Selection of core essential genes

To compile a conservative list of high-confidence core essential genes, we collected 78 published genome-wide CRISPR essentiality screens performed in 64 different human and 2 murine cell lines[1–7] and calculated the gene-level log2 fold changes (LFC) by taking the geometric mean of probe-level LFCs over reference. To assess the dynamic range of all publicly available screens, we defined the overlap of genes commonly essential in 2 haploid gene-trap mutagenesis[8] and 4 early landmark CRISPR screens[2] as crude core essentialome and calculated the average LFC of these genes for every screen. Screens not passing an average LFC threshold ≤ -1, as well as redundant screens were excluded from further analyses. To normalize the remaining 62 CRISPR screens, we scaled each dataset to an average LFC of -2 for the previously used crude core essential genes. Finally, we generate a refined list of 625 high-confidence core essential genes by filtering genes that: (1) are predicted to be essential by haploid genetic screens in HAP1 and KBM7[8], (2) were tested in ≥ 70% of the 62 filtered CRISPR screens, (3) were detected as essential (normalized LFC ≤ -1) in ≥ 85% of the 62 filtered CRISPR screens.

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