efficiently;
https://phys.org/news/2019-05-transgenic-fungus-rapidly-malaria-mosquitoes.html

Pollen carries CRISPR to its target;
https://www.sciencemag.org/news/2019/03/corn-and-other-important-crops-can-now-be-gene-edited-pollen-carrying-crispr

An AI that quickly synthesises and identifies protein structures;
https://www.chemistryworld.com/news/neural-network-folds-proteins-a-million-times-faster-than-its-competitors/3010451.article

4 General conclusions

The development of genetic engineering increases both threats and possibilities. In a global world, the weaker and narrower the national ability to detect and respond to threats, the more the threats multiply. The possibilities offered by genetic engineering are great in solving many major challenges, and promising development should not be obstructed with unnecessary restrictions. Some of the development is still at a stage in which investment from society is necessary in order to achieve a leap forwards before businesses are prepared to invest in the development. It is necessary to make changes to regulation, invest in expertise and support development.

PARLIAMENT
OF FINLAND

ISBN 978-951-53-3760-3 (PAPERBACK) • ISBN 978-951-53-3761-0 (PDF)