**SUPPLEMENTARY METHODS**

**Enzymatic tumor tissue dissociation**

For side-by-side comparisons of tumor dissociation methods, chopped tumor slurries were divided into 3 equal portions (confirmed and adjusted by weighing). Each tumor or portion was enzymatically digested according to one of three methods.

Method one (adapted from Quintana et al (9)): The tumor slurry was resuspended in HBSS (without Ca2+ and Mg2+ (HBSS-/-)), Sigma, St Louis) containing 200U/ml Collengase IV (Worthington, Lakewood, NJ) with 50U/ml DNase and 1mg/ml CaCl2 (10ml of digestion media per gram of tissue), and placed in a at 37°C water bath for 20 mins, with agitation and mixing every 5 mins. The resultant digest was made up to 50ml with HBSS-/- and spun down at 220xg for 4 mins at 4°C. The cell/tissue pellet was then gently resuspended in warmed 0.05% trypsin-EGTA (Gibco Glasgow, Scotland) with 200U/ml DNase, followed by incubation at 37°C for 5 mins. More DNase (50-200U/ml) was added when necessary to reduce cell clumping during digestion. An equal volume of chilled staining media (L15 medium containing, 1mg/ml BSA, 1% penicillin/streptomycin, 10mM Hepes (pH7.4)) was added to quench the trypsin, followed by centrifugation at 220xg for 4 mins at 4°C. The cell pellet was resuspended in staining media and filtered (40µm cell strainer) to obtain a single cell suspension.

Method two (adapted from Civenni et al (6)): The tumor slurry was resuspended in HBSS-/- (Sigma, St Louis) containing 1 mg/ml Collengase III (Worthington, Lakewood, NJ) and 0.5mg/ml dispase (Roche, Indianapolis, IN) (5ml of digestion media per gram of tissue) for 1 hour at 37°C, with concurrent agitation and intermittent mixing mins. The digest was then made up to 50ml with HBSS-/- and cells filtered (40µm cell strainer) to obtain a single cell suspension. The sample was spun at 220xg for 4 mins at 4°C and the cell pellet resuspended in staining media.

Method three (adapted from Boiko et al (5)): The tumor slurry was resuspended in Media 199 (Invitrogen, Carlsbad, CA)) containing 60µg/ml Liberase Blendzyme TM mix (Roche, Indianapolis, IN) (10ml of digestion media per gram of tissue) and placed in a water bath for 1 hour at 37°C, followed by the addition of more 60µg/ml of Liberase Blendzyme TH mix for at least 40 mins to reduce cell clumping. After ≥100 min digestion, the digest was made up to 50ml with HBSS-/- and the cells were filtered (40µm cell strainer) to obtain a single cell suspension, which was centrifuged at 220xg for 4 mins at 4°C and resuspended in staining media. Dead cells and debris were reduced using density centrifugation (1:1 g/ml Optiprep; Sigma, St Louis) when necessary.

**The ‘t-statistic’ method: determination from SNP array data of genomic differences between tumors and between cell subopulations.** Two-way comparisons of CN profiles were compared by calculating t-statistics in 100 SNP-windows across the genome. Log R ratios (LRR) and B allele frequencies (BAF) were compared independently. BAF signals were filtered to remove homogeneous SNPs by applying upper and lower thresholds, which were set to account for different levels of noise between samples. Only BAF signals between these thresholds in at least one of the two samples were retained. Trimmed BAF signals in each window were transformed to ensure unimodal distributions. This transformation involved splitting SNPs into two groups: one with BAF signals larger than 0.5 and one with BAF signals lower than 0.5. The two resulting distributions were then merged using a mirror transformation along the mean of their modes:

where

This is similar to traditional mirrored BAF transformation, but corrects for asymmetry of BAF bands around the BAF=0.5 line due to a dye intensity bias between the two channels of the assay (43). Finally, in order to avoid overestimating regions of difference, windows containing SNPs separated by more than 200,000 nucleotides were discarded. As a change in ploidy between two tumors causes a global offset in the LRR, which propagates into the LRR t-statistic, this was translated so that its mode was 0.

Regions of CN difference were defined by substantial runs of t-statistics departing from 0. These regions were found by applying a min-run-max-gap (MRMG) algorithm on both LRR and BAF statistics and identifying the union of the two resulting binary signals. The 3 parameters of the MRMG algorithm were used to adjust the sensitivity of the comparison.