This is the T-cell, this is the antigen presenting cell. I told you this was the MHC complex, this is the T-cell receptor itself. Here is CD4 and Lck, ZAP-70 we talked about. Here is this link molecule, LAT, and this is the phospholipase-C-γ enzyme. Now what we're going to see herein thereafter is see these waves of calcium being produced in the cell. And one of the major things that calcium does is that it binds a protein called calmodulin, which is just a binding partner, but the most important thing in terms of this particular cascade, and what we're going to be talking about, is it activates this other enzyme called calcineurin, and calcineurin is an enzyme that actually removes phosphate, not from tyrosine, but from serine-threonine residues, and it will allow this nuclear factor of activated T-cells called NFAT to go from the cytoplasm into the nucleus, and it will bind certain promoter elements that regulate the synthesis of the interleukin-2 gene. OK? And of course once you have interleukin-2 made, it will go through the ribosome and it will be translated, made into a protein and it will be secreted through the ER Golgi apparatus so that now you can get interleukin-2 into the extracellular milieu Ok so in this movie what we're going to see is basically see that particular event. So here we're just going to concentrate in the T-cell receptor, itself. The initiating event here. Here first we're going to have the APC coming down and engaging the T-cell as you would see in an initiation of the response. And upon initial contact, which is a low affinity interaction, the CD4 molecule increases the avidity, the Lck molecule phosphorylates these particular tyrosine residues within the receptor, provides docking sites now for the ZAP-70 enzyme, and in turn allows Lck to phosphorylate and activate the ZAP-70 enzyme. Now the activated ZAP-70 enzyme can go on and phosphorylate a number of proteins, one of which is this linker protein called LAT. It itself will provide a docking site for this phospholipase-C-γ1 enzyme and activate it, and the enzyme itself will then hydrolyze to certain phospholipids that are present within the plasma membrane called PIP2, to release it to give rise to a number of intermediates and products. But one of which is this second messenger called IP3. These are phospholipids that will then go on, these are also a second messenger, and so these IP3 molecules - now we are going to talk about how these IP3 molecules modulate calcium in this other signaling pathway on the left here. So the IP3 molecules will diffuse into the cell and engage the IP3 receptors that are typically present within the endoplasmic reticulum. You're going to get waves of these particular calcium bursts. And what we're going to see is that the calcium is released from the endoplasmic reticulum, again another second messenger, and it's going to come over here and activate this particular enzyme complex, it's going to activate this calcineurin enzyme and now this transcription factor, which is typically in the cytosol of the cell will get de-phosphorylated and move into the nucleus of the cell where it, along with other transcription factors, which we're not talking about will result in the synthesis and transcriptional activation of the interleukin-2 gene, where it will be made into protein in the ribosome, and secreted out through the secretory complex. So all these IL-2 molecules then will accumulate into the extracellular milieu and of course one of the other things that occurs following T-cell activation is not... the T-cell does not just activate IL-2, but will also make IL-2 receptors on the cell surface, and these high affinity IL-2 receptors will then bind IL-2, and that, I told you is the signal through other signaling pathways we don't have time to talk about today to induce that cell to proliferate and differentiate. And the end result then, is that this initial single cell, with a single antigen specificity against this particular viral protein over a several day period will then be able to multiply.