# Research & Design Phase Model Summary

## Grafton High School SMART Team

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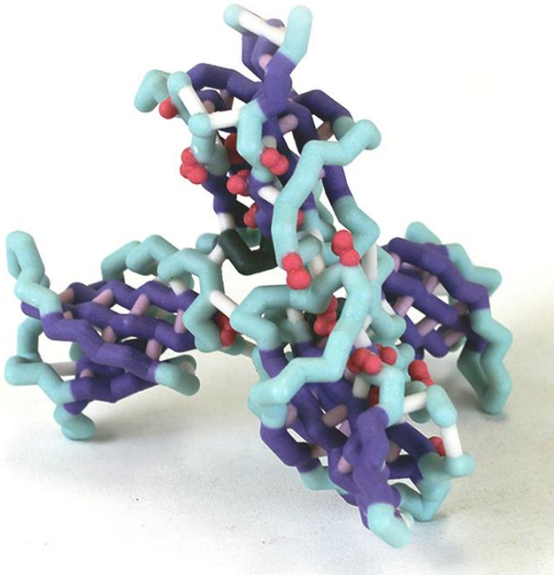
## Dynamic Duo: Leptin and PACAP Receptors Fight Obesity

**PDB File:** 3V6O



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**Format:** Alpha carbon backbone

**RP:** Zcorp with plaster

**Description:** Obesity is a risk factor for cancer, diabetes, and strokes, causing 300,000 deaths annually in the U.S.[1] Facets of obesity, such as adipose-tissue mass, hunger, and energy use are, in part, regulated by leptin, which binds to the leptin receptor (LR) within the hypothalamus, regulating mammalian feeding behaviors and promoting metabolic homeostasis. The LR is a homodimer belonging to the cytokine family. It binds leptin at ten residues between amino acids 433 and 617. Leptin binding activates the JAK-STAT signaling cascade, which promotes gene transcription altering feeding behavior and metabolism. The putative structure of the LR is composed of 206 amino acids, containing two exposed tryptophan residues, four-helical bundle cytokines, and four antiparallel α-helices. Understanding LR activation is crucial for obesity as studies have shown that defects in LR binding may disrupt normal metabolic function and overeating leading to metabolic disorders such as obesity. Overeating also occurs when PACAP (pituitary adenylate cyclase activating polypeptide) which functions similarly to leptin, is blocked. Importantly, leptin is blocked from producing its anorexic effects when PACAP receptors are blocked. Understanding how leptin receptors function with PACAP receptors would advance the understanding of leptin signaling in obesity. The Grafton High School SMART (Students Modeling A Research Topic) Team designed a leptin receptor model using 3D printing technology to specifically explore the structure-function relationship between PACAP and leptin, and their shared common pathway. To date, effective treatments for obesity are lacking, therefore research focused on the relationship between PACAP and LR activation could lead to the development of new therapeutic medications.

[1] West Virginia Department of Health and Human Resources

**Specific Model Information:**

Amino acid side chains involved and WHY: Leptin interaction site-these amino acids are the ones that directly interact with the leptin molecules to facilitate the cascade reaction

- Asn433
- Ile434
- Cys473
- Asp 475
- Ser450
- Pro526
- Asp617
- Thr527
- Cys528
- Val529

Highlighted protein structures & Colors:

- Hbond is colored-Thistle
- Alpha helix is colored-Dim gray
- Beta sheet is colored-Medium Slate Blue
- Backbone is colored-Powder Blue
- Leptin interaction site is colored-Pink

Supporting Features:

- Struts are colored-Azure