

**Protocol S1.** Approximation of allele frequency evolution.

To obtain an approximate solution of equation (3), we derive two approximate solutions of equation (1) in which mutation is assumed to be unidirectional with host-specific selection, giving:

$$p_{\text{HLA}^+}(t) = \frac{\mu \left( e^{t(s_{\text{esc}} + \mu)} - 1 \right)}{s_{\text{esc}} + \mu e^{t(s_{\text{esc}} + \mu)}}$$

and

$$p_{\text{HLA}^-}(t) = \frac{s_{\text{rev}} + \nu}{s_{\text{rev}} + \nu e^{t(s_{\text{rev}} + \nu)}}.$$

These approximations have the initial conditions  $p_{\text{HLA}^+}(0) = 0$  and  $p_{\text{HLA}^-}(0) = 1$  and are reasonably accurate when selection is stronger than mutation and the effective population size is large.