

Table S3. Numerical screen of large-population model with “monotonic” mutation rates (Figs. 2J, K)

<u>Parameter</u>	<u>Physical meaning</u>	<u>Range of values</u>
N	Population size	$10^4 - 10^9$ stem cells
L	Organism lifetime	$10^2 - 10^3$ cell cycles
$u_i; i = 0 \dots k$	Early mutation rates	$10^{-9} - 10^{-6}$ (Fig. 2J) $10^{-5} - 10^{-2}$ (Fig. 2K)
$u_i; i = k+1 \dots K-1$	Late mutation rates	$10^{-5} - 10^{-2}$ (Fig. 2J) $10^{-9} - 10^{-6}$ (Fig. 2K)
k	Transition stage	0 ... K-2 (chosen uniformly)
K	# accumulated mutations	2 – 10 (chosen uniformly)