**SUPPLEMENTARY METHODS**

**Genomic analysis of Cohort 1**

We performed WES on 11 sets of fresh-frozen PTs, synchronous metastatic biopsies, and non-neoplastic tissue from patients with untreated gastric adenocarcinoma at Samsung Medical Center (Seoul, South Korea) after institutional review board (IRB) approval. For exome sequencing, samples were subjected to exon hybrid selection capture using the Agilent SureSelect v2 Kit (1) and sequenced on the Illumina HiSeq platform at the Broad Institute. The median coverage for the tumors and their matched normals is 87x and 86x, respectively (range: 67~100x for tumors and 74~102x for normals). Raw reads were processed and aligned to the reference genome using the Picard tools as previously described (2). Sample contamination was estimated using ContEst (3) and all samples had less than 1% of estimated contamination.

Somatic SNVs and indels were called using the Mutect and Indelocator as previously described (2). Somatic copy number alterations were obtained from the mapped reads using the ReCapSeg software (http://www.broadinstitute.org/cancer/cga/acsbeta) which estimates copy ratios using read depths compared to a panel of normal diploid genomes, and then the copy ratios were segmented using the circular binary segmentation (CBS) algorithm (4). Allelic copy ratios were refined from the total copy ratios as described previously (5).

The ABSOLUTE computational algorithm was then performed to estimate tumor purity, ploidy, absolute copy numbers of the SCNAs, and cancer cell fractions (CCFs) of the somatic mutations (6). SCNAs such as amplifications and homozygous deletions were determined based on the absolute copy numbers as previously described (7). After the initial estimation of CCF distributions of all mutations by ABSOLUTE, a Bayesian clustering algorithm was used to refine the initial CCF estimates based on the prior assumption that each sample had a small number of subclones (clusters) that had mutations with the same CCFs, as described previously (8). Mutations were determined as clonal or absent if the refined CCF estimate was higher than 0.95 or lower than 0.05, respectively; otherwise the mutations were determined as subclonal. A shared mutation of two tumors was determined if a mutation was not absent in either tumor (both present), otherwise the mutation was not shared. The CCF clustering of the mutations, which reflected their clonality/subclonality in the primary and metastatic tumors, was used by the Phylogic algorithm to establish evolutionary relationship of the primary and metastatic tumors, as described previously (7).

**Genomic analysis of Cohort 2**

FFPE samples of gastric cancer and matched normal mucosa containing >40% tumor cellularity were dissected under a light microscope, using 4-μm-thick unstained sections (10 to 20 slides), by comparison with hematoxylin and eosin-stained slides. Briefly, DNA was extracted using standard procedures (Qiagen) and extracted genomic DNA was sheared to 150–200 base pairs (bp) in size using a Covaris S220 ultrasonicator (Covaris, Woburn, MA, USA). Extracted DNA underwent massively parallel sequencing of exons of 243 genes commonly altered in gastric cancer (Supplementary material, Table 1). The MuTect algorithm was used to identify somatic mutations (9) and annotated by Variant Effect Predictor (VEP) (10). Mutations detected in the normal tissue most likely represented germline variants and were filtered out from further analysis. Only mutations that have been recurrently (≥3 times) reported in COSMIC were included in our analysis. For variants of interest not detected in all samples from an individual, an additional variant caller termed the "naïve caller" was employed at the selected locations. After using MuTect’s normal short read preprocessing steps to remove common alignment artifacts, reads covering regions of interest were evaluated for any evidence of missense mutations.  If two or more reads at any location contained the same variant that was called in another sample from the individual, it was flagged as being postive for the variant.   Copy number variants were identified using RobustCNV. Read depth at informative capture targets in tumor samples was calibrated to estimate the copy ratio using depths observed in a panel of normal (non-cancer) diploid genomes. The resulting copy-ratio profiles were then segmented using the circular binary segmentation (CBS) algorithm (11). Finally, segments are assigned gain, loss, or normal-copy calls using a cutoff derived from the within-segment standard deviation of post-normalized mapping depths and a tuning parameter which was set based on comparisons to array-CGH calls in separate validation experiments.

**Fluorescence in situ hybridization (FISH) for Cohort 2**

Fluorescence in situ hybridization (FISH) analysis was performed on formalin-fixed paraffin-embedded (FFPE) tissue. After deparaffinization and dehydration, the sections of FFPE tissue were digested in 0.1-0.5% pepsin/0.1 N HCl for 5-20 min, and then washed by phosphate-buffered saline (PBS). After dehydration and dry up, the following FISH probes, customized by Chromosomescience laboratory (Sappro, Japan), were applied to each targeted area, and then the slides were sealed with coverslips. The probe for *KRAS* was constructed with bacterial artificial chromosomes (BACs) RP11-636P12, RP11-62I19, and RP11-65C2, and labeled with Cy3 (visualized by orange) or Cy5 (visualized by red). The probe for *EGFR* was constructed with BACs RP11-815K24, and RP11-81B20, then labeled with Cy3 (visualized by green) or FITC (visualized by green). The probe for *MET* was constructed with BACs RP11-163C9, and RP11-95I20, then labeled with Cy3 (visualized by yellow) or Cy5 (visualized by red). The probe for *CCND1* was constructed with BACs RP11-825J6, and RP11-266K14, then labeled with Cy3 (visualized by yellow). The section was denatured at 90ºC for 10 min, followed by overnight hybridization at 37°C in a wet chamber. Hybridized slides were washed in 2x saline-sodium citrate buffer (SSC) for 5 min and coverslips were removed gently. The slides were stringently washed in 50% formamide/ 2x SSC for 20 min at 37°C, and the kept in 1x SSC for 15 min at room temperature. The slides were counterstained with 4′,6-diamidino-2-phenylindole (DAPI). The FISH images were captured with a fluorescence microscope (IX83, OLYMPUS, Tokyo, Japan).

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