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Proposal for curing multiple sclerosis by genetically engineering oligodendrocytes
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What is Multiple Sclerosis?
- A chronic T cell mediated autoimmune disease
- Affects the central nervous system (CNS) by causing irreversible damage to the myelin sheath
- Two stages:
  1. Relapsing-Remitting
  2. Progressive

Possible Causes of Multiple Sclerosis
- CD4+ T cells are activated in the periphery
- B Cells are the key effectors for onset of the disease
- Low serum levels of Vitamin D
- Smoking
- Childhood obesity
- Repeated infections of the Epstein-Barr virus
- Genetics

Why try to find a cure?
- Current treatments/therapies only slow the progression of the disease
- ~2.5 million people worldwide are affected - Between 400,000 and 570,000 in the U.S.
- Diagnoses usually occurs between the ages of 20 and 40
- Affects women more commonly than men
- No two cases are the same

Specific Aim
- Find a cure for Multiple Sclerosis through genetically engineering neural stem cells, specifically the oligodendrocytes.
- Oligodendrocytes will be treated with chemotherapy in order to forget their memory of Multiple Sclerosis
- The three key myelin genes (PLP1, MBP, and MOG) will be introduced to cause remyelination when introduced
- Hypothesis: Genetically engineering the neural stem cells will remyelinate the myelin sheath and stop lesions from forming.

Methods
- Mouse model used in study
- Chemotherapy to forget memory of M.S
- MRI to determine disease activity
- Response to tx measured
- 3 key myelin genes split into txt groups
- GraphPad Prism 4 and one way ANOVA for statistical analysis
- Txt response tested by MRI and amount of lesions

References

Potential Conclusions
- 1. The 3 key myelin producing genes together work as hypothesized
- 2. Two of the 3 key genes together fix the myelin sheath
- 3. One of the 3 key myelin genes by itself causes remyelination
- For this to support the hypothesis:
  - Remyelination occurs
  - Disease progression is halted
  - No new symptoms occur
  - Old symptoms disappear
- If this occurs, then a possible new treatment and cure could become available (Figure 5).

Hypothesis: Genetically engineering the neural stem cells will remyelinate the myelin sheath and stop lesions from forming.

Figure 1. Multiple Sclerosis. The driver for M.S is the lesions that form in the myelin sheath causing issues in communication between the brain and the muscles

Figure 2. Causes for M.S. The possible causes broken down by category.

Figure 3. M.S stats. The highest risk

Figure 4. MRI of M.S. A healthy brain vs a brain that has been damaged due to the lesions that form as a result of multiple sclerosis

Figure 5. An MRI is done to determine disease activity in a multiple sclerosis patient.

Potential Pitfalls
- Using neural stem cells for remyelination is a novel concept
- Mice do not respond to any of the three key myelin producing genes (Figure 4)
- If mice do not respond to the three key myelin producing genes, change it to the seven myelin peptides

Image 1: Multiple Sclerosis
Image 2: Causes for M.S.
Image 3: MRI of M.S
Image 4: M.S stats
Image 5: An MRI is done to determine disease activity in a multiple sclerosis patient.