

What I'm going to show you is the adipose tissue, which was next to some muscle tissue, and we zoom in on it, we see that the adipose tissue is composed of millions of individual cells. I'm going to focus on one cell as a model, but remember this event is going on in all cells and a sample of fat tissue has been included in your packet which we looked at yesterday. Here's the fat cell which contains a nucleus, it contains cytoplasm and a specialized structure in this fat cell is the lipid droplet, or the fat droplet, that stores triglycerides as the energy source and can release them depending on the communication with the rest of the body. The fat cell is a hormone secreting cell, Dr. Friedman spoke about leptin yesterday, it also secretes hormones such as adiponectin, in red, and resistin, in blue. Changes in the size of the fat cell and the amount of lipid it contains can change the balance of these informational hormones and shifting things such as insulin sensitivity and appetite. So the nature of the fat cell and how large it is, is very important to us. Now in 1995 we discovered that PPAR-gamma can respond to a certain class of drugs, which are shown here in blue, and these drugs, we give them to the cell, diffuse across the membrane and the cytoplasm, and are able to interact with a PPAR-gamma receptor in the nucleus as is shown here on genes. Here is the drug coming in, which when it binds will trigger a conformational change in the receptor, shown there, which causes the dissociation of the repressor mechanism for genes, and allows activators to come in. This stimulates the activity of this gene, and because PPAR-gamma is in several locations in the nucleus, a network of genes becomes activated, it changes the balance of proteins that are produced by the cell. Changes the function of the cell by activating this network. As the fat cell grows, the balance of these hormones can shift. Here it is growing because more lipids are contained. This shifts the balance; however, if we give it the drug for PPAR-gamma, you can increase the production of adiponectin. So giving the drug causes this increase and this promotes insulin sensitivity, which is an important feature because big fat cells often lead to insulin resistance. By doing this, that adipose, or fat pad can be large, and yet the patient or the individual who has this can be insulin sensitive, without the drug, they would be insulin resistant.