

Let's review how HIV's reverse transcriptase works. The yellow strand is HIV RNA; it's attached to the reverse transcriptase enzyme. Reverse transcriptase uses the host's cell nucleotides. It makes DNA using HIV RNA as the template and the viral RNA is destroyed in the process. Now let's see how AZT works. Here's the RNA and reverse transcriptase again. The purple pieces are host cell nucleotides being assembled into a DNA strand, the green molecule is AZT. Here it's shown next to a thymidine molecule one of the 4 nucleotide bases A, T, C and G. AZT is very similar to thymidine only one part of the molecule is different and because they are so similar reverse transcriptase mistakes AZT for thymidine and incorporates it into the DNA chain. But the difference is crucial because when AZT is incorporated into the DNA chain, the chain cannot be extended and the process shuts down. When that happens the HIV life cycle is disrupted. Here is a mutant form of reverse transcriptase that is resistant to AZT. It is resistant because its mutant molecular structure does not allow AZT to be used as a substitute for thymidine. AZT is therefore rejected, DNA synthesis can proceed and HIV continues to infect the cell.