As seen in Figure 4, small RNA viruses and ssDNA viruses (both with relatively small genomes) are the primary drivers of evolution-by-*de novo* mutation. Although (as shown below) far from their exclusive evolutionary mechanism, their high rate of replication and error-prone RNA-dependent RNA polymerase allow for relatively high rates of random mutation without catastrophic consequences to the overall fitness of the whole viral population within the host. (I.e., although many mutants may be non-viable, the rate of replication is high enough and the error rate of the RDRP high, but nonetheless low enough that enough virions remain viable to allow for sustained proliferation.) In higher-order organisms (e.g., eukaryotes), the rate of *de novo* mutation remains low, largely due to the proofreading mechanisms that exist to correct for errors in genome replication.

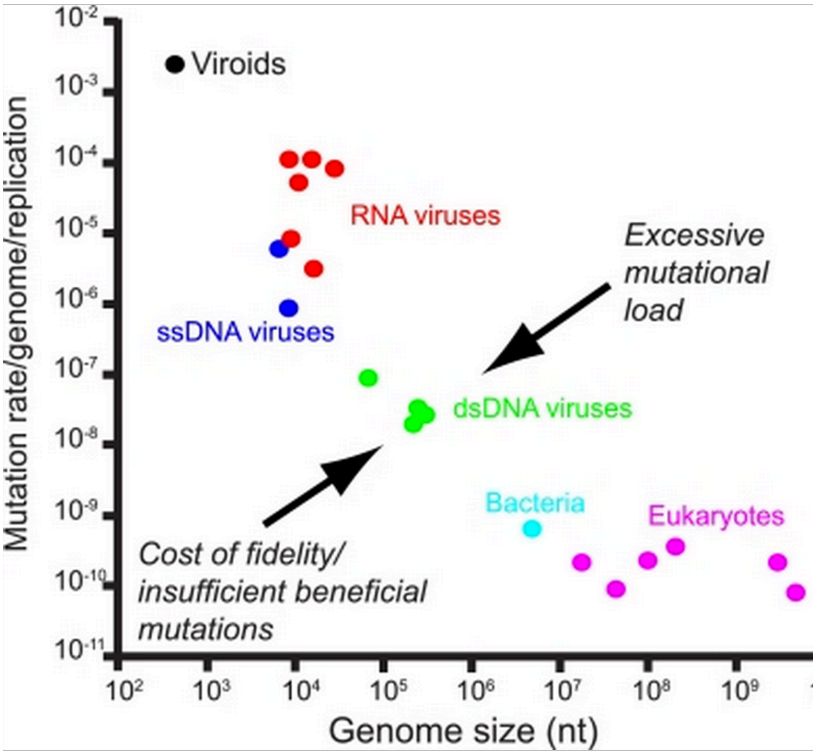

Figure 4: Mutation rate versus genome size. Excerpted from Holmes (2011).

Among viruses, we see that this strategy is employed quite successfully, primarily with the goal of immune evasion. Influenza, for instance, is highly antigenically variable with respect to its HA and NA surface proteins: the high rate of mutation on these regions (typically the targets of annual flu vaccines) allows the virus to persist easily despite concerted annual vaccination and prevention efforts. Likewise, among, for instance, parasites such as *P. falciparum* we see a similar evolutionary mechanism employed in the evolution of resistance to quinine and chloroquinine, via mutations to the *pfcrt* allele (Valderramos et al., 2010).

Alternately, many bacteria, such as *V. cholera*, will employ horizontal gene transfer systems. In the case of cholera, we observe horizontal transfer of genes is mediated by a type VI secretion system. In this way, the bacteria respond to inter-serogroup competition and external environmental pressures by the direct cell-to-cell exchange of genetic material (Unterweger et al., 2013).

With respect to genetic reassortment and recombination, we see these strategies broadly employed by diverse pathogens. Returning to influenza, having a segmented genome, multiple strains co-infecting a single host have the capability to swap gene segments with one another during replica-