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Multiancestry genomic and transcriptomic analysis of gastric cancer

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Supplementary Information guide

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Supplementary information for Figure 5b legend

Distribution of non-protein truncating mutations in human CDH1 protein

Side-chains of the residues contributing to the dimer interface are shown as a stick model generated by crystallographic structural analysis[53, 54]. Upper left: one of the intermediate dimeric states is termed the “X-dimer”. The peptide-mimetic ligand (P159) is shown as a surface model that takes the place of hydrophobic interaction. Lower left: trans-dimer formation in swapping adhesion arms (155-DWVIPP-160) into each acceptor pocket. Right: cis-interface formed between EC1 and EC2 domain of its dimerization partner in

parallel orientation. For the symmetrical dimer, only one side of the surface was annotated with residues for figure conciseness.

Supplementary information for Extended Data Figure 2d legend

Validation of somatic mutations in *TRIM49/49B/49C*

We performed deep genomic sequence analyses of S327R/G/C mutations in *TRIM49/49B/49C* using the Illumina PCR amplicon workflow for ten paired DNA samples. Briefly, genomic PCR amplicons of 290 bp were prepared using the primers listed in **Supplementary Table 28**. Nextera XT index kits v2 (Illumina) was used to add the index by secondary PCR. The amplified libraries were quantified, pooled, and sequenced in paired-end 301 base mode on a MiSeq sequencer (Illumina). Multi-hit reads were removed. Uniquely mapped gene-specific reads were counted and calculated as TVAF (tumor variant allele frequency) and NVAF (variant allele frequency of the matched non-tumor sample) in the tumor and normal DNA, respectively. The detected TVAF values were compared with the results of WES (Whole-exome sequencing**)**.

Supplementary information for Extended Data Figure 8a legend

Clustering of gastric cancer cases by the contribution of COSMIC mutational signatures

The following nine clusters and one mixed group were identified with characteristic combinations of mutational signatures. Signature Cluster 1 (defective mismatch repair: MMR): high mutation burden with DNA repair deficiency-associated signatures, such

as SBS6, 15, and 26; Signature Cluster 2 (SBS5/6): enriched with SBS6 with low mutation burden (non-defective MMR); Signature Cluster 3 (SBS1/3): enriched with SBS1 and 3; Signature Cluster 4 (SBS1/16): enriched with SBS1 and 16; Signature Cluster 5 (SBS1/18): enriched with SBS1 and 18; Signature Cluster 6 (SBS3): SBS3 is dominant; Signature Cluster 7 (SBS17/28): enriched with SBS17 and 28; Signature Cluster 8 (SBS17): SBS17 is dominant; Signature Cluster 9 (SBS17/1): enriched with SBS17 and 1; Signature Cluster 10 (Mixed group): collection of small cases with various combinations of mutational signature. Few patients had a high mutational burden. For example, SBS10 (associated with polymerase epsilon (*POLE*) exonuclease domain mutations) is dominant in one of these cases.

Supplementary references for Supplementary Table 25

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