Biochemistry 401 Lecture 30
Today we're going to talk about cholesterol transport. We're going to talk about the origin, function, and fate of lipoprotein particles, good cholesterol versus bad cholesterol, and then we're going to talk about lipoprotein particles and disease, including atherosclerosis, and metabolic disorder. So let's get started.

Lipoprotein particles are comprised of both lipids and proteins, just as the name suggests. The lipids include phospholipids, triacylglycerols, cholesterols, and cholesterol esters, and other lipids, such as lipid soluble vitamins. The proteins are called apolipoproteins and sometimes they're called apoproteins. Apolipoproteins serve many purposes. They help to organize the lipoprotein particle, and they help to target it to the right place. Some apolipoproteins also act as enzyme cofactors. Lipoprotein particles have a polar exterior that faces the aqueous solution, and a hydrophobic interior.

Lipoprotein particles are constructed such that the polar groups are situated facing the outside, toward the aqueous solution, and the hydrophobic portions face the inside of the lipoprotein particle, and that's as you would expect. Cholesterol is oriented with the hydroxyl facing the outside and the ring structure, and long hydrocarbon tail pointing toward the inside. Here we see phosphatidylethanolamine. The long hydrocarbon tails are facing inward, and the ester linkage, and phosphate-alcohol head group are pointing toward the outside. The same thing is true for triacylglycerols. The fatty acids are pointing toward the inside of lipoprotein particle, and the ester linkages are pointing toward the outside. This makes the ester linkages accessible to lipases, and this is important in the hydrolysis of triacylglycerols. Lipoprotein particles also contain apolipoproteins, and these are also found toward the outside. And packed in the center of lipoprotein particles, we find cholesterol esters. This is cholesterol that has been acylated. A fatty acid has been added at the hydroxyl, so that it can pack more tightly into the center of the lipoprotein particle.

Plasma lipoproteins we're originally isolated and characterized based on their relative densities. Plasma lipoproteins are shown in the figure below and are listed in this chart. The name of the plasma lipoprotein is shown first, then its density, its diameter, the type of apolipoprotein it contains, its physiologic role in the body, and its percent composition of triacylglycerols, cholesterol esters

cholesterol, phospholipids, and protein. We're going to start with chylomicrons. These are the least dense, and they have the highest diameter. They contain the apolipoprotein B48 and C and E. Chylomicrons primarily contain triacylglycerols of dietary origin, and therefore the physiological role of chylomicrons is to transport fats. The rest of these plasma lipoproteins are constructed in the liver. They range from very low density lipoprotein, which is the least dense of those that are generated the liver, all the way down to high density lipoprotein particles. They vary not only in their density, and diameter, but also in their physiological role. For instance, high density lipoprotein is what you may have heard referred to as good cholesterol. This is a lipoprotein particle that is engaged in reverse cholesterol transport. High density lipoproteins take cholesterol from the tissues and bring it back to the liver. The rest of these, the very low density lipoproteins, intermediate density lipoproteins, and low density lipoproteins all carry endogenous lipids from the liver to the tissues. Very low density lipoproteins are constructed in the liver and like chylomicrons they primarily contain triacylglycerols. Their role is to carry endogenous fat in the body and to transport it to the tissues, primarily the muscles and the adipose tissue, and as more and more triacylglycerols are given off, very low density lipoproteins become intermediate density lipoprotein particles. As they give off more of their lipids they become smaller, and therefore more dense. Intermediate density lipoproteins are then tumed into low-density lipoprotein particles and these are primarily involved in cholesterol transport. They primarily contain cholesterol esters, and so low density lipoprotein is known as the “bad cholesterol”. It is involved in transport of cholesterol, originally from the liver, to the tissues. Now the apolipoproteins that are found in chylomicrons differ from those that are found in lipoprotein particles that arise in the liver. Chylomicrons contain B48 for instance. Those lipoprotein particles that contain endogenous lipids contain B100 apolipoprotein. And so what you need to know about this chart. There's a lot of inflammation. Well, you need to know the names of the plasma lipoproteins, and whether they’re larger or smaller in comparison to one another, and whether they’re more dense or less dense in comparison with each other. You also need to know what sort of B apolipoprotein they contain and which component has the highest percentage composition in each lipoprotein particle. For instance in chylomicrons, and in very low density lipoproteins, the component with the highest percentage are triacylglycerols. In intermediate density lipoprotein, it's about a 50-50 split between triacylglycerol and cholesterol esters, whereas in low density lipoprotein particles this is cholesterol ester, and in high density lipoprotein it’s protein, and

that's it. Please do not memorize these numbers. You do not have to memorize the numbers. I hope this helps.

So why is it that chylomicrons, which are formed in the small intestines, have a different apolipoprotein B than those lipoprotein particles that are constructed in the liver? The small intestine contains an enzyme, a deaminase, that removes the amino group in cytosine to form uracil. This introduces a stop codon into the messenger RNA. Therefore. the ribosome stops short and translates a shorter B apolipoprotein. In fact, it's only about half as long as apoB100. This is an intestinal-specific apolipoprotein, and it's only found in chylomicrons.

Now chylomicrons, as we said, are formed in the small intestines, and they have three stages of development. They start off as a nascent chylomicron. They have all their lipids, but they don't have all their proteins, and we'll talk about that in just a minute, and therefore, they're not functional. These nascent chylomicrons are found in the intestines, and in the lymphatic vessels, and are found early on in the bloodstream. In the bloodstream, chylomicrons become mature chylomicrons. This is due to the addition of apolipoprotein CII. Once they give off the majority of their triacylglycerols through hydrolysis, they become known as chylomicron remnants. These are the leftovers, and they returned to the liver for recycling. Let's take a look at this.

Here we see epithelial cells of the intestine. These are enterocytes. In the enterocytes, apolipoproteins and lipids come together to form chylomicrons. These consist of triacylglycerols, cholesterol esters, phospholipids, and other lipids, and they contain apoB48, as we just saw, and another apoprotein, apoA1. These are constructed and then they enter the lymphatic vessels…

…that underlie the epithelial cells. They travel in the lymphatic system,

and enter the bloodstream in a place close to the neck, believe it or not.

And these chylomicrons as they travel in the lymphatic system, and as they just enter the bloodstream are nascent chylomicrons. They're not functional yet. But in comes HDL, good cholesterol, and it's going to take apoA1 from the chylomicron, and in exchange, is going to transfer apoCII to apoE to the chylomicron and now, because the chylomicron has the apolipoprotein apoCII, it