UNIT 13 - THE FUTURE OF GENOMICS AND NURSING

Precision Healthcare: Genomics-Informed Nursing by Andrea Gretchev

Please visit the web version of Precision Healthcare: Genomics-Informed Nursing (https://ecampusontario.pressbooks.pub/personalizedhealthnursing/) to access the complete book, interactive activities and ancillary resources.

Unit 13 Contents

Attribution

13.1 UNIT OVERVIEW

Learning Objectives

- Identify current and emerging gene therapies
- Explore ethical issues involving gene therapy and regulatory oversight
- Compare somatic-cell and germ-line gene therapy
- Examine additional biotechnologies that can contribute to health and wellness
- Envision the future of genomics nursing in the context of Canada's readiness for genomics integration

Outline

Topics covered in this chapter include:

- Gene editing
- Other genomic technologies
- Health system readiness for the genomic era

Competencies Nurses will Develop in this Chapter

ANA (2023):

Identification:

- Identifies credible, accurate, appropriate, and current genomic information, resources, services, and technologies specific to given clients.
- Identifies ethical, ethnic or ancestral, cultural, religious, legal, fiscal, and societal issues related to genomic

information and technologies.

NHS (2023):

Identify individuals who might benefit from genomic services and/or information as part of assessing needs and planning care:

- recognizing the key indicators of a potential genetic condition, or clinical situation where genomics-informed healthcare would be appropriate; and
- recognizing the importance of family history in assessing predisposition to a genetic condition.

Demonstrate a knowledge and understanding of genomics in human development, variation and health to underpin effective practice:

- relating it to the maintenance of health and manifestation of conditions;
- relating it to the prevention and management of a genomic condition or response to treatment; and
- underpinned by core genomic concepts that form a sufficient knowledge base for understanding the implications of different conditions and clinical situations that may be encountered.

Apply knowledge, understanding and context of genomic testing and information to underpin care and support for individuals and families prior to, during and following decision-making:

- incorporating awareness of the ethical, legal and social issues related to testing, recording, sharing and storage of genomic information and data.

Examine your own competency of practice on a regular basis:

- recognizing areas where professional development related to genomics would be beneficial;
- maintaining awareness of clinical developments in genomics that are likely to be of most relevance to your area of practice, seeking further information on a case-by-case basis; and
- based on an understanding of the boundaries of your professional role in delivering genomic healthcare including the referral, provision or follow-up to genomic services.

Obtain and communicate reliable, current information about genomics, for self, patients, families and colleagues:

- using information technologies and other information sources effectively to do so;
- applying critical appraisal skills to assess the quality of information accessed; and
- ensuring the information is appropriate for the intended audience.

Key terminology

Bio-hacking

A movement in which people are experimenting with biotechnology research and development methods outside of traditional research institutions (Parker et al., 2016).

CRISPR

CRISPR (short for "clustered regularly interspaced short palindromic repeats") is a technology that research scientists use to selectively modify the DNA of living organisms. CRISPR was adapted for use in the laboratory from naturally occurring genome editing systems found in bacteria.

Gene drives

A natural phenomenon whereby the inheritance of a particular gene or set of genes is favorably biased, resulting in the increase in its frequency in the population. Gene drives can arise through a variety of mechanisms, and scientists have proposed using gene editing to engineer gene drives for specific purposes (Parker et al., 2016).

Gene therapy

Gene therapy is a technique that uses a gene(s) to treat, prevent or cure a disease or medical disorder. Often, gene therapy works by adding new copies of a gene that is broken, or by replacing a defective or missing gene in a patient's cells with a healthy version of that gene. Both inherited genetic diseases (e.g., hemophilia and sickle cell disease) and acquired disorders (e.g., leukemia) have been treated with gene therapy.

Genetically modified organisms

GMO (short for "genetically modified organism") is a plant, animal or microbe in which one or more changes have been made to the genome, typically using high-tech genetic engineering, in an attempt to alter the characteristics of an organism. Genes can be introduced, enhanced or deleted within a species, across species or even across kingdoms. GMOs may be used for a variety of purposes, such as making human insulin, producing fermented beverages and developing pesticide resistance in crop plants.

Germline gene therapy

Alteration of a germline cells using gene therapy. These changes can be passed on to offspring, leading to unintended consequences for future generations (Parker et al., 2016).

Off-target effects

Potential alterations induced by CRISPR that are unintended, such as changing a beneficial gene, altering its product (Parker et al., 2016).

Recombinant DNA technology

Recombinant DNA technology involves using enzymes and various laboratory techniques to manipulate and isolate DNA segments of interest. This method can be used to combine (or splice) DNA from different species or to create genes with new functions. The resulting copies are often referred to as recombinant DNA. Such work typically involves propagating the recombinant DNA in a bacterial or yeast cell, whose cellular machinery copies the engineered DNA along with its own.

Transgenic

Transgenic refers to an organism or cell whose genome has been altered by the introduction of one or more foreign DNA sequences from another species by artificial means. Transgenic organisms are generated in the laboratory for research purposes.

Attribution & References

Except where otherwise noted, this page is adapted from:

- Talking Glossary of Genomic and Genetic Terms, Courtesy of: National Human Genome Research institute (NGHRI), Public Domain with attribution.
- 12.4 Gene Therapy In *Microbiology* by Nina Parker, Mark Schneegurt, Anh-Hue Thi Tu, Philip Lister and Brian M. Forster, CC BY 4.0. Access for free at *Microbiology (OpenStax) (https://openstax.org/books/microbiology/pages/1-introduction)*

Definitions adapted from the two sources and combined.

References

American Nurses Association (ANA). (2023). *Essentials of genomic nursing: Competencies and outcome indicators* (3rd ed.). https://www.nursingworld.org/nurses-books/ana-books/ebook-essentials-of-genomic-nursing-competencies-/

National Health Service (NHS). (2023). *The 2023 genomic competency framework for UK nurses*. https://www.genomicseducation.hee.nhs.uk/wp-content/uploads/2023/12/2023-Genomic-Competency-Framework-for-UK-Nurses.pdf

National Human Genome Research Institute (NHGRI). (n.d.). *Talking glossary of genetic and genomic terms*. https://www.genome.gov/genetics-glossary

Parker, N., Schneegurt, M., Tu, A. T., Lister, P., & Forster, B. M. (2016, November 1). *12.4 Gene therapy – Microbiology*. OpenStax. https://openstax.org/books/microbiology/pages/12-4-gene-therapy

13.2 GENE EDITING

Genetic Engineering

Many types of genetic engineering have yielded clear benefits with few apparent risks. Few would question, for example, the value of our now abundant supply of human insulin produced by genetically engineered bacteria. However, many emerging applications of genetic engineering are much more controversial, often because their potential benefits are pitted against significant risks, real or perceived. This is certainly the case for gene therapy, a clinical application of genetic engineering that may one day provide a cure for many diseases but is still largely an experimental approach to treatment.

Historically, clinical trials have shown the clear hazards of attempting genetic manipulation in complex multicellular organisms like humans. In some patients, the use of an adenovirus vector can trigger an unanticipated inflammatory response from the immune system, which may lead to organ failure. Moreover, because viruses can often target multiple cell types, the virus vector may infect cells not targeted for the therapy, damaging these other cells and possibly leading to illnesses such as cancer. Another potential risk is that the modified virus could revert to being infectious and cause disease in the patient. Lastly, there is a risk that the inserted gene could unintentionally inactivate another important gene in the patient's genome, disrupting normal cell cycling and possibly leading to tumor formation and cancer. Because gene therapy involves so many risks, candidates for gene therapy need to be fully informed of these risks before providing informed consent to undergo the therapy.

Case in Point: Gene Therapy Gone Wrong

The risks of gene therapy were realized in the 1999 case of Jesse Gelsinger, an 18-year-old patient who received gene therapy as part of a clinical trial at the University of Pennsylvania. Jesse received gene therapy for a condition called ornithine transcarbamylase (OTC) deficiency, which leads to ammonia accumulation in the blood due to deficient ammonia processing. Four days after the treatment, Jesse died after a severe immune response to the adenovirus vector (Sibbald, 2001).

Until that point, researchers had not really considered an immune response to the vector to be a legitimate risk, but on investigation, it appears that the researchers had some evidence suggesting that this was a possible outcome. Prior to Jesse's treatment, several other human patients had suffered side effects of the treatment, and three monkeys used in a trial had died as a result of inflammation

and clotting disorders. Despite this information, it appears that neither Jesse nor his family were made aware of these risks when they consented to the therapy. Jesse's death was the first patient death due to a gene therapy treatment and resulted in the immediate halting of the clinical trial in which he was involved, the subsequent halting of all other gene therapy trials at the University of Pennsylvania, and the investigation of all other gene therapy trials in the United States. As a result, regulation and oversight of gene therapy in general was reexamined, resulting in new regulatory protocols that are still in place today.

Source: Sibbald, B.. (2001). Death but one unintended consequence of gene-therapy trial. *Canadian Medical Association Journal,* 164(11), 1612–1612. https://pmc.ncbi.nlm.nih.gov/articles/PMC81135/

No discussion of gene editing would be complete without introducing CRISPR. Genome editing (also called gene editing) is a group of technologies that give scientists the ability to change an organism's DNA. These technologies allow genetic material to be added, removed, or altered at particular locations in the genome. Several approaches to genome editing have been developed. A well-known one is called CRISPR-Cas9, which is short for clustered regularly interspaced short palindromic repeats and CRISPR-associated protein 9. The CRISPR-Cas9 system has generated a lot of excitement in the scientific community because it is faster, cheaper, more accurate, and more efficient than other genome editing methods.

CRISPR-Cas9 was adapted from a naturally occurring genome editing system that bacteria use as an immune defense. When infected with viruses, bacteria capture small pieces of the viruses' DNA and insert them into their own DNA in a particular pattern to create segments known as CRISPR arrays. The CRISPR arrays allow the bacteria to "remember" the viruses (or closely related ones). If the viruses attack again, the bacteria produce RNA segments from the CRISPR arrays that recognize and attach to specific regions of the viruses' DNA. The bacteria then use Cas9 or a similar enzyme to cut the DNA apart, which disables the virus.

Researchers adapted this immune defense system to edit DNA. They create a small piece of RNA with a short "guide" sequence that attaches (binds) to a specific target sequence in a cell's DNA, much like the RNA segments bacteria produce from the CRISPR array. This guide RNA also attaches to the Cas9 enzyme. When introduced into cells, the guide RNA recognizes the intended DNA sequence, and the Cas9 enzyme cuts the DNA at the targeted location, mirroring the process in bacteria. Although Cas9 is the enzyme that is used most often, other enzymes (for example Cpf1) can also be used. Once the DNA is cut, researchers use the cell's own DNA repair machinery to add or delete pieces of genetic material, or to make changes to the DNA by replacing an existing segment with a customized DNA sequence.

Genome editing is of great interest in the prevention and treatment of human diseases. Currently, genome editing is used in cells and animal models in research labs to understand diseases. Scientists are still working to determine whether this approach is safe and effective for use in people.

CRISPR – Applications in Humans

Applications of CRISPR in humans include treatment for sickle cell disease, (https://ghr.nlm.nih.gov/condition/sickle-cell-disease) which causes severe pain and premature death in millions of people worldwide. Scientists use CRISPR to treat sickle cell disease by removing blood stem cells from a patient with sickle cell disease, editing the genome of those cells to remove the sickle cell variant, and then re-insert the modified cells into the person's bone marrow.

Another CRISPR application now entering human clinical trials aims to combat human immunodeficiency virus (or HIV) infection (https://www.drugtargetreview.com/news/145203/eliminating-the-hiv-virus-from-infected-cells-with-crispr-cas/). HIV enters human white blood cells and then alters those cells' genomes. Then, it makes copies of itself to infect the person's immune system, making them vulnerable to other infections. CRISPR is now being investigated for use in either cutting out the HIV-derived DNA from the genome as well as engineering a person's genome so that HIV cannot enter their cells. However, it is important to stress that these techniques are still relatively new and very much still in testing mode.

Concept in Action

Oversight of Gene Therapy

Presently, there is significant oversight of gene therapy clinical trials. In the US, at the federal level, three agencies regulate gene therapy in parallel: the Food and Drug Administration (FDA), the Office of Human Research Protection (OHRP), and the Recombinant DNA Advisory Committee (RAC) at the National Institutes of Health (NIH). Along with several local agencies, these federal agencies interact with the institutional review board to ensure that protocols are in place to protect patient safety during clinical trials. Compliance with these protocols is enforced mostly on the local level in cooperation with the federal agencies. Gene therapies are currently under the most extensive federal and local review compared to other types of therapies, which are more typically only under the review of the FDA. Some researchers believe that these extensive regulations actually inhibit progress in gene therapy research. In 2013, the Institute of Medicine (now the National Academy of Medicine) called upon the NIH to relax its review of gene therapy trials in most cases (Grens, 2013). However, ensuring patient safety continues to be of utmost concern.

In Canada, gene therapy products are regulated in the same way as other pharmaceuticals, under the *Food and Drugs Act* and *Food and Drug Regulations* (Jorgensen et al., 2024). Gene therapy products are classified by Health Canada as biologic drugs, which are under the purview of the Health Canada (HC) Biologic and Radiopharmaceutical Drugs Directorate (Jorgensen et al., 2024). Gene therapy products qualify for expedited

approval via HC Notice of Compliance with Conditions (NOC/c), approving drugs that have evidence of potential to treat serious life-threatening or life-limiting conditions, subject to further testing. As such, these drugs are usually not subject to phase 3 clinical trials (Jorgensen et al., 2024).

As of June 6, 2024, there were ten approved gene therapy products in Canada, including treatments targeting rare and severe conditions such as blood cancers and spinal muscular atrophy (Jorgensen et al., 2024). Six of these are CAR-T therapies for blood cancer treatment and the other four are AAV-based therapies that restore gene function (Jorgensen et al., 2024). As of November 21, 2024, there were 41 FDA-approved gene and cell therapies in the US, including treatment for several types of cancer, Duchenne muscular dystrophy, hemophilia A and B, type 1 diabetes, spinal muscular atrophy, and sickle cell disease (USFDA, 2024).

In 2024 Health Canada approved CASGEVY® (exagamglogene autotemcel), an autologous CRISPR-Cas9 genome-edited hematopoietic stem cell therapy to treat sickle cell disease (SCD). This is the first CRISPER-based gene editing therapy approved in Canada. For those who qualify, this will bring relief for this severely debilitating and progressive disease. However, the cost of these medications is exorbitant and it is unclear in the long term whether provincial healthcare plans or insurance companies will continue to pay. CASGEVY, for example, costs $2.2 million for a one-time treatment (Watt, 2024). According to Watt (2024), LENMELDY is one of the most expensive at $4.25 million per dose. However, the cost of managing SCD using other previously existing therapies, including hospital stays for crisis management, is comparable, if not more (Watt, 2024).

Ethical Concerns

Beyond the health risks of gene therapy, the ability to genetically modify humans poses a number of ethical issues related to the limits of such "therapy." While current research is focused on gene therapy for genetic diseases, scientists might one day apply these methods to manipulate other genetic traits not perceived as desirable, which brings us back to the discussion on eugenics. This raises questions such as:

- Which genetic traits are worthy of being "corrected"?
- Should gene therapy be used for cosmetic reasons or to enhance human abilities?
- Should genetic manipulation be used to impart desirable traits to the unborn?
- Is everyone entitled to gene therapy, or could the cost of gene therapy create new forms of social inequality?
- Who should be responsible for regulating and policing inappropriate use of gene therapies?

What are off-target effects?

There are concerns that CRISPR might inadvertently alter regions of the genome other than the intended

ones. These are called "**off-target effects**." The worry is that CRISPR could change a beneficial gene, such as disabling a tumor-suppressing gene or activating one that causes cancer. Another concern is that because no two people's genomes are identical, identifying off-target effects in individuals may be impossible. Researchers attempt to predict where in the genome off-target effects might occur using web-based algorithms, but there are concerns that this approach is not accurate enough.

In May 2017, an article published in the journal Nature Methods (http://www.nature.com/nmeth/journal/v14/n6/full/nmeth.4293.html) reported an alarming number of off-target variants in mice whose genomes had been edited using CRISPR. However, experts voiced skepticism (https://geneticliteracyproject.org/2017/06/02/crispr-study-reporting-off-target-mutations-draws-skepticism-researchers/) of the finding because only two mice were edited and unusual methods used. Scientists are attempting to address these concerns by developing more precise variants of the Cas9 enzyme used in the CRISPR system. Some of these enzymes have been shown to improve targeting in human tissue in the lab. Researchers have also focused on developing methods to more efficiently locate off-target variants in the animals they study.

Somatic vs. Germline Editing

The ability to alter reproductive cells using gene therapy could also generate new ethical dilemmas. To date, the various types of gene therapies have been targeted to somatic cells, the non-reproductive cells within the body. Because somatic cell traits are not inherited, any genetic changes accomplished by somatic-cell gene therapy would not be passed on to offspring. However, should scientists successfully introduce new genes to germ cells, the resulting traits could be passed on to offspring. This approach, called **germ-line gene therapy**, could potentially be used to combat heritable diseases, but it could also lead to unintended consequences for future generations. Moreover, there is the question of informed consent, because those impacted by germ-line gene therapy are unborn and therefore unable to choose whether they receive the therapy. For these reasons, the U.S. government does not currently fund research projects investigating germ-line gene therapies in humans.

Ethical Issues Spotlight

In 2018, Chinese researcher He Jiankui edited twin embryos using CRISPER to disable the CCR5 gene to make them immune to HIV infection and transplanted them into a human uterus. He only announced his work to the world once the twins were born. As a result, the Chinese government arrested him and he served jail time. There was immense backlash following his announcement among the scientific community. This expedited the conversation around the ethical issues on the use of this technology.

Read this short article that highlight the concerns

Bai, N. (2018, November 30). *What's so controversial about the first gene-edited babies? Experts explain*. University of California San Francisco. https://www.ucsf.edu/news/2018/11/412461/whats-so-controversial-about-first-gene-edited-babies-experts-explain

Following the announcement about the work of He Jiankui, in 2019, scientists called for a five-year global moratorium on all clinical uses of human germline editing (Ladner et al., 2019). The aim was to allow for a period of discussion about the potential medical, societal, and ethical issues germline editing might pose. This was to be followed by a period where nations would choose how to proceed and whether they would continue to impose a ban. The hope was for transparency and open communication amongst the scientific community. The ban did not apply to research using germline editing, provided there was no transfer of embryos to a human uterus (Ladner et al., 2019). In Canada, the TCPS2 guidelines, article 13.7, section G, addresses research involving gene transfer. It directs readers to the *Assisted Human Reproduction Act* which prohibits altering the human genome or in vitro embryo such that the alteration can be passed on to subsequent generations (Government of Canada, 2022). While there are no laws or regulations in many countries prohibiting germline editing, the moratorium is strictly voluntary. It has now been five years and, despite the potential ethical issues remaining, there is discussion that South Africa might be the first country to accept germline editing (https://www.nature.com/articles/d41586-024-03643-4).

What are gene drives?

A **gene drive** is a natural phenomenon whereby the inheritance of a particular gene or set of genes is favorably biased, resulting in the increase in its frequency in the population. Gene drives can arise through a variety of mechanisms, and scientists have proposed using gene editing to engineer gene drives for specific purposes. These include preventing the spread of insects that carry pathogens, such as mosquitoes that transmit malaria, dengue, Zika and other diseases.

Here is how it works: This system uses genetically modified male mosquitos to deliver new genes along with a mechanism for copying the new sequences from one member of a chromosome pair to the other. In other words, a mosquito larva has a gene that came only from its father, yet has it as both a paternal and maternal copy. Thus, even a recessive gene will manifest its trait in all offspring. Furthermore, the offspring will spread the gene and trait to their own offspring. Since mosquitoes have a short life cycle, this means that in the course of just a summer, we could alter almost the entire population of a particular mosquito species in

say the Brazilian rain forest, possibly wiping out the Zika disease. In August 2016 the U.S. Food And Drug Administration (FDA) issued a "Finding of No Significant Impact (https://www.fda.gov/AnimalVeterinary/NewsEvents/CVMUpdates/ucm490246.htm)" to biotech company Oxitec's plan to release genetically modified male Aedes aegypti mosquitoes into the Florida Keys.

Engineered gene drives have also been proposed (https://geneticliteracyproject.org/2017/11/16/saving-galapagos-gene-drives-help-rid-invasive-pests/) to control invasive species, such as rodents that eat the eggs of endangered bird species in New Zealand, and for eliminating herbicide and pesticide resistance in crops.

Concerns about gene drives (https://geneticliteracyproject.org/2017/11/17/gene-drive-trials-risky-field-studies/) include the possibility that a variant could happen during the engineered gene drive, which could spread unwanted traits with the drive. The spread of some other disease could be unexpectedly facilitated. Or the elimination of a link in the food chain could harm the local ecology. It's also plausible that something could happen akin to the introduction of rabbits in 19th century Australia (http://www.nma.gov.au/online_features/defining_moments/featured/rabbits_introduced), where the population exploded, due to lack of predators, with major consequences for the ecosystem. There are also worries that an engineered gene drive could move beyond its target population, causing unintended impacts on other species and ecosystems.

Anti-biotechnology activists including Vandana Shiva, Jane Goodall and David Suzuki have advocated against the use of gene drives. In August 2017, they joined with other radical environmental groups (https://globaljusticeecology.org/30-environmental-leaders-say-no-to-gene-drives-in-conservation/) to issue a well-publicized opposition statement [PDF] (http://www.etcgroup.org/files/files/final_gene_drive_letter.pdf) to gene drive technology, writing:

Given the obvious dangers of irretrievably releasing genocidal genes into the natural world, and the moral implications of taking such action, we call for a halt to all proposals for the use of gene drive technologies, but especially in conservation.

In 2016, the National Academy of Sciences issued its wide-ranging review of dozens of studies, Report on Gene Drives in Non-Human Organisms [PDF] (https://www.nap.edu/resource/23405/Gene-Drives-Brief.pdf), which outlined a number of potential risks but urged more research and gave a cautious green light to "highly controlled field trials." Some studies have come to different conclusions, among them: researchers at the University of California, San Diego and colleagues at Harvard created a mathematical model (https://www.nytimes.com/2017/11/16/science/gene-drives-crispr.html) for CRISPRs likely success, concluding the a gene drive could be remarkably aggressive in the wild, spreading a new gene beyond its targeted population—possibly meaning that experiments in the real world are too risky on a case by case basis at this stage in the technology's development.

If you are interested in learning how CRISPR-Cas9 is being used by consumers and bio-hackers,

What is "bio-hacking" and "DIY-bio?"

Do-it-yourself biology, also called "**biohacking**" or "DIY bio," is a movement in which people are experimenting with biotechnology

research and development methods outside of traditional research institutions. Some "biohackers" are trying to make these methods easier and more accessible, so that even non-scientists can use them. Because of its relative ease to deploy, CRISPR experiments can be performed even by high school students.

watch this fascinating and horrifying documentary on Netflix – Unnatural Selection (https://www.netflix.com/ca/title/80208910)

One of the most accessible forms of biohacking is through engineering microorganisms or plants. Experiments range from using plasmids to create fluorescent bacteria, controlling gene expression using light in bacteria and even using CRISPR to engineer the genomes of bacteria or yeast. Some biohackers have begun selling kits that allow you to use CRISPR at home (https://geneticliteracyproject.org/2017/11/09/crispr-home-easy-hack-dna/). One kit, created as part of an Indiegogo crowd-funding project, was sold for $130 by biohacker Josiah Zayner.

The Future of CRISPR

Despite the serious ethical challenges, CRISPR/Cas 9 is a promising technology to treat a multitude of conditions.

Concept in Action

Watch this brief Ted Talk given by Nobel Prize recipient Jennifer Doudna, the scientist credited with CRISPR's creation, speak about how metagenomics and CRISPR are being combined to create a new field of science called Precision Microbiome editing. This could provide a transformative solution targeting the microbiome to treat diseases and disorders such as asthma, obesity, diabetes, Alzheimer's and climate change.

Watch CRISPR's Next Advance is Bigger Than You Think | Jennifer Doudna | TED (8 mins) on YouTube (https://youtu.be/HANo__Z8K6s)

Attribution & References

- CRISPR – Applications in Humans from Genome Editing, courtesy of National Human Genome Research Institute (NHGRI), Public Domain with attribution
- Paragraphs on gene therapy products in Canada and Ethical Issues spotlight written by Andrea Gretchev, CC BY-NC 4.0
- Genome Editing and Human Disease from What are genome editing and CRISPR-Cas9? In *Help Me Understand Genetics* Courtesy of MedlinePlus from the National Library of Medicine, Public Domain with attribution

References

Jorgensen, P.l., Heir, P., Daniele, D., & Wall, K. (2024, June 6). *IP monitor: Gene therapy products in Canada: Regulation, IP and emerging issue*s. Norton Rose Fulbright.

Government of Canada Panel on Research Ethics. (2022). TCPS2 (2022) – Chapter 13: Human genetic research.

Grens, K. (2013, December 9). *Ease Gene Therapy Reviews* [Report]. The Scientist.

Lander, E. S., Baylis, F., Zhang, F., Charpentier, E., Berg, P., Bourgain, C., Friedrich, B., Joung, J. K., Li, J., Liu, D., Naldini, L., Nie, J. B., Qiu, R., Schoene-Seifert, B., Shao, F., Terry, S., Wei, W., & Winnacker, E. L. (2019). Adopt a moratorium on heritable genome editing. *Nature*, *567*(7747), 165–168. https://doi.org/10.1038/d41586-019-00726-5

Sibbald, B.. (2001). Death but one unintended consequence of gene-therapy trial. *Canadian Medical Association Journal,* 164(11), 1612–1612. https://pmc.ncbi.nlm.nih.gov/articles/PMC81135/

US Food and Drug Administration (USFDA). (2024, November 21). *Approved Cellular and Gene Therapy Products*. https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products

Watt, A. (2024, August 2). *Casgevy: Launch sequence and price analysis of the first marketed CRISPR therapy*. Pharmaceutical Technology.

13.3 OTHER GENOMIC TECHNOLOGIES

It is easy to see how biotechnology can be used for medicinal purposes. Knowledge of the genetic makeup of our species, the genetic basis of heritable diseases, and the invention of technology to manipulate and fix gene variants provides methods to treat diseases. Biotechnology in agriculture can enhance resistance to disease, pests, and environmental stress to improve both crop yield and quality. Genomic technologies have the potential to transform the future of health and healthcare.

Production of Vaccines, Antibiotics, and Hormones

Traditional vaccination strategies use weakened or inactive forms of microorganisms or viruses to stimulate the immune system. Modern techniques use specific genes of microorganisms cloned into vectors and mass-produced in bacteria to make large quantities of specific substances to stimulate the immune system. The substance is then used as a vaccine. In some cases, such as the H1N1 flu vaccine, genes cloned from the virus have been used to combat the constantly changing strains of this virus.

Antibiotics kill bacteria and are naturally produced by microorganisms such as fungi; penicillin is perhaps the most well-known example. Antibiotics are produced on a large scale by cultivating and manipulating fungal cells. The fungal cells have typically been genetically modified to improve the yields of the antibiotic compound.

Recombinant DNA technology was used to produce large-scale quantities of the human hormone insulin in *E. coli* as early as 1978. Previously, it was only possible to treat diabetes with pig insulin, which caused allergic reactions in many humans because of differences in the insulin molecule. In addition, human growth hormone (HGH) is used to treat growth disorders in children. The HGH gene was cloned from a cDNA (complementary DNA) library and inserted into *E. coli* cells by cloning it into a bacterial vector.

Transgenic Animals

Although several recombinant proteins used in medicine are successfully produced in bacteria, some proteins need a eukaryotic animal host for proper processing. For this reason, genes have been cloned and expressed in animals such as sheep, goats, chickens, and mice. Animals that have been modified to express recombinant DNA are called **transgenic animals**. Several human proteins are expressed in the milk of transgenic sheep and goats. In one commercial example, the FDA has approved a blood anticoagulant protein that is produced in the milk of transgenic goats for use in humans. Mice have been used extensively for expressing and studying the effects of recombinant genes and variants.

Figure 13.1 It can be seen that two of these mice are transgenic because they have a gene that causes them to fluoresce under a UV light. The non-transgenic mouse does not have the gene that causes fluorescence. **Source:** Moen et al., CC BY 2.0)

Cloning

The term cloning describes a number of different processes that can be used to produce genetically identical copies of a biological entity. The copied material, which has the same genetic makeup as the original, is referred to as a clone. Researchers have cloned a wide range of biological materials, including genes, cells, tissues and even entire organisms, such as a sheep.

Do clones ever occur naturally?

Yes. In nature, some plants and single-celled organisms, such as bacteria (https://www.genome.gov/Glossary/?id=15), produce genetically identical offspring through a process called asexual reproduction. In asexual reproduction, a new individual is generated from a copy of a single cell from the parent organism.

Natural clones, also known as identical twins, occur in humans and other mammals. These twins are produced when a fertilized egg splits, creating two or more embryos that carry almost identical DNA (https://www.genome.gov/Glossary/?id=48). Identical twins have nearly the same genetic makeup as each other, but they are genetically different from either parent.

What are the types of artificial cloning?

There are three different types of artificial cloning: gene cloning, reproductive cloning and therapeutic cloning.

Gene cloning produces copies of genes or segments of DNA. Reproductive cloning produces copies of whole animals. Therapeutic cloning produces embryonic stem cells for experiments aimed at creating tissues to replace injured or diseased tissues.

Gene cloning, also known as DNA cloning, is a very different process from reproductive and therapeutic cloning. Reproductive and therapeutic cloning share many of the same techniques, but are done for different purposes.

How are genes cloned?

Researchers routinely use cloning techniques to make copies of genes that they wish to study. The procedure consists of inserting a gene from one organism, often referred to as "foreign DNA," into the genetic material of a carrier called a vector. Examples of vectors include bacteria, yeast cells, viruses or plasmids, which are small DNA circles carried by bacteria. After the gene is inserted, the vector is placed in laboratory conditions that prompt it to multiply, resulting in the gene being copied many times over.

How are animals cloned?

In reproductive cloning, researchers remove a mature somatic cell (http://www.genome.gov/Glossary/?id=186), such as a skin cell, from an animal that they wish to copy. They then transfer the DNA of the donor animal's somatic cell into an egg cell, or oocyte, that has had its own DNA-containing nucleus removed.

Researchers can add the DNA from the somatic cell to the empty egg in two different ways. In the first method, they remove the DNA-containing nucleus of the somatic cell with a needle and inject it into the empty egg. In the second approach, they use an electrical current to fuse the entire somatic cell with the empty egg.

In both processes, the egg is allowed to develop into an early-stage embryo in the test-tube and then is implanted into the womb of an adult female animal.

Ultimately, the adult female gives birth to an animal that has the same genetic make up as the animal that donated the somatic cell. This young animal is referred to as a clone. Reproductive cloning may require the use of a surrogate mother to allow development of the cloned embryo, as was the case for the most famous cloned organism, Dolly the sheep.

What animals have been cloned?

Over the last 50 years, scientists have conducted cloning experiments in a wide range of animals using a variety of techniques. In 1979, researchers produced the first genetically identical mice by splitting mouse embryos in the test tube and then implanting the resulting embryos into the wombs of adult female mice. Shortly after that, researchers produced the first genetically identical cows, sheep and chickens by transferring the nucleus of a cell taken from an early embryo into an egg that had been emptied of its nucleus.

It was not until 1996, however, that researchers succeeded in cloning the first mammal from a mature (somatic) cell taken from an adult animal. After 276 attempts, Scottish researchers finally produced Dolly, the lamb from the udder cell of a 6-year-old sheep. Two years later, researchers in Japan cloned eight calves from a single cow, but only four survived.

Besides cattle and sheep, other mammals that have been cloned from somatic cells include: cat, deer, dog, horse, mule, ox, rabbit and rat. In addition, a rhesus monkey has been cloned by embryo splitting.

Have humans been cloned?

Despite several highly publicized claims, human cloning still appears to be fiction. There currently is no solid scientific evidence that anyone has cloned human embryos.

In 1998, scientists in South Korea claimed to have successfully cloned a human embryo, but said the experiment was interrupted very early when the clone was just a group of four cells. In 2002, Clonaid, part of a religious group that believes humans were created by extraterrestrials, held a news conference to announce the birth of what it claimed to be the first cloned human, a girl named Eve. However, despite repeated requests by the research community and the news media, Clonaid never provided any evidence to confirm the existence of this clone or the other 12 human clones it purportedly created.

In 2004, a group led by Woo-Suk Hwang of Seoul National University in South Korea published a paper in the journal *Science* in which it claimed to have created a cloned human embryo in a test tube. However, an independent scientific committee later found no proof to support the claim and, in January 2006, *Science* announced that Hwang's paper had been retracted.

From a technical perspective, cloning humans and other primates is more difficult than in other mammals. One reason is that two proteins essential to cell division, known as spindle proteins, are located very close to the chromosomes in primate eggs. Consequently, removal of the egg's nucleus to make room for the donor nucleus also removes the spindle proteins, interfering with cell division. In other mammals, such as cats, rabbits and mice, the two spindle proteins are spread throughout the egg. So, removal of the egg's nucleus does not result in loss of spindle proteins. In addition, some dyes and the ultraviolet light used to remove the egg's nucleus can damage the primate cell and prevent it from growing.

What are the potential applications of cloned animals?

Reproductive cloning may enable researchers to make copies of animals with the potential benefits for the fields of medicine and agriculture.

For instance, the same Scottish researchers who cloned Dolly have cloned other sheep that have been genetically modified to produce milk that contains a human protein essential for blood clotting. The hope is that someday this protein can be purified from the milk and given to humans whose blood does not clot properly. Another possible use of cloned animals is for testing new drugs and treatment strategies. The great advantage of using cloned animals for drug testing is that they are all genetically identical, which means their responses to the drugs should be uniform rather than variable as seen in animals with different genetic make-ups.

After consulting with many independent scientists and experts in cloning, the U.S. Food and Drug Administration (FDA) decided in January 2008 that meat and milk from cloned animals, such as cattle, pigs and goats, are as safe as those from non-cloned animals. The FDA action means that researchers are now free to using cloning methods to make copies of animals with desirable agricultural traits, such as high milk production or lean meat. However, because cloning is still very expensive, it will likely take many years until food products from cloned animals actually appear in supermarkets.

Another application is to create clones to build populations of endangered, or possibly even extinct, species of animals. In 2001, researchers produced the first clone of an endangered species: a type of Asian ox known as a guar. Sadly, the baby guar, which had developed inside a surrogate cow mother, died just a few days after its birth. In 2003, another endangered type of ox, called the Banteg, was successfully cloned. Soon after, three African wildcats were cloned using frozen embryos as a source of DNA. Although some experts think cloning can save many species that would otherwise disappear, others argue that cloning produces a population of genetically identical individuals that lack the genetic variability necessary for species survival.

Some people also have expressed interest in having their deceased pets cloned in the hope of getting a similar animal to replace the dead one. But as shown by Cc the cloned cat, a clone may not turn out exactly like the original pet whose DNA was used to make the clone.

What are the potential drawbacks of cloning animals?

Reproductive cloning is a very inefficient technique and most cloned animal embryos cannot develop into healthy individuals. For instance, Dolly was the only clone to be born live out of a total of 277 cloned embryos. This very low efficiency, combined with safety concerns, presents a serious obstacle to the application of reproductive cloning.

Researchers have observed some adverse health effects in sheep and other mammals that have been cloned. These include an increase in birth size and a variety of defects in vital organs, such as the liver, brain and heart. Other consequences include premature aging and problems with the immune system. Another potential

problem centers on the relative age of the cloned cell's chromosomes. As cells go through their normal rounds of division, the tips of the chromosomes, called telomeres, shrink. Over time, the telomeres become so short that the cell can no longer divide and, consequently, the cell dies. This is part of the natural aging process that seems to happen in all cell types. As a consequence, clones created from a cell taken from an adult might have chromosomes that are already shorter than normal, which may condemn the clones' cells to a shorter life span. Indeed, Dolly, who was cloned from the cell of a 6-year-old sheep, had chromosomes that were shorter than those of other sheep her age. Dolly died when she was six years old, about half the average sheep's 12-year lifespan.

What is therapeutic cloning?

Therapeutic cloning involves creating a cloned embryo for the sole purpose of producing embryonic stem cells with the same DNA as the donor cell. These stem cells can be used in experiments aimed at understanding disease and developing new treatments for disease. To date, there is no evidence that human embryos have been produced for therapeutic cloning.

The richest source of embryonic stem cells is tissue formed during the first five days after the egg has started to divide. At this stage of development, called the blastocyst, the embryo consists of a cluster of about 100 cells that can become any cell type. Stem cells are harvested from cloned embryos at this stage of development, resulting in destruction of the embryo while it is still in the test tube.

What are the potential applications of therapeutic cloning?

Researchers hope to use embryonic stem cells, which have the unique ability to generate virtually all types of cells in an organism, to grow healthy tissues in the laboratory that can be used replace injured or diseased tissues. In addition, it may be possible to learn more about the molecular causes of disease by studying embryonic stem cell lines from cloned embryos derived from the cells of animals or humans with different diseases. Finally, differentiated tissues derived from ES cells are excellent tools to test new therapeutic drugs.

What are the potential drawbacks of therapeutic cloning?

Many researchers think it is worthwhile to explore the use of embryonic stem cells as a path for treating human diseases. However, some experts are concerned about the striking similarities between stem cells and cancer cells. Both cell types have the ability to proliferate indefinitely and some studies show that after 60 cycles of cell division, stem cells can accumulate variants that could lead to cancer. Therefore, the relationship between stem cells and cancer cells needs to be more clearly understood if stem cells are to be used to treat human disease.

What are some of the ethical issues related to cloning?

Gene cloning is a carefully regulated technique that is largely accepted today and used routinely in many labs worldwide. However, both reproductive and therapeutic cloning raise important ethical issues, especially as related to the potential use of these techniques in humans.

Reproductive cloning would present the potential of creating a human that is genetically identical to another person who has previously existed or who still exists. This may conflict with long-standing religious and societal values about human dignity, possibly infringing upon principles of individual freedom, identity and autonomy. However, some argue that reproductive cloning could help sterile couples fulfill their dream of parenthood. Others see human cloning as a way to avoid passing on a deleterious gene that runs in the family without having to undergo embryo screening or embryo selection.

Therapeutic cloning, while offering the potential for treating humans suffering from disease or injury, would require the destruction of human embryos in the test tube. Consequently, opponents argue that using this technique to collect embryonic stem cells is wrong, regardless of whether such cells are used to benefit sick or injured people.

Attribution & References

References

Moen, I., Jevne, C., Wang, J., Kalland, K., Chekenya, M., Akslen, L. A., Sleire, L., Enger, P. Ø., Reed, R. K., Øyan, A. M., & Stuhr, L. E. (2012). Gene expression in tumor cells and stroma in dsRed 4T1 tumors in eGFP-expressing mice with and without enhanced oxygenation. *BMC Cancer*, *12*(1). https://doi.org/10.1186/1471-2407-12-21

13.4 HEALTH SYSTEM READINESS FOR THE GENOMIC ERA

Nursing & The Future of Genomics

The future of genomics in healthcare is poised to transform the prevention, diagnosis, and treatment of diseases through precision medicine. As healthcare evolves to integrate these technologies, nurses will play a pivotal role as educators, advocates, and leaders. They will guide patients in understanding genetic information, support informed decision-making, and bridge the gap between complex genomic data and patient-centred care. Additionally, nurses will contribute to interdisciplinary teams by addressing ethical considerations, ensuring equitable access to genomic interventions, and fostering genomic literacy within healthcare systems. Their holistic perspective positions them as vital contributors to the equitable implementation of genomics in improving population health outcomes.

Watch The Future of Genomics (1 mins) on YouTube (https://youtu.be/Ghkrzc0QxrA)

What will the future of genomics look like?

Watch Siddhartha Mukherjee, biologist, physician, and Pulitzer Prize-winning author of the Gene: An Intimate History, describe 10 bold predictions for the future of genomics.

Note: This is an amazing book that everyone should read! There is also a full length PBS series by Ken Burns based on the book by Mukherjee (https://www.pbslearningmedia.org/resource/the-gene-full-film/the-gene-intimate-history/).

Watch The Future of Genomics: 10 Bold Predictions (4 mins) on YouTube (https://youtu.be/5kAL11m_fwM)

Visit the NHGRI website for an interactive web-based application detailing the NHGRI 2020 Strategic Vision (https://www.genome.gov/2020SV). You can also access the full document in .pdf format [PDF]

(https://www.genome.gov/sites/default/files/media/files/2022-11/Strategic-vision-for-improving-human-health-at-The-Forefront-of-Genomics.pdf).

Canada's Readiness for Genomics Integration

In this course, we have discussed the benefits of genomics, alongside the challenges associated with its implementation. In 2021, Canada committed $400 million dollars to the Pan-Canadian Genomics Strategy (PCGS), aiming to position Canada as a global leader in genomics innovation (Government of Canada, 2023). To guide this initiative, the government engaged interested parties to identify strategic priorities, resulting in publishing a consultation paper (https://ised-isde.canada.ca/site/genomics/en/consultation-paper-developing-pan-canadian-genomics-strategy).

The consultation paper (Government of Canada, 2023) outlines that a major challenge to genomics integration lies in the fragmentation of genomics services due to federated health systems, which hinder a unified national approach. Addressing these gaps requires enhanced coordination and collaboration across jurisdictions. Building a robust genomics workforce is also critical, involving initiatives to develop expertise, create employment opportunities, and attract and retain top talent. Furthermore, the standardization and secure sharing of genomic data across regions must be prioritized to maximize the utility of genomics research. The Global Alliance for Genomics and Health (GA4GH, n.d) provides a framework for responsible sharing of genomic and health-related data (https://www.ga4gh.org/framework/). Additionally, the World Health Organization (2024) just released guidance for human genome data collection, access, use and data sharing (https://www.who.int/publications/i/item/9789240102149).Overcoming barriers in transitioning genomics technologies from research to commercialization, including pharmaceuticals, is essential for Canada to lead in the genomic era. Finally, the integration of genomics across diverse sectors—such as healthcare, environmental stewardship, and the food industry—will be pivotal in realizing the full potential of genomics in advancing Canadian society (Government of Canada, 2023). The Canadian Institutes of Health Research strategic plan Sequencing Our Future: 2020-2027, (https://cihr-irsc.gc.ca/e/52973.html) mentioned in a previous unit, also commits to enabling genomic medicine through research, including streamlining data access through developing a Canadian Human Genome Library (https://genomelibrary.ca/). Husereau et al. (2023) evaluated Canada's readiness to adopt widespread genomic testing through a comprehensive literature review and interviews with key informants. Their analysis assessed the healthcare system against established readiness conditions, revealing that Canada remains in the early stages of preparing for a genomic future. Among the provinces examined by the authors (British Columbia, Alberta, Ontario, Quebec, and Nova Scotia), Alberta and Quebec have made the most significant strides in genomics integration, attributed to their establishment of centralized laboratories and service organizations, which mitigate fragmentation within these provinces. In contrast, provinces with multiple health authorities face heightened challenges in coordinating genomic services. These findings align with priorities identified in the consultation paper and underscore the need for provider education and navigation tools to facilitate integration into healthcare

systems. A major barrier highlighted is funding, which will require substantial attention to ensure successful implementation (Husereau et al., 2023).

Attribution & References

References

Global Alliance for Genomics & Health. (n.d). *Framework for responsible sharing of genomic and health-related data* . https://www.ga4gh.org/framework/

Government of Canada. (2023, August 24). *Consultation paper: Developing a pan-Canadian genomics strategy*. https://ised-isde.canada.ca/site/genomics/en/consultation-paper-developing-pan-canadian-genomics-strategy

Husereau, D., Villalba, E., Muthu, V., Mengel, M., Ivany, C., Steuten, L., Spinner, D. S., Sheffield, B., Yip, S., Jacobs, P., Sullivan, T., & Arshoff, L. (2023). Progress toward Health System Readiness for Genome-Based Testing in Canada. *Current oncology (Toronto, Ont.)*, *30*(6), 5379–5394. https://doi.org/10.3390/curroncol30060408

World Health Organization. (2024, November 20). *Guidance for human genome data collection, access, use and data sharing*. https://www.who.int/publications/i/item/9789240102149

13.6 UNIT SUMMARY AND REVIEW

Key Takeaways

Genetic engineering has produced significant benefits, such as insulin production, but applications like gene therapy remain controversial due to significant risks and ethical issues. Gene therapy shows potential to cure diseases but has faced challenges, including immune reactions to viral vectors, off-target effects, and tumor risks, as highlighted by the 1999 case of Jesse Gelsinger, whose death spurred stricter regulations.

Advancements in genome editing, particularly CRISPR-Cas9, have revolutionized DNA manipulation by enabling precise, efficient, and cost-effective edits. Adapted from bacterial immune systems, CRISPR-Cas9 introduces targeted DNA cuts, allowing researchers to modify genetic material. Applications include promising but experimental treatments for conditions such as sickle cell disease and HIV, though these approaches remain under evaluation for safety and efficacy in humans.

Biotechnology has broad applications in medicine, leveraging genetic knowledge and technology to address challenges such as disease treatment. In medicine, biotechnology enables the production of vaccines, antibiotics, and hormones, often using recombinant DNA technology and genetically engineered microorganisms or transgenic animals. For example, insulin and human growth hormone are now produced in bacteria, while transgenic animals produce complex proteins for therapeutic use.

The integration of genomics into healthcare is set to revolutionize disease prevention, diagnosis, and treatment through precision medicine, with nurses playing critical roles as educators, advocates, and leaders in supporting patient understanding and equitable implementation. In Canada, efforts to advance genomics include the Pan-Canadian Genomics Strategy and strategic initiatives to address challenges such as service fragmentation, workforce development, and data standardization. Alberta and Quebec have made notable progress through centralized services, but funding and coordination remain significant barriers nationally. Continued investment in

infrastructure, education, and collaboration is essential to fully realize the potential of genomics in healthcare and beyond.

Genomics is reshaping healthcare by enabling personalized approaches to patient care. As genomics becomes integral to healthcare practice, nurses must adapt by acquiring the knowledge and skills necessary to provide safe, equitable, and accessible care. This book has equipped readers with foundational genomic literacy, emphasizing the significance of genetic, environmental, and lifestyle factors in disease susceptibility and progression. By understanding the interconnection of these factors and integrating evidence-based, genomics-informed practices, nurses can assess risks, interpret data, and advocate for personalized care strategies. Furthermore, the text highlights the critical role of nurses within interdisciplinary teams, advancing the delivery of genomic services and fostering improved health outcomes for individuals and populations through advocacy and policy. The hope is that this book empowers nursing professionals to participate as leaders in the evolution of genomics-integration for precision healthcare.

Attribution and References

- Key takeaways generated using ChatGPT. Prompt: "summarize this text in a few sentences, ignoring images, captions, citations and web references." The output was then edited by Andrea Gretchev.
- Closing summary written by Andrea Gretchev.

References

ChatGPT: OpenAI. (2024). *ChatGPT (Version 4.0)* [Large language model]. https://openai.com