References and Contributions

Investigating and Modeling the Mechanism between Fingolimod and Sphingosine-1-Phosphate Receptor

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Background

- The Sphingosine-1-Phosphate Receptor is involved with the central memory T-cells (TCM) of the immune system (Vermersch 2018).
- Fingolimod, a Multiple Sclerosis drug, binds to the S1P receptor causing the recruitment of β-arrestin which induces receptor internalization. This prevents TCM migration into the CNS, a key part of autoimmune reactions (Park & Im, 2017).

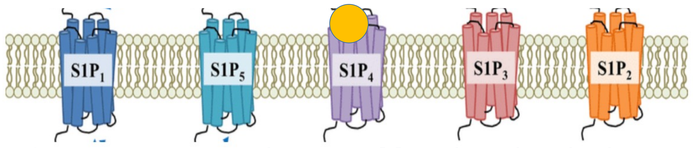


***Figure 1**. Action mechanism of fingolimod and other S1P receptors*

Objective: Model the mechanism of how fingolimod acts as a receptor modulator when it interacts with the sphingosine-1-phosphate receptor.

Materials and Methods

1. Research with academic journals

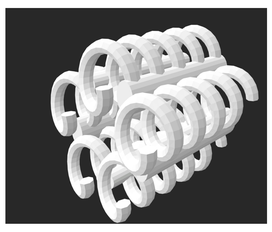
2. Initial Prototype Design with Craft Kit

3. Hand-Drawn Sketches

4. Digital Design with TinkerCAD

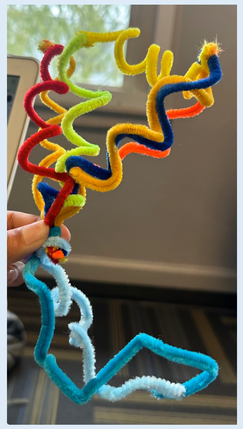
5. Printing and Assembly with MakerSpace 3D printers

BEAM BE A MAKER

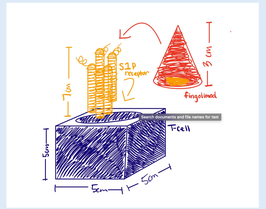


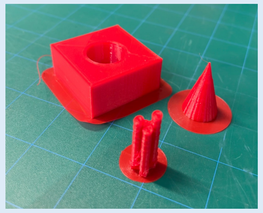
S1P Receptor Design

Design Process



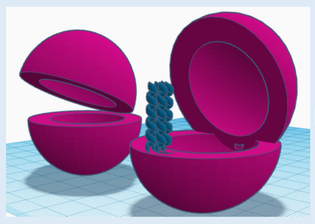
Initial Prototype using Craft Kit





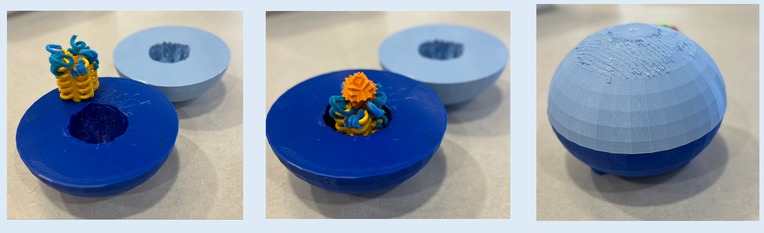
2nd Prototype Sketch & 3D Print

3rd Prototype Sketch



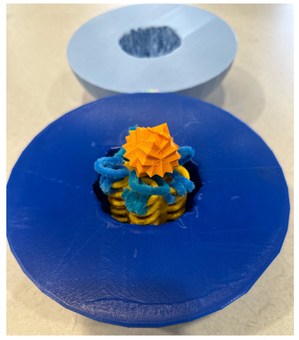
3rd Prototype TinkerCAD Design

3rd Prototype 3D Print



S1P receptor on TCM, fingolimod bound, and internalized by TCM

Final Model



Drug-receptor complex internalized by the TCM

LIVE MODEL

Discussion

- This model illustrates the inward movement and internalization of the receptor-drug complex within the TCM once the drug binds.
- The internalization of the S1P receptor and fingolimod drug complex in the TCM blocks further signaling which prevents circulating lymphocytes from entering the CNS. This will reduce the autoimmune reaction that typically leads to myelin sheath degradation in Multiple Sclerosis.

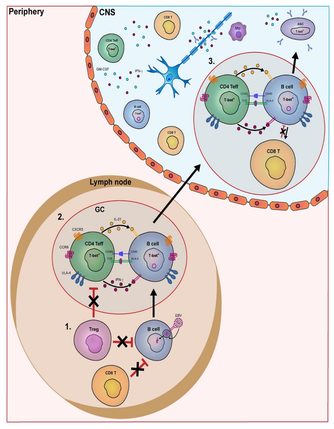


***Figure 2**. T-cell migration in Multiple Sclerosis*

- Our model can facilitate understanding the mechanisms between the fingolimod drug, the S1P receptor, and the TCM to guide future research toward treating other T- cell mediated autoimmune diseases.