What do I mean by a conformational change mutation? What I mean is, if you recall back to the first video, BCR-ABL is a machine. It's moving back and forth between this inactive and active shape. What these mutations do is force the protein into the active conformation. If you'll also remember, I made the point that when Gleevec binds it very cleverly locks the BCR-ABL protein in the inactive conformation. So if you have a mutation now that is making the protein stay in the active form all the time Gleevec's not going to be able to bind. So what I'm showing you on the left is the inactive conformation, and on the right is the mutant form, which creates this active conformation. Now in both forms ATP, the yellow molecule can bind no problem, but now when you try to fit Gleevec in, because of how nicely and tightly it fits into the inactive conformation, it can't fit into the mutant BCR-ABL. So, the drug that was sent to us, the one that worked the best was the drug that now goes by the name Dasatinib let's see how that works in the next video, if you could please roll that one? So some of you I think have Dasatinib in your bag I think it's green, you can see that Dasatinib fits nicely in either pocket. And in both cases, it prevents ATP from binding so it accomplishes the mission. And when you go outside in the hall, you'll also see a red version of BCR-ABL. This is the active conformation and I'll show you and I'll let you play with it yourself, it's very difficult to get Gleevec to fit into this shape. Can't fit it in this way, if I take it apart I can't jam it into the pocket, just doesn't work. But if you take Dasatinib in green it fits in very nicely and tightly and prevents ATP from binding.