How to Solve a World Problem

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Problem

How can we use biotechnology to solve a current issue in the world?

Hypothesis

If the mutated gene is replaced by a gene that is the same but healthy, then it will prevent the development of Parkinson’s later in life and save the brain cells from dying.

Research

Parkinson’s Disease (PD) is a recessive protein based disease that gets passed down. Parkinson’s causes depression and tremors due to the death of brain cells. It is a neurodegenerative disorder affecting predominantly dopamine-producing (“dopaminergic”) neurons in the substantia nigra which is found in the brain. Genes known so far to cause pd are mutations in these genes: ATP13A2, GBA, LRRK2, PARK7, PINK1, PRKN, SNCA, UCHL1, VPS35, as well as possible others.

Symptoms

- Tremor, lowed movement (bradykinesia)
- Rigid muscles, impaired posture and balance
- Loss of automatic movements, smell dysfunction
- Speech and writing changes
- Blood pressure changes resulting in feeling dizzy or lightheaded when stand due to a sudden drop in blood pressure (orthostatic hypotension)
- Fatigue in which many people with the disease lack energy
- Pain has been reported throughout the body or in specific areas
- Sexual Organ dysfunction has been reported

Treatable symptoms

Each person depending experiences the disease differently, as every brain and case is different.

- Cognitive difficulties (not really responsive to medication)
- Depression and emotional changes (such as fear, anxiety or loss of motivation)- DRD1
- Problems with swallowing
- Sleep problems and/or disorders (medications may help)
- Rapid eye movement
    - Sleep Disorder involving involuntary movement of limbs to replicate dreams
- Bladder problems which includes difficulty urinating and constipation as well as lack of control leading to leaks

Current treatment

- L-DOPA medication which lasts 5 years before complications
- Musical therapy
- Antidepressants to improve mood

Medications for Parkinson's

- **Carbidopa-levodopa**
- **Carbidopa-levodopa infusion**
- **Dopamine agonists**
- **MAO B inhibitors**
- **Catechol O-methyltransferase (COMT) inhibitors**
- **Anticholinergics**
- **Amantadine**

More information on:
https://www.mayoclinic.org/diseases-conditions/parkinsons-disease/diagnosis-treatment/drc-20376062

Limitations

- There is no known cure, only some treatment
- Parkinson’s sometimes causes brain death
- There is not enough research about PD to find an efficient cure
- There is not a lot known about Neurodegenerative diseases
- Money is also a limitation to it, research is expensive.
- Ways to prevent PD from developing are unknown

Solution

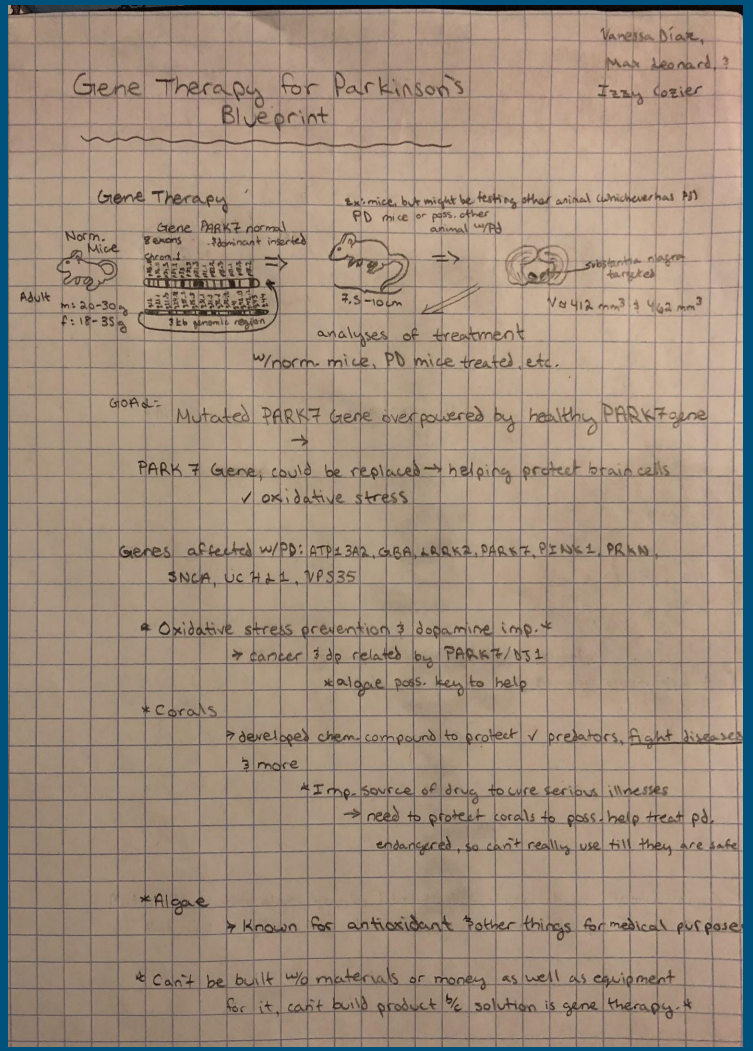
In order to decrease effects of Parkinson's disease and increase life expectancy rates for PD patients, we introduce Gene Therapy. We offer our idea to the BUCK Institute in exchange for recognition rights on the discovery and half of the proceeds from each gene therapy procedure performed.

Product/Our Proposal

Injections to treat effects of genetic mutation. Our product is our proposal since we can not further investigate, nor do we have the materials, or the money to create the product. So our proposal is an injection to the head in the substantia nigra with the gene PARK7 that is not mutated and functioning properly. It could also be with other genes known to pd could be tested. We hope that replacing a gene mutated by the same gene only not mutated and functioning normal that then there is hopefully a chance it could take over and help stop pd in patients. It is only a proposal that has a chance of working, but has not been tested.

Blueprint

Our product is a proposal which in the blueprint at right shows that we are planning to insert healthy genes known to pd into animals that already have pd and compare plus contrast the treatment with a healthy animal to see result of treatment.



Gene Therapy Market

Market estimates for cell therapy, gene therapy, and tissue-engineered products are in the range of $200-400 million, with projected annual growth of 10-15%. Over 150 million people in the United States alone suffer from genetically caused diseases and disorders.

Why did we choose Gene Therapy?

Parkinson’s Disease is a genetic disease which we found could be caused by many mutated genes not working properly leading to the death of brain cells. Gene therapy could ultimately treat it, however without enough research, a cure is still unknown. With gene therapy, the mutated genes would be replaced with a properly coded one which could help lessen the symptoms of Parkinson’s or possibly stop the development.

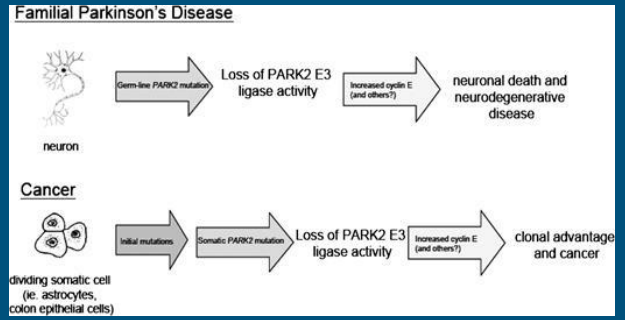
Tests for Efficiency

To test the efficiency of gene therapy before introducing it to humans, we will perform our tests on mice brains. Through insertion of the PARK7 gene to all mice we can test the efficiency of a dominant gene on mice infected with PD, mice with PD and gene therapy, mice without PD but with gene therapy, and mice without PD and gene therapy.. Using gene therapy we are able to increase DNA, translating to RNA, and transcribing to increase proteins.

Safety

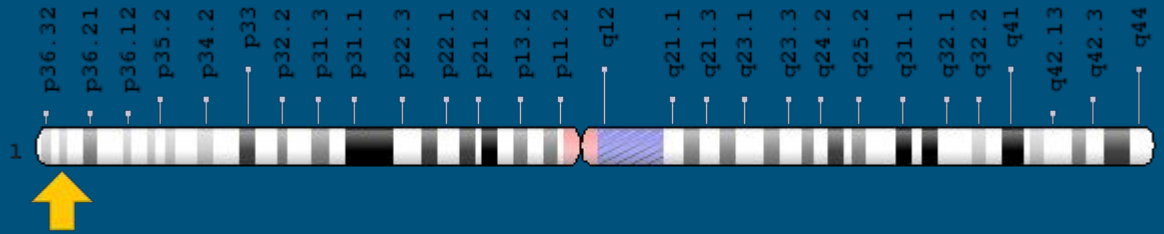
The procedure is relatively safe with the risks of being injected improperly although that is left up to medical professionals to make sure the injection is done properly. However we also facet the possibility of the injection causing deformities and unpredicted dangerous side effects due to humanity’s lack of knowledge of the brain.

PARK7



- Autosomal recessive and has 8 exons
- A mouse with PARK7 will contain these phenotypes
- Located on the 1st chromosome 36th pair
- Provides instructions for DJ1 protein which protects brain cells from oxidative stress which oxidative stress could cause cell death
- Cancer and Parkinson's are in a way related because of PARK7 mutation, yet they are quite opposites because one has abnormal growth while other has death of cells

PARK7 at right



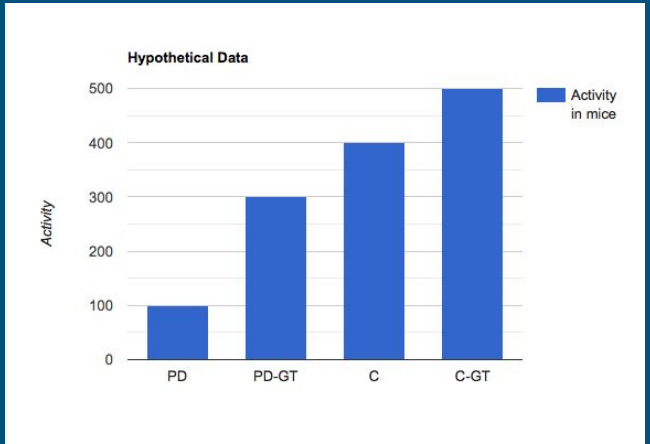
Our Process Steps

1. Acquire PARK7 10 mutated mice and 10 healthy mice from the Jackson Laboratory.

Process Steps

2. Record activity levels in all mice before treatment and create a hypothesis.

- Record disease symptoms
- Focus on activity such as running, burrowing, sleeping, etc.



Process Steps

3. Insert healthy, dominant PARK 7 gene into 5 mice with mutated PARK7 genes and 5 healthy controlled mice (without PD). After insertion there will be 4 groups of mice: 5 untreated PD mice, 5 PD mice with gene therapy, 5 untreated control (No PD) mice, and 5 control (No PD) mice with gene therapy

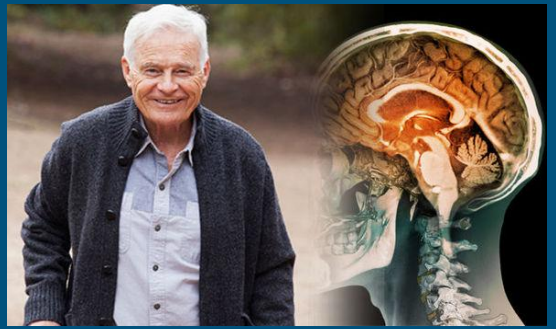
Process Steps

4. Analysis:

- Independent variable: mice
- Dependent variable: activity
- Control: Number of mice
- Figure: To test the effectiveness of inserting a dominant gene into an autosomal-recessive gene, in order to create a healthy and functional gene.

Process Steps

5. Next Steps: After finding the efficiency of our gene therapy we plan on bringing our method into the world for human benefit. Using the same techniques, we plan on inserting a healthy PARK7 gene into PD patients through gene therapy. Although it is known that treatment successful in animals does not mean it will automatically be successful in humans, we keep this in mind with a positive attitude as we move forwards in trials.



Mentor

David Begelman- Intern at the BUCK institute for Research on Aging.

(Resident in Isabelle Cozier’s home.)

A huge thank you to our mentor who was able to help us with any trouble shooting we came across! Teaching my group and I so much about genetic diseases helped tremendously. -Izzy Cozier

How will this make a difference?

This will make a huge difference as it essentially changes the genes in the brain so that Parkinson’s is not passed down and could be stalled or stopped entirely. Also, if it is caught soon enough, there could be possibility to stop Parkinson’s from developing in the first place if it is a successful treatment.

Backup Proposals/ Theories

If that our proposal does not work, other treatments could be with algae to help with oxidative stress which is used due to its antioxidative which could help since oxidative stress plays a major role. Some vitamins could possibly help, and musical therapy as well.

Another thing is somehow looking at cancer and manipulate it to counteract death of cells with Parkinson’s which could either lead to death or successful treatment, it is unpredictable how it will go.

Any questions?

Thank you for listening!
The end! :)

Works Cited

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