Lecture 6: Endoplasmic Recticulum

I want you to look at every single step as a biochemical equation. The reactants of the reaction have to be at the perfect state for them to react and form a designated product. Then if the two molecules that interact with each other because of their chemical characteristics... It is a chemical imperative , every single step needs to makes sense. Now the first example we gave is that protein synthesis in the rough ER and we are talking about a soluble proteins. We said that the end product of a soluble protein is in the lumen of the ER. Where does it start. It starts with the ribosome, and the ribosome of course must be at a particular point for it to react with SRP. The signal sequence is there, the mRNA and the tRNA are there. As we mentioned the signal sequence consists of 6-8 hydrophobic amino acids. Signal recognition particle is a protein that is circulating in the cytosol. What is needed? The SRP particle has a signal sequence binding site and it has to be free and open and available. So they bind and the binding takes place between the signal sequence and the Signal recognition Particle. When this binding occurs it it causes the hinge of this signal recognition particle to bind and wrap itself around the ribosome, by wrapping around the ribosome. The translation pause domain will interact with the ribosome complex with the effect of stopping the synthesis of the nascent peptide. Now what happens when this is bound is that SRP is no longer the same as when it was in the cytosol. It itself has undergone some conformation changes and this protein has a site available to bind to the SRP receptor. It wasn't there previously unless these free SRP will bind to the SRP receptor. But these SRP can only bind to the SRP receptor after it has complexed with the ribosomal complex.

Second key step is that you have this ribosome, the SRP. When it is bound you have the signal sequence bound to the signal sequence binding domain. Now I just mentioned that there are changes to this bound SRP. You have a site that is open that will allow this complex to bind to the SRP receptor protein that is present in the ER membrane. What happens is that you have this binding complex of the ribosome + the SRP and then it binds to the receptor. This net binding brings the ribosome close to the translocator protein. Now what happens at this point, you have the signal sequence of the ribosome. When the SRP complex is brought close to the ER it is in the right position and I mentioned that the signal sequence will trigger the opening of a channel in the translocator protein. So you have signal sequence interacting with the translocator protein and it will open up a channel. There is some details about the channel. It is continuous with the channel in the ribosome where translation is taking place. The binding of the signal sequence also causes the change of the ribosome SRP complex. The SRP will detach itself from the ribosomal complex. When the SRP leaves the ribosome it also changes the configuration of the ribosome. So how does the ribsomes and the signal sequence stay in place? This is the function of the translocator protein where you have seven sites that has strong affinity to ribosome. This is the reason why the ribosome is staying in place and these several points will anchor the protein in place.

One more thing, when the SRP leaves the ribosome the SRP Pause domain that was stopping translation loses its function so translation will start again.

So after the signal sequence interacts with the translocator protein a channel will be opened that will allow the nascent protein to work its way through. But at the same time what will happen is that the