



FIGURE 3.9. HIV evolves resistance to the antiviral drug ritonavir through multiple substitutions in the drug's target, HIV protease. The evolution of this enzyme was followed in 42 patients. The *red bars* show the variants observed in the base population. The *blue bars* show variants that emerged after drug treatment, most of them on multiple occasions. The nine variants marked by an asterisk contributed to resistance, but significant resistance required several substitutions. For example, a change to valine at position 82 appeared first in most patients but does not give resistance by itself.

3.9, redrawn from Molla A. et al., *Nat. Med.* 2: 760–766, © 1996 Macmillan, www.nature.com