SUPPLEMENTARY METHODS

Copy number alteration (CNA) analysis

Copy number alterations (CNAs) were identified using FACETS (1). Read counts for dbSNP (build 137) positions within the target regions were generated for matched tumor and normal samples, and used as input to FACETS. This algorithm performs a joint segmentation of the total and allelic copy ratios and infers allele-specific copy number states. Genes with copy number alterations were determined following the methods described in Curtis *et al*. (2). In brief, the median Log_2 ratio +2 standard deviations (SDs) or +6SDs was computed for the 50% (or 45% or 40%, see below) of the central positions ordered by their Log_2 ratios to define copy number gains and amplifications, respectively, and the median Log_2 ratio -2.5SDs or -7SDs was computed for the 50% (or 45% or 40%) of the central positions to detect copy number losses and homozygous deletions, respectively. To account for the differences in tumor cell content, ploidy and noise between samples, the proportion of central positions, ordered by their Log_2 ratios, was determined based on the median absolute difference between the raw Log_2 ratio and the segmented Log_2 ratio. For samples in which the median absolute difference was ≤0.2, >0.2 and ≤0.3, central positions of >0.3, 50%, 45% and 40% were adopted, respectively Loss of heterozygosity (LOH) was determined using the minor copy number estimates of each segment for genes harboring a somatic mutation. All gene amplifications, homozygous deletions and LOH were visually inspected using plots of raw Log_2 and allelic copy ratios.

Sanger sequencing

PCR amplification of 10ng of genomic DNA was performed using the AmpliTaq 360 Master Mix Kit (Life Technologies) on a Veriti Thermal Cycler (Life Technologies) as previously described (3) (for primers see **Supplementary Table S2**)**.** PCR fragments were purified with ExoSAP-IT (Affymetrix), and the sequencing reactions were performed on an ABI 3730 capillary sequencer

using the ABI BigDye Terminator chemistry (v3.1) (Life Technologies) according to manufacturer's instructions. All analyses were performed in duplicate. Sequences of the forward and reverse strands were analyzed using MacVector software (MacVector, Inc).(3)

Supplementary References

1. Ronglai S, Seshan V. FACETS: Fraction and Allele-Specific Copy Number Estimates from Tumor Sequencing. Memorial Sloan-Kettering Cancer Center, Dept of Epidemiology & Biostatistics Working Paper Series 2015.

2. Curtis C, Shah SP, Chin SF, Turashvili G, Rueda OM, Dunning MJ, et al. The genomic and transcriptomic architecture of 2,000 breast tumours reveals novel subgroups. Nature 2012;486:346-52.

3. Weinreb I, Piscuoglio S, Martelotto LG, Waggott D, Ng CK, Perez-Ordonez B, et al. Hotspot activating PRKD1 somatic mutations in polymorphous low-grade adenocarcinomas of the salivary glands. Nat Genet 2014;46:1166-9.