Project Elevator Pitch

Cardiovascular disease is one of the leading causes of death in the United States today. One risk factor for cardiovascular disease is a high-fat diet, common in the west today. In the intestine, fat is taken up by the body via small spheres made by the intestines called chylomicrons. These chylomicrons allow fats to be moved throughout the bloodstream. The chylomicrons are composed of three elements: the lipids from the meal, phospholipids which make a barrier and the lipoproteins which control the chylomicron size, formation, terminal location, etc. In the past, researchers have found a variety of different proteins that influence how these lipoproteins form chylomicrons. In this project, we will be interrogating the actions of a protein called PRKD2. PRKD2 is a type of protein called a kinase, meaning it modifies other proteins to have different functions, often acting as a messenger between two processes. Previously, researchers have shown that by deleting PRKD2, or by preventing it from doing its job with a drug, mice and human intestine cells could not absorb fat as well, and thus were less fat and had a healthier insulin response. However, the way that PRKD2 influences fat absorption, specifically by influencing chylomicron activity is not clear. In our experiments, we will be targeting PRKD2 in zebrafish with drugs and by changing the protein itself by targeting the zebrafish gene that codes for PRKD2 using CRISPR, which can delete parts of genes. Zebrafish are a great system for looking at fat metabolism, as very young fish have a large, mainly fat-filled yolk will become dark if fat mobilization is broken in some way. Our lab has also developed a system to tag the proteins in chylomicrons with particles that glow. In both the drug and genetic approaches, which target different parts of PRKD2, we should expect to see a dark yolk, and fewer chylomicrons and their associated proteins (less glowing), if PRKD2 is indeed involved in fat transport as is suggested by data from mice. In addition to verifying these results, our experiment should give us a better idea of how PRKD2 functions to encourage fat transport. We are deleting a few different parts of PRKD2, which have different functions. We are also measuring specific levels of a single lipoprotein (ApoB) with our glowing particle, which can verify or eliminate that protein as part of the communication pathway.

Chylomicrons vehicles for transport

Change word for kinase from messenger: switch or traffic signal

What we want to find out: does it affect ApoB biogenesis. Report on number and size of chylomicrons.

Dark yolk: indicator of inability to make chylomicron.