BCR-ABL is a kinase, I want you to watch it change. It's flipping back and forth from an active to an inactive conformation. Now we're looking at the skeleton and you see that loop, called the activation loop moving back and forth. So what is this? Well it happens to be a protein known as a kinase. Kinases have as their job, removing one ATP molecule and putting it onto a substrate. So this is the BCR-ABL protein. ATP is going to come into the mix as the yellow molecule. It binds in what is known as a binding pocket. A phosphate is transferred to the substrate protein in purple. The purple protein then undergoes a conformational change in shape and then it goes off and does its job. This is the very common mechanism by which signals are propagated from the outside of the cell all the way to the nucleus. So it's that switch, active to inactive, it goes back and forth, ATP binds, transferred to substrate. So now I'm going to show you how this works in a model. So and after the lecture in the hallways you can play with these models as well. So here's the BCR-ABL protein, and as another example of amazing technology, this was printed just a few weeks ago on a 3D printer. This is ATP, some of you, if you look into your bag, will have a little molecule of ATP, it fits into this binding pocket and its phosphate is transferred. So let's think about now, making a drug. Since we know how BCR-ABL works it needs this ATP, ATP has this binding pocket. Could you imagine making a binding chemical to fit in that binding pocket and prevent ATP from binding? Where this is exactly where the drug Gleevec came from. So let's now show the next animation in which we'll see how Gleevec fits into that pocket compared to ATP. So some of you might have a purple Gleevec in your bag. It's fitting into that pocket very nicely, now let's see what happens when ATP floats by and tries to get in. It can't fit. So now that's called competition, a competitive antagonist, but there's another clever, really interesting property Gleevec happens to also have. If you remember kinase has this movement, back and forth of the activation move. Let's roll the next video and you'll see when Gleevec binds, as we view the skeleton, the activation loop is in the closed or inactive conformation. As it wants to become active in order to bind to ATP, it can't it bumps into that part of Gleevec, so it's locked into the inactive shape. And we can look at that in the model as well. Gleevec fits so tightly in there, you actually have to take apart the kinase to get it to fit in. Once you fit it in, it's locked in there. So I would encourage you to play with that outside and you can see for yourselves. Alright, this is really cool science, isn't it?