Supplemental Video Captions

S3 (S3.mov) The effect of spatial constraints on heterogeneity (video) Identical simulations and parameterization as figure 1. Cells divide and die on a regular square lattice. A cell selected for birth can divide only into an empty grid location and may accrue passenger or driver mutations. Top: simulations on varied sizes of domains, ranging from 100 cells in diameter to 900 cells, seeded with 100 cells at time zero ($k_d = 1.\ k_p = 0$) at time zero ($T_p = 5 \cdot 10^6$,$T_d = 700$,$s_d = 0.1$, $s_p = 0.01$). Bottom: Identical domain size (seeded with one-third of the domain filled; $k_d = 1.\ k_p = 0$) segregated into varied number of non-interacting regions ($T_p = 10^6$, $T_d = 700$, $s_d = 0.1$, $s_p = 0.01$, $\mu = 10^{-8}$).

S4 (S4.mov) Spatial segregation with cell dispersal accelerates evolution (video) Identical simulations and parameterization as figure 2. Simulations seeded with 100 cells ($k_d = 1$, $k_p = 0$) are allowed to disperse between segregated regions at a low rate (0.01; left column) or high rate (0.1; right column) for varied number of segregated regions, as shown. A Muller plot of tumor evolution represents genotypes color-coded by driver (k_d) value. The horizontal axis is time (cell generations), with height corresponding to genotype frequency. Descendant genotypes are shown emerging from inside their parents. Simulations repeated for 7 by 7 regions, and 11 by 11 regions. Parameters: $T_p = 5 \cdot 10^6$, $T_d = 700$, $s_d = 0.1$, $s_p = 10^{-3}$, $\mu = 10^{-8}$.

S5 (S5.mov) Three dimensional model of tumor evolution constrained by ductal network structure (video) Identical simulations and parameterization as figure 3. Realistic three-dimensional topology of breast ductal networks (reconstructed with data from anthropomorphic breast phantoms in[29]) provides full three-dimensional maps to seed and constrain tumor evolution simulations. Tumor evolution is shown for varied initial conditions ($T_p = 10^6$, $T_d = 700$, $s_d = 0.1$, $s_p = 0.1$, $\mu = 10^{-8}$). Simulations closer to the ductal root (top) in larger, less constrained branches are characterized by more consistently neutral evolution and constant acquisition of new clones (see figure 3B, blue curve). Simulations further from the ductal root (bottom) in smaller, more constrained branches are characterized by clonal sweeping early, but neutral evolution at later times (see figure 3B, purple curve). Each tumor is seeded with 500 cells ($k_d = 1$; $k_p = 0$). Each simulation is run for 3000 cell generations.

S6 (S6.mov) Realistic three-dimensional topology of breast ductal networks (video) Left: realistic three-dimensional topology of breast ductal networks, reconstructed with data from anthropomorphic breast phantoms in[29] provides full three-dimensional maps to seed and constrain tumor evolution simulations. This provides a topology of a continuously connected series of progressively smaller ductal branches. Middle: slices in the z-dimension show fewer, larger ducts for low z-values and many, smaller ducts for high z-values. Right: static images of z-dimension slices.