

Let's talk about what goes on at the single cell level. How does a gene for influenza hemagglutinin get into a human virus? And I've prepared a small video to show you how this goes. Before we roll the tape let me just introduce you to the fact that I'm going to introduce you to two influenza strains here. One of which has red genomic segments, and one, blue. And what you're going to see in the video is that new human hemagglutinin types come about by recombination between two strands. And that recombination requires that the two different strains infect the same cell. And when they do that what you're going to see are the two viruses binding to the cell surface receptors as before, enter the cytoplasm, disassemble, and start replicating their genomes. And then you're going to see an important, new event happen. So let's roll the tape and here you can see particles are going to bind to the cell surface, fuse with the plasma membrane, release their contents, disassemble, and liberate their genomes. Now let's stop the tape for a second. You know from last time that the next event that is going to happen in viral replication is that these RNA segments are going to be... first of all they're going to be transcribed and translated to generate more viral proteins. The RNA is going to undergo RNA-dependent RNA replication, so you're going to get lots of new copies of the subunit. But now because two different strains have infected the same cell their RNA subunits are going to freely admix with one another. So that when the time comes late in infection to reassemble into daughter virus particles, subunits from one strain can occasionally be picked up along with subunits of the other strain and packaged into a single virus particle. So let's roll the tape and watch that process happen. That is a form of recombination that results from the mixing of subunits, and you'll see it shortly. So here are the newly replicated genomes, they're going to go now and assemble now with newly made proteins into progeny particles. Here you can see the process happening and if you concentrate on this particle, you can see, let's stop the tape, that two blue subunits have been incorporated along with six red subunits, and vice versa over here. So you can see from such a dually infected cell a whole host of new recombinant viruses bearing different subunits have occurred. So this is a form of genetic exchange that occurs, not by crossing over, but by swapping whole viral mini-chromosomes, if you will, ok? So we can complete the tape now, and you'll see that these particles will go out, pick up their envelopes and go off into the outside world. This will be a mixed stock of all different varieties of recombinants, and those recombinants that do best in nature will survive. So that at the molecular level, and we can terminate the tape now, is where new recombinant strains come from that is at the cellular and molecular level the ultimate source of all these new shifted variants.