The endocannabinoid system (ECS) plays a role in diverse disorders such as anxiety, addiction, eating and memory disorders. The ECS is found throughout the body and consists of two lipid signaling molecules, N-arachidonylethanolamine (AEA) and 2-arachidonoylglycerol (2-AG), and their target receptor, CB1R. In the brain, these ligands bind to CB1R and modulate the release of neurotransmitters from nerve cells resulting in changes in synaptic transmission. Disorders result when levels of AEA and 2-AG are either too high or too low. While 2-AG is synthesized at the plasma membrane (PM) AEA is produced in the ER and may require an intracellular, carrier protein to move through the cytoplasm to the PM where it is released. The lipid binding protein, sterol carrier protein 2 (SCP-2) is hypothesized to transport AEA due to its ability to bind to membranes and its nonspecific hydrophobic binding pocket. This proposed binding pocket is composed of 2 alpha helices, 3 beta sheets and the core hydrophobic amino acid residues F13, F27, F35, F37 and F80. The Messmer SMART Team (Students Modeling A Research Topic) created a model of SCP-2 using 3D printing technology. Understanding the structure of SCP-2 and how this protein might regulate AEA and 2-AG levels could lead to possible new treatments for debilitating mood, appetite, memory and anxiety disorders.

**AEA and Anxiety**

- ECS in the brain acts as a dimmer switch for the communication between nerve cells.
- The endocannabinoids inhibit neurotransmitter release, slowing down nerve cell communication and contributing to the regulation of synaptic activity.
- Decreases in activity in the ECS in the brain have been hypothesized to result in anxiety disorders (see Figure 4).

**AEA and SCP-2 Relationship**

- AEA is synthesized in the ER and is released and diffuses through the membrane into the synapse.
- When AEA/SCP-2 complex arrives at the membrane, AEA is released and enters the cell through the membrane.
- SCP-2 functions to transport lipids through the cytoplasm. Since AEA is a lipid, it needs a protein to be transported through the watery cell cytoplasm. The common sterol carrier protein, SCP-2, the focus of our research this year, is hypothesized to be that transport protein. It has a hydrophobic pocket (shown in yellow) where the AEA fits. SCP-2 may lead to a new understanding of how AEA is regulated and to new, more effective treatments for these disorders.

**Conclusion**

A better understanding of how the ECS is regulated could give us more effective ways to treat anxiety. SCP-2 transport may be one way that AEA is regulated. Therefore, studying this transporter protein could lead to medical breakthroughs for dealing with many physiological functions that pertain to the ECS.