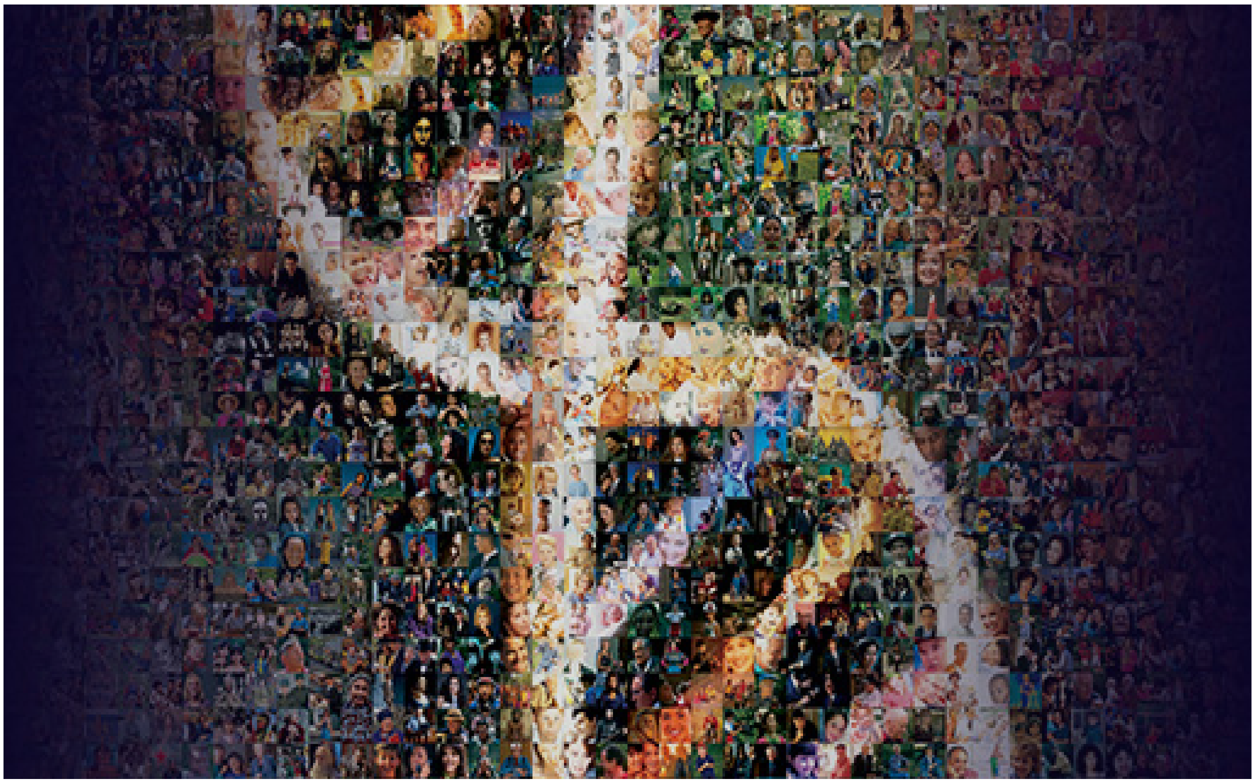
Logbook



The Human Genome Project Pt. 2

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Timeline

November

- Research a little bit and prepare final timeline
- Visit experts

December

- Start designing trifold and slideshow
- Research a lot
- Visit experts

January

- Finalize trifold and online slideshow

Important Dates

- February 9: Coordinator to register project
- March 15: Online project deadline
- April 11: Set up project at Olympic Oval
- April 12: In person judging

Journal

November 14, 2023

- Narrowed down CYSF topics, to: Does weather affect mood? And The Human Genome Project Pt. 2
- Did coin flip and landed on Tails, so our project is The Human Genome Project Pt. 2
- Researched and read articles on The Human Genome
- Got interested in Axolotls and paedomorphic salamander and and limb regeneration
- Asked ourselves lots of questions
- Axolotls have specific “gene” that scientists found that’s the basis of their regeneration
- Could we put this gene in human embryos?
- Could we eradicate certain genetic diseases if in the future, human embryos could get genetically coded?
    - “Ethically wrong” Perception of a “Perfect human”
- Could we potentially eradicate cancer?
    - Yes and No
    - Axolotls, Blue Whales, immune because they have a lot of these kill switch “genes”
        - Also sometimes Blue Whales are too big to notice infinitesimal cancer tumors in their bodies

November 15, 2023

- Researched The Human Genome / The Human Genome Project
- Researched Axolotls
- Looked at tri-fold designs

November 16, 2023

- Researched
- Changed Pt. 2 to Pt. Axolotl (Not permanent just an idea)

November 17, 2023

- Changed back pt. Axolotl to pt. 2 (not permanent)
- Hypothesis idea: can we create synthetic limbs for humans?
    - Or Can humans gain regenerative abilities from Genome Coding (adding Axolotl genes)

November 19, 2023

- Looked at Genome research facilities + Experiment permits

November 21, 2023

- Researched about Human Genome
- Read a few articles on Axolotls and Limb Regeneration

November 24 - 28, 2023

- Watched documentaries
- Researched
- Worked on Slideshow

December 3, 2023

- Researched more about Axolotls

December 7, 2023

- Worked on Slideshow

December 9, 2023

- Met up
- Researched limb regeneration and axolotls
- Worked on logbook
- Worked on slideshow
- Scheduled meeting with Cor Facility Manager Shelley Wegener at U of C

December 12, 2023

- Online meeting with lab manager Shelley Wegener
- Found out that caribou antlers have stem cells in their skin/antlers
- Worked on HeLa/Henrietta Lacks's cells and Cancer cells research

December 15, 2023

- Reviewed recorded meeting with Shelley Wegner
- Wrote notes and revised

December 17, 2023

- Researched

December 18, 2023

- Researched

December 22, 2023
- Added new section called HeLa

December 28, 2023
- Researched
- Added content on slideshow

January 6, 2024
- Met up
- Worked
- Finished research for Limb Regeneration and Axolotls

January 10, 2023
- Researched
- Looked at trif-old designs
- Watched Biotech documentaries

January 20, 2024
- Researched a lot of new ideas
- Focusing on Lulu and Nana CRISPR(Clustered Regularly Interspaced Short Palindromic Repeats)
- HIV important
- Future implications of CRISPR
- Finished all other ideas to start working on new ones

February 5, 2024
- Basic plan for trifold
- Finished up research
- Put rough paper on trifold

February 6, 2024
- Printed out designs for trifold
- Finalized design
- Edited and reformatted for trifold

Key Terms

A: Adenine
- One of the four nucleotide bases in DNA
- Attaches to T's

AIDS: Acquired Immunodeficiency Syndrome
- Most advanced stage of HIV

Alleles
- Alternative versions of a gene

Antiretroviral therapy
- Management of HIV/Aids

Bacillus Thuringiensis
- A gram positive soil dwelling bacterium
- Most commonly used biological pesticide worldwide
- Bacillus thuringiensis naturally occurs in the gut of caterpillars of various types of insects, as well on leaf surfaces, aquatic environments, animal feces, insect-rich environments, and flour mills and grain-storage facilities.
- During sporulation, many Bt strains produce crystal proteins (proteinaceous inclusions), called delta endotoxins, that have insecticidal action

Bacterial Immune System
- Some bacteria and archaea possess an immune system

Blastema
- Regeneration bud
- Mass of undifferentiated cells

Blood Clot
- Gel like clumps of blood
- They form on a cut or injury and stop the bleeding by plugging the injured blood vessel

Blood Vessels
- Channels that carry blood throughout the body
- Your body contains about 60,000 miles of blood vessels

Bones
- Any of the pieces of hard whitish tissue making up the skeleton in humans and other vertebrates

CRISPR: Clustered Regularly Interspaced Short Palindromic Repeats
- Family of DNA sequences found in a bacterial immune system

Cancer
- A disease of tissue growth regulation
- Starts off with one corrupted cell that's no longer able to repair it's genetic code

Cancer Micromovement
- Borderland hard for Killer T cells and other defenses to cross

Carbohydrate
- Sugar Molecules
- Body breaks them down into glucose

Cas-9
- An endonuclease which causes a double-stranded DNA break
- A 160 kilodalton protein

Cell
- The basic membrane-bound unit that contains the fundamental molecules of life and of which all living things are composed

Central Nervous System
- The brain and spinal cord

Clone
- Genetically identical copies of a biological entity

Cloning
- Different processes that can be used to produce genetically identical copies of a biological entity

Common Sequence
- Commonly found sequence in genome

Communication
- Cells/organs/different bodily systems exerting chemicals to warn/talk to other parts of the body

Cystic fibrosis

- A genetic disorder affecting the lungs, digestive tract and other organs

Cytidine

- Mutation of thymine

C: Cytosine

- One of the four nucleotide bases in DNA
- Attaches to G's

DNA: Deoxyribonucleic Acid

- A complex molecule that guides the growth, development, function and reproduction of everything alive
- Information is encoded in the structure of the molecule
- Four nucleotides are paired and make up code that carries instructions
- Change the instructions and you change the being carrying it

Deafness

- This occurs when a person cannot understand speech through hearing, even when sound is amplified

Dedifferentiate

- Where regular cells dedifferentiate (meaning they lose their identity) and transform back into stem cells

Dendritic Cells

- The intelligence officers of your immune system

Drug

- A drug is any chemical substance that when consumed causes a change in an organism's physiology, including its psychology, if applicable

Endonuclease

- A group of enzymes that break the phosphodiester bond present within the polynucleotide chain of a DNA molecule

Epidermis

- Top layer of skin on your body

Ethical

- Relating to moral principles or the branch of knowledge dealing with these

Evolution

- The process by which new species or populations of living things develop from preexisting forms through successive generations

FgF2: Fibroblast Growth Factor 2

- Growth factor that plays important role with tissue

Frameworks

- A structure intended to serve as a guide for the building of something that expands the structure into something useful

Genetic Lineage

- A series of mutations or changes in the genetic code which connect an ancestor's genetic code to their descendant's genetic code

Genome

- The entire set of DNA instructions found in a cell

Germline Editing

- Gene editing of the human embryo or germline that results in genetic changes that are passed down to the next generation. This is the most controversial process as it causes a ripple effect.

GJB2: Gap junction beta-2 protein

- Instructions to make Gap junction beta-2 protein

Glycoproteins

- Any of a class of proteins that have carbohydrate groups attached to the polypeptide chain.

Gram Positive

- In bacteriology, gram-positive bacteria are bacteria that give a positive result in the Gram stain test.

Gram Stain Test

- A test used to determine/identify bacteria

Growth factor

- Naturally occurring substances that helps with cell proliferation, wound healing and sometimes cell differentiation

Gut

- Gastrointestinal tract

G: Guanine

- One of the four nucleotide bases in DNA
- Attaches to C’s

HIV: Human Immunodeficiency Virus

- It weakens a person's immune system by destroying important cells that fight disease and infection.
- There is currently no effective cure for HIV. But with proper medical care, HIV can be controlled.

HeLa

- First line of immortal cells
- Cells of a tumor ridden woman named Henrietta Lacks

Homozygous

- Having inherited the same versions (alleles) of a genomic marker from each biological parent

IVF: In Vitro Fertilization

- The process of fertilization where the egg is fertilized by injecting sperm in vitro

Immune

- Resistance to a disease

Immune System

- Body’s protection to viruses and diseases

Informed Consent

- Where the healthcare provider gives the full details about the risks and benefits of a given procedure and intervention

Kilodalton

- A unit of mass to express molecular mass

Lulu and Nana

- Two genetically modified babies born in 2018
- Genetically-modified using CRISPR in order to make them resistant to HIV and Aids

Macrophages

- A type of white blood cell that surrounds and kills microorganisms, removes dead cells and stimulates the actions of other cells

Molecules

- The smallest particle of a substance

Mosaicism Inherent

- Where someone has one or more different sets of genes
- If the abnormal cells begin to outnumber the normal cells, it can lead to disease

Mutation

- When there's a change in a gene

Natural Selection

- Survival of the fittest

Nerves

- Channels that carry electrical signals/impulsives through the body

Nervous System

- A system that sends messages back and forth from the brain and the body

PAM: Protospacer Adjacent Motif

- A "system" that lets CRISPR know if a region of DNA is ok to cut or not.

Peripheral Nervous System

- Part of your nervous system outside of you brain and spinal cord

Phosphate Backbone

- The bordering portion of the DNA double helix that provides support to the molecule

Physiology

- The study of how the human body works

Polio

- A life threatening paralysis disease

Polygenic

- A characteristic that is influence by two or more genes

Polynucleotide

- Linear biopolymers, that are composed of several nucleotide monomers with covalent bonds in a chain

Polypeptide

- Unbranched amino acids

Preimplantation

- Of, involved or being an embryo before uterine implantation

Proliferation
- Rapid cell reproduction

Prohibited
- Not allowed/banned

Regeneration
- Regrowth of an organ/cell/limb

RNA: Ribonucleic Acid
- A molecule present in almost everything

Scar Tissue
- A collection of cells and collagen that covers a wound

Scientific Validity
- Straight up facts

Skin
- Largest organ in the human body
- Covers up the entire external surface

Stem Cell
- Immature cells able to make other blood cells that mature and function as needed

Synthetic Embryos
- Synthetic embryos created by using stem cells

T-cells
- White blood cells that are your deadliest cancer killers

TGF - Beta: Transforming Growth Factor β
- A molecule essential to regeneration
- Also acts as tumor suppressor

Therapeutic
- Healing of a disease

T: Thymine
- One of the four nucleotide bases in DNA
- Attaches to A's

Thyroid Gland

- Butterfly shaped organ that produces hormones to regulate the body's metabolic rate, growth and development

Thyroid Gland Tissue

- Tissue from Thyroid gland

Tissue Development and Repair

- Repairs with cell proliferation
- Can develop new tissue with scars and not original

Trauma

- A deeply distressing or disturbing experience
- A physical injury

Tumor

- a swelling of a part of the body, generally without inflammation, caused by an abnormal growth of tissue, whether benign or malignant

WNT: (Wingless-related integration site)

- Code for protein that regulates cell growth, motility, and differentiation during embryonic development

Wound

- An injury to living tissue caused by a cut, blow or other impact

Tissue

- A type of material that animals and plants are made of
- Consists of special cells

Zygote

- A fertilized egg cell

Current Guidelines

The AHRA specifically states that “[n]o person shall knowingly […] alter the genome of a cell of a human being or *in vitro* embryo such that the alteration is capable of being transmitted to descendants” (s 5(1)(f)). Those who violate this provision may be guilty of an offense and subject to a fine up to $500,000 and/or 10 years in prison (s 60) - PubMed Central National Library of Medicine US

Proposed Guidelines to change Assisted Human Reproduction Act (“AHRA”):

1. Research/Experiments shall be conducted under the supervision of authorized and qualified researchers approved by the The Federal Government
    a. Ethics:
        i. The Federal Government, or any government responsible for overseeing research activities, has a ton of interest in safeguarding the well-being of both researchers and participants involved in germline editing. By only allowing the research to be conducted under the supervision of authorized and qualified individuals, authorities can enforce obedience to safety protocols and ethical standards to minimize potential risks and ensure the protection of human subjects and the generations after.
        ii. Ensuring that research is overseen by qualified researchers helps maintain the quality and integrity of scientific investigations. Qualified researchers have the necessary expertise and experience to conduct research effectively. Their supervision helps leave no space for errors and biases that could compromise the reliability of research findings.
        iii. By regulating the research, the Federal Government tries to maintain public trust in the scientific enterprise and demonstrate accountability for the use of taxes and resources. Transparent and accountable research fosters confidence among research institutions, and the general public, regarding the credibility, reliability, and social relevance of germline.

2. Research/Experiments on synthetic embryos must first be approved by The Federal Government
    a. Ethics:
        i. Synthetic embryos, which are typically created using stem cells or other cellular materials, attract a ton of ethical questions regarding the beginning of human life, the safety of the embryos, and what being human even means anymore. Ethical concerns surrounding the creation, manipulation, and destruction of synthetic embryos need careful regulations and protocols to ensure that research activities respect the fundamental principles of human dignity and rights.

ii. The manipulation and experimentation with synthetic embryos pose potential risks to human health done many generations, as well as scientific uncertainties regarding the safety and long-term consequences of germline. Regulatory handling by the Federal Government helps assess the scientific validity and risk-benefit considerations associated with research on synthetic embryos, thereby protecting the well-being of researchers, participants, and future generations.
iii. Many countries have established legal and regulatory frameworks to govern research involving human embryos, including synthetic embryos. These frameworks often require researchers to obtain explicit approval or permits from government agencies, ethics committees, or regulatory bodies before initiating research activities involving synthetic embryos. Exactly what we are suggesting. Compliance with regulatory requirements helps ensure transparency, accountability, and obedience to established ethical standards.
iv. Transparent and accountable governance of research on synthetic embryos is essential for gaining public trust in the scientific community and regulatory institutions. By subjecting research proposals to review processes and the public eye, regulatory authorities demonstrate a commitment to ethical governing responsible stewardship of resources, and responsiveness to societal values, concerns, and expectations.

3. Randomized controlled checks to provide transparency.
   Context: Researchers should maintain transparency regarding their motivations and objectives when conducting experiments. Institutions and funding agencies can promote accountability by requiring researchers to justify the significance of their work and demonstrate its potential contribution to knowledge advancement or societal welfare.
   a. Ethics:
      i. Ethical research requires that participants provide informed consent before engaging in any study or experiment. Secret experiments steal participants of the opportunity to make informed decisions about their involvement, including understanding potential risks, benefits, and alternatives. Without informed consent, individuals may be unknowingly subjected to harm or exploitation, violating their autonomy and dignity.
      ii. Secret experiments pose significant risks to the well-being and rights of participants, as well as the participants' descendants. Without proper oversight and ethical review, researchers may disregard safety protocols, experimental standards, and risk strategies, leading to adverse consequences such as physical or psychological harm, privacy violations, and irreparable damage. The lack of transparency exacerbates these risks by concealing potential hazards and limiting opportunities for accountability.
      iii. Ethical concerns about secret experiments reflect core principles and guidelines established within the field of research ethics, including respect for persons,

beneficence, justice, and transparency. These principles emphasize the importance of protecting the rights and welfare of individuals, promoting the common good, and ensuring fairness and accountability in the conduct of research. Secret experiments completely disregard these principles, destroying the ethical foundation of scientific inquiry.

4. Research/Experiments/Alterations should be performed on synthetic embryos in general
    a. Ethics:
        i. Despite their scientific promise, research and experimentation on synthetic embryos attract a ton of ethical concerns related to the beginning of human life, the moral status of embryos, and the implications of human genetic manipulation. Ethical debates often revolve around questions of personhood, dignity, and the permissibility of altering embryonic genomes for therapeutic or enhancement purposes.
        ii. Many countries have established legal and regulatory frameworks to govern research involving human embryos, including synthetic embryos. These frameworks usually require researchers to obtain approval from government agencies, ethics committees, or regulatory bodies before conducting experiments on synthetic embryos. Regulations help to ensure compliance with ethical standards, safety protocols, and legal requirements while balancing scientific freedom with ethical responsibilities.

5. Embryo alterations are only allowed after full approval of the Federal, Provincial and Municipal governments and full consent from participants.
    a. Ethics:

        i. Full consent from patients undergoing embryo alterations is essential to uphold principles of autonomy, informed decision-making, and respect for individual rights and preferences. Patients must be fully informed about absolutely everything, potential risks and benefits, alternative options, and the implications for themselves and future offspring and generations to come. Informed consent processes empower patients to make autonomous choices about their reproductive health and genetic interventions, ensuring that their values, beliefs, and priorities are respected throughout the decision-making process.
        ii. Regulatory authorities play a critical role in ensuring that embryo alterations adhere to ethical standards, legal requirements, and professional guidelines, thereby promoting confidence in the safety and integrity of government services and genetic interventions.

6. Embryo alterations should only be attempted if
    a. One of the parents is homozygous with a dominant disease
    b. Both of the parents are homozygous with a recessive disease,

c. The disease is polygenic (such as cancer or diabetes) and involves, for example, 20 genes, in which case the couple cannot produce a large enough set of embryos allowing an embryo with the right combination of all alleles to be selected.
d. Ethics:
   i. The use of embryo alterations for preventing the transmission of genetic diseases raises ethical considerations related to safety, and informed consent, and social implications. Ethical debates revolve around questions of genetic enhancement, unintended consequences, and the potential for creating designer babies. Ethical frameworks and regulations are essential for ensuring responsible use of embryo alterations and safeguarding the well-being of individuals and future generations.

7. Genetic Altering for the purpose of vanity is strictly prohibited with offenders subjected to a fine up to $750,000 and/or 10 years in prison and/or stripped of right to research germline therapy.
   a) Ethics
      i. Regulatory frameworks governing genetic technologies must balance innovation with safety, ethical considerations, and respect for human rights.
      ii. Prohibiting genetic altering for vanity purposes serves as a means of protecting public health and ensuring that genetic technologies are used responsibly and in accordance with established ethical principles.
      iii. The risks of fines and prison sentences, along with the potential loss of research privileges in the field of germline therapy, serves as a deterrent against violating the prohibition on genetic altering for vanity.
      iv. By imposing significant penalties, authorities aim to discourage individuals and organizations from engaging in activities that could have detrimental effects on individuals and society as a whole.

Pros of CRISPR

CRISPR technology stands out for its cost-effectiveness, efficiency, and accuracy but also for its ability to be coded to whatever desire, and potential to change the premise of various areas of science, including medicine, agriculture, and biotechnology.

Versatile Applications:

One of the remarkable aspects of CRISPR is its versatility. There are many ways to use CRISPR, including the classic CRISPR Cas-9 RNA pair which edits and silences, replacing cytidine with thymidine fixing mutations, or a more challenging method, attaching fluorescent proteins to find specific genes. And this is only the beginning, with more acceptance, and funding, the limits of CRISPR will know no bounds.

Personalized Medicine:

CRISPR's precision allows for the development of personalized medicine approaches. By targeting specific genes associated with diseases and mutations, CRISPR-based therapies can potentially offer personalized treatments for individuals based on their genetic makeup. This precision CRISPR offers, minimizes the risk of mutations and enhances the effectiveness of therapeutic interventions.

Continued Research and Innovation:

Ongoing research is focused on improving the efficiency, and safety of CRISPR technology. From exploring alternative CRISPR systems to developing sci-fi delivery methods, researchers are continuously innovating to overcome existing limitations and unlock the full potential of CRISPR across all fields of science.

Conclusion

In conclusion, CRISPR technology represents a world-changing tool that can be used for addressing pressing global challenges, advancing scientific knowledge, and improving human health and well-being. However, it is imperative to proceed thoughtfully, considering the ethical, social, and regulatory implications associated with its acceptance.

Cons of CRISPR

Even though CRISPR is an incredibly versatile and extraordinary scientific tool, it has received a ton of backlash regarding its ethicality, accuracy and unknown side effects.

Lot of Ethical concerns:

In 2018, a scientist named He Jiankui genetically modified two embryos to make them immune to HIV and AIDS. The Scientific community raised a ton of concerns surrounding unknown side effects, safety and the fact that these traits would be passed down onto the following generations. Jiankui was then sentenced to three years in prison.

Prohibited:

Out of all the countries in the world, only 11 of them have approved gene editing with CRISPR. The other 184 countries have either not taken action or have CRISPR completely prohibited. Some of these countries include but are not limited to, Canada, Belarus, Switzerland and Sweden.

What it means to be human anymore:

Another ethicality concern surrounding CRISPR is the fact of what it even means to be human anymore. Many have voiced their concerns on the near uncanny future of Designer Babies and what being human even means anymore.

Conclusion

Although CRISPR could possibly be the world's greatest technological advancement, it still has many unignorable flaws. But as more and more support is gained, CRISPR could advance towards the betterment of our world.

The Future Implications of CRISPR

The future implications of CRISPR are vast and hold the potential to reshape various aspects not only medicine but many areas of science.

Medicine:

CRISPR could lead to breakthroughs in treating genetic diseases, including cancer, cystic fibrosis, sickle cell disease, and down syndrome. By targeting and editing specific genes causing these conditions, CRISPR offers the possibility of personalized medicine and more effective treatments.

Genetic Engineering:

CRISPR allows for precise changes to the genetic makeup of organisms, including plants, animals, and microbes. This tool could revolutionize agriculture by creating crops with enhanced nutritional value, improved yield, and resistance to pests and diseases. In livestock, CRISPR could be used to breed healthier animals and higher immunity to diseases.

Drug Development:

CRISPR technology allows for the easier creation of more accurate disease models for drug discovery and development. By mimicking genetic mutations associated with specific diseases, scientists can identify potential drug targets and test new therapies more efficiently.

Regenerative Medicine:

CRISPR has opportunities for regenerative medicine by editing stem cells to repair damaged tissues and organs. This could lead to advancements in treating conditions such as spinal cord injuries, heart disease, and degenerative disorders.

Biotechnology Industry:

CRISPR technology has implications beyond healthcare and agriculture, extending to biotechnology, environmental conservation, and industrial processes. It could be used to develop biodegradable materials, enhance biofuel production, and mitigate pollution.

Global Health:

CRISPR has the potential to relieve global health challenges, including infectious diseases, malnutrition, and access to healthcare in third world communities. Affordable and accessible CRISPR-based diagnostics and therapies could improve health outcomes worldwide.

Conclusion

In summary, the future implications of CRISPR are diverse and unlimited, spanning from medicine and agriculture to the biotechnology industry. As research and development in CRISPR technology continues to advance, it is important to consider the ethical, social, and regulatory frameworks necessary to ensure its responsible and equitable use for the benefit of humanity.

Importance

CRISPR is indeed crucial for shaping our future in profound ways. Its potential to revolutionize not only disease treatment but also numerous other areas of science. CRISPR is known far and wide as a potent and versatile instrument for manipulating genetic makeup, presenting far-reaching implications across medicine, agriculture, and scientific endeavours.
In medicine, CRISPR holds promise as a transformative tool for treating genetic diseases. By precisely targeting and editing specific DNA sequences, scientists envision correcting mutations responsible for various inherited disorders. This approach offers hope for previously untreatable conditions, potentially ushering in an era of personalized medicine tailored to individual genetic profiles.

CRISPR's impact extends beyond medical applications. In agriculture, it offers the potential to address pressing challenges such as food security and sustainability. By modifying crop genomes, researchers aim to enhance yield, improve nutritional content, and confer resistance to pests and diseases. Such advancements could bolster global efforts to mitigate hunger and reduce reliance on environmentally harmful agricultural practices.

However, with its immense potential, comes the ethical, legal, and social implications of CRISPR. The prospect of editing the human germline raises ethical questions regarding the nature of human identity, equality, and consent. Concerns also arise regarding the fair distribution of CRISPR-based therapies, ensuring access for all individuals regardless of socioeconomic status.

However, the potential for unintended consequences and the risk of misuse underscore the need for strong regulatory frameworks and ethical guidelines governing CRISPR research and applications. Balancing innovation with responsible stewardship is paramount to harnessing the full potential of CRISPR while safeguarding against potential harm.

In conclusion, CRISPR stands as a revolutionary force with the power to reshape medicine, agriculture, and scientific inquiry. Its importance lies not only in its technical capabilities but also in the ethical considerations that accompany its use. By navigating these complexities with diligence and an open mind, we can harness the promise of CRISPR for the betterment of humanity, ensuring a future where its benefits are equitably shared and responsibly managed.

The He Jiankui Affair: A Critical Examination

Introduction

The He Jiankui Affair, occurring in late 2018, brought the world's attention to the controversial field of genetic engineering when Chinese scientist He Jiankui claimed to have successfully created the first genetically modified babies. This critical study aims to analyze the key aspects of this event, including the genetic editing process, ethical concerns, long-term implications and the legal aftermath.

Recruitment of Couples

Jiankui and his team enlisted eight couples, comprising HIV-positive fathers and HIV-negative mothers, through the Baihualin Chinese League, a volunteer-run HIV group. This recruitment process raises questions regarding informed consent and the motivations of the couples involved.

Genetic Editing Process

During the in vitro fertilization (IVF) process, He employed CRISPR Cas-9 technology to modify the embryos. Specifically, he targeted the CCR5 gene, which plays a crucial role in HIV-1 infection. This method aimed to confer HIV resistance by introducing a specific mutation (CCR5-Δ32). However, concerns persisted as some strains of HIV employ alternative receptors.

Ethical Considerations

One of the central ethical issues surrounding the He Jiankui Affair pertains to informed consent. While He claimed that parents were given the choice between edited and unedited embryos, questions remain about the depth of understanding and autonomy of the couples involved.

Long-Term Implications

The birth of the genetically modified twins, Lulu and Nana, in October 2018 raised concerns about the unknown long-term effects of gene editing on their health and development. This aspect underscores the importance of thorough scientific investigation and monitoring.

Scientific Community Response

In February 2022, Chinese scientists advocated for a dedicated facility to study and care for the genetically edited children, highlighting concerns about potential errors in the gene editing process. However, this proposal faced criticism internationally for perceived privacy invasion and abuse of power.

Legal Consequences

On December 30, 2019, He Jiankui was sentenced to three years in prison and fined 3 million RMB for his actions. Collaborators Zhang Renli and Qin Jinzhou received lesser penalties, highlighting the legal consequences of their involvement in forging ethical review documents.

Regulatory Developments

In response to the He Jiankui Affair, China began drafting regulations holding individuals accountable for manipulating the human genome through gene-editing techniques, reflecting growing concerns about the ethical and safety aspects of genetic engineering.

Conclusion

The He Jiankui Affair serves as a pivotal case study in the ethical, scientific, and legal dimensions of genetic engineering. It has prompted global discussions on the implications of gene editing and the necessity of stringent regulations to ensure responsible research in this field.

References

https://en.wikipedia.org/wiki/He_Jiankui

Denis Rebrikov: A Critical Examination

Introduction
In June 2019, Denis Rebrikov at the Kulakov National Medical Research Center for Obstetrics, Gynecology and Perinatology in Moscow announced through Nature that he was planning to repeat He's experiment once he got permission from the Russian Ministry of Health and other governing bodies. Denis Rebrikov asserted that he would use a safer and better method than that of He Jiankui, saying, "I think I'm crazy enough to do it." On 17 October, Rebrikov said that he was approached by a deaf couple for help. He already started an in vitro experiment to repair a gene that causes deafness, GJB2, using CRISPR.

Difference
Yet unlike He Jiankui, Denis Rebrikov has been transparent. He plans to seek rigorous ethical and regulatory review. Rebrikov says he has a detailed research plan to find the risks of altering embryos with CRISPR before he makes any attempt to implant them.

Genetic Editing Process
Working with synthetic embryos made at his IVF clinic, part of the Kulakov National Medical Research Center for Obstetrics, Gynecology and Perinatology. Rebrikov and his co-workers used CRISPR to introduce a delete mutation into a gene for a protein, CCR5, that studs the surface of white blood cells. People who naturally inherit a defective *CCR5* gene from both parents are highly resistant to HIV. This is the same gene that He Jiankui tried to remove in the twin girls. Denis Rebrikov's initial CRISPR embryo experiments wanted to better see the risks and challenges. Most commonly, CRISPR is introduced right after an egg is fertilized, it will make its desired edit at the one-cell zygote stage, so that as the embryo divides, all cells are corrected. But if CRISPR enters at the two-cell stage or later, it may create a child who has the desired change in some cells but not others. This mosaic child could still be vulnerable to HIV. But out of eight embryos edited using CRISPR, Denis Rebrikov and his team found evidence of mosaicism in only three of them at the blastocyst stage, when they are 5 days old and have about 250 cells. Still, the study did not assess the concerning possibility that the editing would create accidental, "off-target" mutations, theoretically, these could trigger cancer or cause other health problems.

His Plan
Denis Rebrikov couldn't find any HIV-infected women who didn't respond to antiretroviral therapy (Management of HIVs and AIDS) and also wanted to get pregnant. So he changed plans and sought out hearing-impaired couples who are homozygous for a mutation known as 35delG in a gene, *GJB2*, that produces a protein in gap junctions, the channels that help move chemical signals like potassium between cells, including in the inner ear. The 35delG mutation, in which a single incorrect DNA base destroys the protein the gene codes for, is one of the most common genetic causes of hearing loss. Denis Rebrikov wants to use CRISPR to replace the abnormal DNA base with the correct one.

Safety First

Denis Rebrikov told *Science* that he plans to do extremely detailed safety checks before seeking approval to implant an edited embryo. First, he wants to sequence the entire genomes of each parent to get a baseline for assessing off-target mutations in their edited embryos. He then wants to stimulate the woman's ovaries, obtain about 20 eggs, fertilize them with her partner's sperm, and finally add the mutation-fixing CRISPR. He'll grow these embryos for 5 days, where they will have about 250 cells and be in the blastocyst stage. Then he will do repeated rounds of whole-genome sequencing of 10 of these blastocysts, to reveal all mutations that differ from the genomes of the parents.

Recruitment of Couples

With help from a Moscow hearing clinic, this summer Rebrikov identified five couples who are likely homozygous for 35delG and certain to have a deaf child. He has met one, though the husband and wife have yet to decide whether they want to participate in his experiment.

Backlash

Right now there are several specialized hearing loss clinicians who disagree with the experiment as there are currently cochlear implants and hearing aids that can help with the condition.

References

https://en.wikipedia.org/wiki/He_Jiankui_affair

https://www.science.org/content/article/embattled-russian-scientist-sharpens-plans-create-gene-edited-babies

Current Technology/Events

CRISPR-Cas9

Overview

- (Clustered Regularly Interspaced Short Palindromic Repeats)
- Cas-9: A 160 kilodalton protein
- A tool for cutting DNA in a specific location
- Revolutionized gene editing but still a first generation tool
- Discovered in bacterial immune system
- Has been adapted into a powerful tool for gene research
- Made up of two main parts,
  - Cas9 a DNA-cutting protein
  - A RNA molecule known as the guide RNA
  - Bond together they form a complex that can identify and cut specific sections of DNA

Editing

- First, Cas9 has to locate and bind to a common sequence in the genome called a PAM (protospacer adjacent motif)
  - Once found the guide RNA unwinds part of the double helix (physical structure of DNA)
  - The RNA strand is designed to match and bind a particular sequence in the DNA
  - Once the correct sequence is found, it's cut by Cas9
  - It's two nuclease domains each make a nick, leading to a double strand break
  - The cells may try to repair this break, the process is error prone and often inadvertently introduces mutations that disable the gene
  - Making CRISPR a great tool for knocking out specific genes
- Some researchers are deactivating one or both of Cas9's cutting domains and fusing new enzymes onto the protein
- Cas9 can then transport those enzymes to a specific DNA sequence
- For example, Cas9 can be fused to an enzyme, a deaminase, with mutates specific DNA bases
  - Replacing cytidine with thymidine fixing mutations
  - Very useful and very precise

Transcription

- Not just gene editing but also gene transcription
- Deactivating Cas9 completely so it can no longer cut DNA
- Instead, transcriptional activators are added to the Cas9 wither fusing them directly or via a string of peptides
- Activators can be used to guide RNA as well
  - They recruit the cell's transcription machinery bringing RNA polymerase and other factors to the target and increasing gene transcription

Silencing

- The same principle applies to gene silencing
  - A KRAB domain fused to the Cas9 inactivates transcription by recruiting more factors that physically block the gene
- A more outside the box idea for using CRISPR is to attach fluorescent proteins so you can see where particular DNA sequences are found in the cell.

GMOs ("Genetically modified organisms")

History

- One of the most controversial areas of Science
- Humans have been genetically modifying plants for years, just look at a watermelon today versus four hundred years ago
  - Maybe a few of your crops had good yields
  - Maybe one of your wolves was a bit more loyal
  - So you did the smart thing and bred the plants/animals with the traits beneficial to you
  - Traits are suggested by genes, so with each generation the specific traits/genes are more pronounced
- Selective breeding is basically just looking for lucky hits
- Genetic engineering completely eliminates this

Issues

- Why are people so concerned?
  - Gene Flow
    - GMOs could potentially mix with traditional plants and introduce unwanted characteristics in the mix.
    - One solution: Terminator Seeds

                - Sterile seeds that require farmers to buy new seeds every year
                - Absolute public outcry
            - A ton of unintentional spreading of engineered DNA
            - However GM plants can't run wild entirely
                - Many plants pollinate themselves
                - Need to be related to mingle
    - Is the food from GM plants and non GM plants different?
        - Same risk of eating either
        - bacillus thuringiensis plants
            - Gene borrowed from Bacillus Thuringiensis lets engineered plants produce protein that destroys the digestive system of specific insect pests
            - Concerning?
            - Unlike pesticides which can be washed off, the poison is inside of these BT plants
            - Not harmless to humans (i.e. coffee or chocolate)
    - Opposite approach
        - Plants resistant to certain weed killers
        - Dark underbelly of GMO
            - For the pesticide industry, they are big business
            - Over 90% of US's cash crops are herbicide resistant, mostly to glyphosate
            - Use of glyphosate skyrocketed
            - Glyphosate not very harmful to humans as other herbicides
            - Farmers pretty much relied on this one method only

Agriculture

- A lot of criticism of GMO is actually more of criticism of modern agriculture (Monoculture)
- GMO could be a powerful ally to minimize our impact on the environment
- Positive examples of GM use
    - Bangladesh
        - Eggplant is an important crop but often, whole harvests were destroyed by pests
        - Farmers relied heavily on pesticides and herbicides
        - Introduction of GM eggplant in 2013 stopped this with the same BT protein
        - Reduced insecticides use by 80%
    - Hawaii

        - In the 1990's the Hawaiian papaya almost wiped out by ringspot virus
        - GM papaya saved industry
    - Cavendish Bananas
        - Cavendish bananas are almost extinct as TR4, also known as the cancer of bananas, is wiping out the plant species.
        - James, a banana farmer, has spent the last ten years trying to genetically modify cavendish bananas to withstand TR4.
        - He has received a lot of hate and it is a very controversial topic.

Looking Forward

- Scientists are working on GMOs that improve our diet (i.e. higher levels nutrients and antioxidants)
- On a larger scale we are trying to engineer plants resistant to climate change or making more adaptable
- GM plants can also help protect environment like taking nitrogen from the air fixing nitrogen pollution and fertilizer use
- GMOs could be our most powerful weapon to save our biosphere

References:

https://www.youtube.com/watch?v=4YKFw2KZA5o
https://www.youtube.com/watch?v=7TmcXYp8xu4

Shelley Wegener Meeting

This meeting was on December 12, 2023 and lasted from 12:00 pm to 12:17 pm

Questions

- How do you sequence the Human Genome and what's the process?
- How would limb regeneration work for humans?
- What's a Synthetic Human Genome?
- Are birthmarks the result of failed TGF-Beta cells?
- What are the future implications of your and our research?
- Could you talk about the future and importance of the work you're doing?

Answers

Shelley started off with talking a little bit about what they do at the lab.

- Center of Health Genomics and Informatics at U of C
- A core lab for entire University
- Very expensive equipment and tools

How do you sequence the Human Genome and what's the process?

- Get the DNA first
- Sample blood sample/cheek swab
- 23 pairs of chromosomes
- 4 different bases: A, C, G, T's
- Looking for changes
- Chop into smaller pieces and add known parts

Are birthmarks the result of failed TGF-beta cells

- Some (not all) birthmarks are when TGF-beta cells fail

How would limb regeneration work for humans

Synthetic Human Limbs

- Synthesizing a human limb may be theoretically possible but are very far into the future

Future Implications of our project

- With our project testing the regulations and ethicality of one of the most controversial

Future implications and importance of Shelley's work

- Trying to stop scar tissue especially for burn victims
- Testing on moose and then possibly implicate on humans

Human Genome/ The Human Genome Project

- Your genome is basically the code that tells your body what to do/function
- Determines your physical attributes
- One of Science's Greatest Feats
    - Started in October 1990, Completed April 2003
    - "Race" to generate first sequence of the Human Genome
    - 99.99% accurate
- In December 2002 an advanced draft of the mouse genome sequence was published
- Initial draft of rat genome sequence produced in November 2002
- A single gene is only 8 atoms wide
- Complete opposite genes stick together
- A's to T's and G's to C's
- Human Genome is used to sequence complete gene lines to be able to study in the future

References

https://www.genome.gov/human-genome-project
https://www.genome.gov/about-genomics/educational-resources/fact-sheets/human-genome-project
https://www.youtube.com/watch?v=MvuYATh7Y74
https://www.genome.gov/About-Genomics/Educational-Resources
https://www.economist.com/graphic-detail/2020/06/27/the-human-genome-project-transformed-

Timeline

1984-1986: Early meetings assess the feasibility of a Human Genome Project.

1988: National Institute of Health assembles scientists, administrators and science policy experts to plan for a possible Human Genome Project. The National Research Council on Life Sciences and the U.S. Congress Office of Technology Assessment recommends a concerted genome research program. NIH and DOE signed a memorandum of understanding to “coordinate research and technical activities related to human genome.

1989: HHS establishes the National Center for Human Genome Research (NCHGR) with James D. Watson as the first director.

1989-1990: The NIH and Department of Energy each establish an Ethical, Legal and Social Implications (ELSI) Research Program.

1990: The Human Genome Project begins with an initial five-year plan.

1992: James D. Watson resigns as the first director of NCHGR.

1993: The Human Genome Project revises its five-year goals.

1994: Human Genome Project researchers publish a detailed genetic linkage map of the human genome.

1995: Human Genome Project researchers publish a physical map of the human genome.

1996: Bermuda Principles encourage open data access for the Human Genome Project.

1997: NCHGR becomes the National Human Genome Research Institute (NHGRI).

1998: The Human Genome Project sets new five-year goals.

1999: The Human Genome Project successfully completes the pilot phase of sequencing the human genome. The International Human Genome Sequencing Consortium backs the rapid construction of a "working draft" sequence of the human genome and stands firm on open data access. Human Genome Project researchers decode the DNA sequence of the first human chromosome.

2000: The International Human Genome Sequencing Consortium announces the completion of a "working draft" human genome sequence.

2001: The International Human Genome Sequencing Consortium publishes an initial analysis of the human genome sequence.

2003: The Human Genome Project is completed.

2004: The International Human Genome Sequence Consortium publishes their finished human genome sequence.

Axolotls

Overview

- Paedomorphic salamander
- Scientific name: Ambystoma mexicanum
- Never leaves water
- Stays in Juvenile form, doesn't transform into adult form
    - Sexually Matures at 6 months
    - When exposed to certain chemicals/substances they may morph into adults
    - Lose regenerative ability as adult
    - As babies, would playfully munch on each other, wasn't problem because of regenerative abilities

Evolution

- Scientists believe"Forever young" condition called neoteny evolved from stable environment
    - Native to the wetlands in Mexico City
        - Only about 10,000 left in Lake Xochimilco
        - Ancient Aztec people considered it the incarnation of a God named Xolotl
        - Axolotl roughly equals water monster
        - Large Lakes with only dessert surrounding
        - Lakes the axolotls evolved in were unchanging year round
        - Not many aquatic predators

Regeneration

- Metamorphosis? Not necessary
    - Don't undergo normal metamorphosis into adults like other salamanders
    - Salamanders in general have a lot more DNA than other vertebrates because they lose parts of it regularly
    - Lots of repeating unfamiliar sequences that don't code for a protein/unknown function
    - Key genes in regeneration
    - Salamanders are the only four legged vertebrates that can transform regular cells back into stem cells
        - Regeneration may not be from the genes but the order of them
- Can regenerate heart, and various limbs and organs.
- Can amazingly regenerate parts of it's brain
- In most animals in general, neurons typically only grow in the embryonic stage
- Any neurogenesis that happens in adulthood is limited, but axolotls can
- Severed spinal cord will heal in roughly three weeks
- ⅓ of heart will regenerate
- After a certain age, lose regeneration

History

- First shipped from Mexico to prominent French zoologist Auguste Dumeril in the 1860's
    - Thought were larvae of unknown salamander
    - 6 months later, unexpectedly reproduced
    - In 1865 some axolotls transformed into their adult forms which somewhat resembled a tiger salamander but different enough to be another species
    - Early 1900's researchers were narrowing in on thyroid gland tissues as a mechanism for amphibian metamorphosis
        - What better guinea pig than Axolotls?
        - Were fed thyroid tissue from livestock and underwent metamorphosis
        - Lost external gills, shedding their larval skin, venturing onto land as well as it's cuteness
        - Can also morph when forced to breath air but takes longer and a toll on the axolotl

Other

- Lots of creatures who can regenerate body parts are invertebrates
- In vertebrates like us, regeneration is pretty much limited to regrowing skin or scar tissue and regrowing our liver
- Only vertebrate that can regenerate are frogs but they lose the ability after fully morphing into an adult

References

https://www.youtube.com/watch?v=uooR4293p_4
https://www.youtube.com/watch?v=bFkIG9S2Mmg&ab_channel=RealScience
https://www.youtube.com/watch?v=uUw4NJmAUNI&ab_channel=InsiderTech

Limb Regeneration

Human Regeneration

- Humans and mice can regenerate a partially amputated finger or toe due to stem cells under fingernails
  - Regrowth of mice digits studied depended on two proteins
    - WNT Proteins: Glycoproteins that allow for communication between cells
    - FgF2 Proteins: Growth factor that plays important role with tissue development and repair
    - Same as those in salamander regeneration
    - Partially retain regenerative abilities?
    - One day reawakened?
  - Humans lose this ability as they age
  - Stem cell that allows nails to perpetually grow
  - Remnant of when our ability to regenerate was stronger?

Axolotl

- Starts with surviving cells of the severed limb
- Blood clot quickly forms to stop bleeding
- Cells cover amputation
- Cells under epidermis start rapidly divide
- Forms blastema around wound

Macrophages

- In our bodies
- Known to be linked to regeneration
- When scientists injected a drug that eliminates the macrophages in an axolotl's limb, before it can regenerate it formed scar tissue instead
- Showing they are a key component of regeneration

TGF - Beta

- Molecule essential to regeneration

Blastema

- Forms Blastema
- Blastema is required in order to start limb regeneration after a wound
- Blastema is also known as the regeneration bud

- After trauma, blastema forms around wound and starts cloning tissue
- Key to regeneration
- Where regular cells dedifferentiate (meaning they lose their identity) and transform back into stem cells
- These Cells then start reforming bones skin and veins, just like when the creature is developing
- Then continuing on to divide, nerves and blood vessels connect it to the rest of the body
- The limb then completely regrows identical to the prior one

Cancer

Evidence shows that cancer has existed since the dawn of mankind

Phase 1: Elimination Phase

- Starts with one corrupted cell who no longer is able to repair it's genetic code
- Doesn't die and starts multiplying
- Over few weeks grows continuously
- Mutates into different genetic lineages, clans working together and competing
- Some mutate weaker, some mutate into stronger and more fitter versions
- Tiny tumor formed
- Needs resources, without food and oxygen, the cells die off.
- But a few surviving cells unlock a new mutation, the ability to order the growth of new blood vessels
- Body supplies tumor unknowingly
- Tumor grows and grows and starts causing harm and fatalities to nearby cells

In a sense, this tiny tumor is like a rogue town. Imagine a group of rebels in Calgary decided that they were not a part of the city no more. Starting a new city branded Tumor town. Occupying the same space, the new city wants to expand, ordering steel beams and drywall. The new buildings are far from logical, ugly, hazardous and just dangerous in general. They are built right in the middle of streets, on top of playgrounds and existing infrastructure. The old neighborhood is destroyed to make way for the new one, while former residents are trapped and begin to starve. This goes on for a while until police and building inspectors arrive.

- In your body, the immune system is activated by the stench of dying cells.
- First responders arrive (i.e. Macrophages and Natural Killer Cells)
    - Police forces that get right to work
    - Killing and consuming cancer cells
    - Release chemical that lets body know that there's cancer to be killed
- Dendritic Cells, the intelligence officers of your immune system collect samples of your dead tumor cells and begin activating the BIG GUNS
- AKA Helper and Killer T Cells
    - Has list of every bad thing that could come into your body
    - Each cancer is unique, but they're still are genetic corruptions that they can't hide
    - T Cells are the deadliest cancer eradicators you have
    - By the time they arrive the tumor has grown to hundreds of thousands of cells

    - However T cells can block the growth of new blood vessels starving the tumor cells, halting their growth

Imagine the police and building inspectors switching off electricity and water and putting up roadblocks to prevent further expansion

- Cells are massacred and their carcasses are cleaned up by Macrophages
- Who then order the construction of healthy tissue
- Your body has now crushed the illegal Tumor town without mercy

Phase 2: Equilibrium Phase

- Natural selection in a nutshell is where the most well suited genes are more likely to survive
- Natural selection spoils your victory over cancer
- Accidently, your immune system leaves the most fittest mutation to start it all over again.
- This cell is better than the ones who've came before

It's like the surviving rebels of Tumor Town have learned their lessons, the law and how to break it better.

- The remaining starts replicating and replicating until it once again becomes an even better tumor.

However the immune system with experience, gets to work starting with SWAT teams instead of police. Tearing through Tumor Town without mercy. But once again, one survives. An even fitter cell from an even fitter mutation lineage. This time it gets a cheap suit and studies building codes pretending to be a lawyer to start the process all over again. The struggle repeats a few times, with the tumor getting stronger and stronger each time. Finally a tumor changes into cancer, making it dangerous. Yes, the type that kills over 10 million a year. How though?

- Immune cells have an off switch that deactivate them before they attack
    - Immune system is incredibly powerful and needs be shut down especially near the central nervous system
    - This could be exploited
    - Mutated cancer cell finds a way to switch the immune system off by targeting the inhibitor receptors on anti cancer cells
    - Stops cell from killing cancer

Start of an even stronger cancer cell lineage, starting Tumor Town yet again.

Phase 3: The Escape Phase

- New cancer cells immune to the immune system and everything is much much more different

Tumor Town has been rebuilt bigger and uglier than ever before. But now the Tumor Town Council has forged numerous types of permits. As building inspectors come to shut down the building, they get confused, unable to ward off the construction of buildings. Police come next ready to arrest and take down when Tumor Town erects its own roadblock keeping them out. Confused officers stand around helplessly as Tumor Town engulfs Calgary in a fiery haze. T Cell SWAT teams attempt to stop the rampant violence, but to no avail as newer and newer cancer lineages emerge for blood, sending fake documents to the police, ordering them to shoot at the SWAT teams. Actively shutting down the body's defenses, the tumor has now begun creating the Cancer Micromovement, a sort of borderland that's hard to cross. All avenues of attack are now shut down and the tumor growth is uncontrollable. A dangerous tumor. If this goes on, new lineages will begin to explore the world, expand into other tissue and build new towns. This is exactly what makes the disease so harmful, it takes nutrients from your body and starves to the point where it can't function properly. Leading to, death of the human, and death of the cancer, as if the body dies, the cancer along with it. Truly a game without winners.

References

https://www.youtube.com/watch?v=uoJwt9l-XhQ&t=355s

HeLa

Introduction

- HeLa cells are deemed to be immortal
- Whenever Henrietta's cells died, they always regenerated in perfect or just rarely died in the first place
- HeLa cells are extremely rare and have only been found in 1 person: Henrietta Lacks

History

- They are used for studies to possibly eradicate certain types of cancer
- Scientists grow human cells to study how they function, understand disease
  - To examine and compare with other scientists
  - Need cells that multiply for years
  - But all human cells scientists tried to grow died after a few days
  - Then a John Hopkins scientist George Gey received a sample of a strange looking tumor
    - Dark-purple, shiny, jelly like
    - Some of it's cells kept on dividing
    - Endless source of cells still around today
    - Can divide an unlimited amount of times on a cell structure plate

Importance

- Henrietta died of aggressive cervical cancer a few months after her tumorous cells were harvested
- How though? We don't know
- Normally cells have a built in function that allows them to multiply 50 times before self destructing
- This prevents genetic mutation after repeated multiplication
- Not HeLa though, which unlike normal cells also don't die outside the body, and that's the part we can't yet explain
- After he realized he had the first line of immortal cells, he shipped them all around the world

Use

- The Polio epidemic was at its peak in the early 50's
  - HeLa cells which easily took up and replicated the virus, allowed Jonas Salk to test his vaccine
- HeLa's been used to study various diseases

- We know that human cells have 46 chromosomes because he exposed HeLa to a chemical that makes chromosomes visible
- HeLa cells actually have around 80 mutated chromosomes

References

https://www.youtube.com/watch?v=22lGbAVWhro&t=34s