Hungry Like PACAP Man: 
The Role of PACAP and PACAP6-38 in Eating Behaviors

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A. Obesity and Related Health Concerns in the United States

- Obesity and eating disorders are a major health concern in the United States. Up to 24 million people involved in eating behaviors could improve people’s lives and decrease obesity-related US medical costs. Program printing technology to investigate their relationships. Studying PACAP and PACAP6-38 regulation and brain chemistry

Modeling A Research Topic) Team modeled PAC1R’s ECD and its two ligands, PACAP and PACAP6-38, using 3D printing technology to investigate their relationships. Studying PACAP and PACAP6-38 regulation and brain chemistry involved in eating behaviors could improve people’s lives and decrease obesity-related US medical costs. Program supported by a grant from NIH-CTS.

Abstract:
According to the CDC, 34.9% of United States adults are obese, which is linked to premature death, heart disease, cancer, respiratory disorders, fertility problems, Type 2 diabetes, and stroke. Over- and under-eating are related to brain chemistry. A 38 amino acid peptide hormone in the hypothalamus, called pituitary adenylate cyclase-activating peptide (PACAP), may be linked to weight gain and eating disorders. PACAP binds to PACAP type 1 receptor (PAC1R), a G-protein coupled receptor. Seven hydrophobic transmembrane (TM) domains hold PAC1R in hypothalamic cell membranes. PAC1R’s extracellular domain (ECD) contains a ligand binding site. PAC1R’s many negative residues attract PACAP to its many positive ECD residues. PACAP’s V19, K20, and 127 affect PACAP binding to PAC1R. K20 forms a possible salt bridge with PAC1R’s G104, allowing PACAP to align parallel to PAC1R or PACAP’s N-terminus interacts with PAC1R’s TM domains. This activates PAC1R, sending a signal into the cell. Too much PACAP may cause a person to stop eating and lead to eating disorders. PACAP6-38 is an antagonist formed when a protease removes the first five PACAP residues. When PACAP6-38 binds to PAC1R, eating increases, possibly leading to obesity. SuJeAn Choi, PhD wants to determine how ratios of PACAP and PACA6-38 are regulated. The Greenfield SMART (Students Modeling A Research Topic) Team modeled PAC1R’s ECD and its two ligands, PACAP and PACAP6-38, using 3D printing technology to investigate their relationships. Studying PACAP and PACAP6-38 regulation and brain chemistry involved in eating behaviors could improve people’s lives and decrease obesity-related US medical costs. Program supported by a grant from NIH-CTS.

B. Eating Behavior and Brain Chemistry

Researchers know the hypothalamus regulates eating behaviors. However, more needs to be studied regarding the specific regions of the hypothalamus involved in regulating eating. Two possible areas of the hypothalamus that regulate eating and brain chemistry are the PVN (Paraventricular Nuclei) and VMN (Ventromedial Nuclei).

Comparing the Hypothalamic PVN & VMN Regions
Two regions within the hypothalamus were examined to see if they produce the PAC1R receptor, a protein involved in eating and brain chemistry. White dots appear where mRNA molecules coding for PAC1R are expressed in the hypothalamus. High concentrations of PAC1R mRNA were found in the VMN, and also in PVN. Due to the high concentration of PAC1R mRNA in the VMN, the VMN is a target for administering chemicals related to pituitary adenylate cyclase-activating protein (PACAP) signaling in lab animals.

C. Applying PACAP to the Hypothalamic VMN Decreases Food Intake in Rats

A guide cannula injector system was used to administer chemicals to the VMN to determine if they would alter eating behavior.

D. How Different Ratios of PACAP and PACAP6-38 Affect Eating Behaviors

E. Structures of PAC1R, PACAP, and PACAP6-38

PAC1R has 7 transmembrane domains, an extracellular domain (ECD) for binding, and an intracellular domain.

F. The Future of PACAP and Eating Behaviors

PACAP research can help prevent prolonged by reducing eating disorders, such as binge-eating, obesity, and anorexia. PACAP could help find a balance between over- and under-eating. PACAP can also solve many different types of disease, such as diabetes and heart disease, through controlling food intake and ultimately excess weight gain. Some of the treatments for these diseases are expensive, so if weight gain and some of these diseases are prevented by PACAP, the country will save money and be more healthy overall. Additionally, this medical research can help researchers understand brain signaling and know what is causing over- and under-eating.

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