Supplementary Table Legends

Table S1. Characteristics of the HNSCC cell lines. HNSCC cell line information on the site origin (primary tumor, metastatic site, or recurrence post-chemo/radiation therapy), the metastatic status of the patient, TP53 mutational status of each cell line, and phenotypic validation of cell line in an orthotopic *in vivo* model of HNSCC.

Table S2. Characteristics of the MSCC cell lines with germline mutations in p53 pathway genes. MSCC cell line information on germline mutation (genotype), Trp53 mutational status, Hras status, and murine inbred strain of derivation. A reference list to published studies is also provided in which murine germline mutations in p53 pathway genes and the resulting phenotypes were characterized in a chemical carcinogenesis model (DMBA/TPA) of squamous cell carcinoma.

Table S3. Human kinome (713 kinases). Sigma kinome library available through the Quellos High Throughput Facility at the University of Washington Institute for Stem Cell and Regenerative Medicine (http://depts.washington.edu/uwhts/).

Table S4. Murine kinome (572 kinases). Ambion kinome library available through the Quellos High Throughput Facility at the University of Washington Institute for Stem Cell and Regenerative Medicine (http://depts.washington.edu/uwhts/).

Table S5. Interspecies kinome (508 kinases). Comparative analysis of human kinome (Table S3) and murine kinome (Table S4) cross-referenced utilizing Mouse Genomics Informatics (MGI) (http://www.informatics.jax.org/) and National Center for Biotechnology Information (NCBI) (http://www.ncbi.nlm.nih.gov/) database nomenclature to generate a common list of 508 kinases referred to as the interspecies kinome

Table S6. Primary validation siRNAs. List of 84 unique siRNAs with 3 siRNAs per gene to 28 kinase targets used in the primary validation screen (Qiagen, FR).

Table S7. Secondary validation siRNAs. List of 57 siRNAs to 2-3 siRNAs per gene target, to 20 kinase targets used in the secondary validation assay (Qiagen, FR).

Table S8. Interspecies kinase targets selected for validation. Kinase targets (38 kinases) selected from interspecies kinome comparisons for validation. Interspecies comparisons included cell line stratification by genotype (p53mutant/ p53 deficiency) and metastatic *in vivo* phenotype. All cell lines comparison included: [HNSCC: UMSCC-14A, UMSCC-14C, UMSCC-15A, UMSCC-15B, UMSCC-O19 & MSCC: MSCC-CK101, MSCC-CK102, MSCC-CK103, MSCC-CK104], p53 mutant comparison [HNSCC: UMSCC-14A, UMSCC-14C, JHU-O19 & MSCC: MSCC-CK102 ($Hras^{Q61L}$ $Trp53^{+/-}$)], metastatic comparison included

[HNSCC: UMSCC-14C, UMSCC-15B & MSCC: MSCC-CK102 (*Hras^{Q61L} Trp53 $^{+/-}$*), MSCC-CK103 (*Hras^{wt} p19Arf$^{-/-}$*)]. Global Z-score calculations utilized to select 38 kinases from these three comparisons [Z-score $_{\text{Mean All}}$ < -1.0, Z-score $_{\text{p53 mutant}}$ < -2.0, Z-score $_{\text{Mean Met}}$ < -1.5]; denoted in column format.

Table S9. HT RNAi primary validation screen with siRNA pool deconvolution. Primary validation screen normalized cell viability data (CellTiterGlo assay) and caspase 3/7 dependent apoptosis data (Apotox, caspase reagent) from 384-well high throughput screening.

Table S10. Differential analysis of primary validation screen (CTG) N=12. Differential viability calculated using mean of cell viability measures at day 4.5 and day 1.5 (d4.5-d1.5) for all 28 kinase targets utilizing all 12 data points from three separate siRNAs per gene plus a pool of all three siRNAs each in triplicate.

Table S11. Differential analysis of primary validation screen (CTG) N=3 pooled. Differential viability calculated using mean of cell viability measures at day 4.5 and day 1.5 (d4.5-d1.5) for all 28 kinase targets utilizing pool of all three siRNAs each in triplicate.

Table S12. Statistical analysis summary of differential viability (CTG). Statistically significant differences in differential viabilities resulting from RNAi mediated knockdown of 28 kinase targets using N=12 and N=3 pooled siRNA data evaluated versus the universal negative control siRNA using one-way ANOVA with Dunnetts post-test for multiple comparisons, $P<0.05$ as significant.

Table S13. Statistical analysis (absolute viability) of primary validation screen (CTG). Results (i.e. scored 'hits') from negative control-independent and negative control-dependent statistical analysis of absolute viability at day 4.5 post-transfection on independent siRNA triplicates and pooled siRNAs in triplicate; positive controls Kif11 (N=24), and universal negative control UNI (N=24) indicated.

Table S14. HT RNAi primary validation screen summary of 'hits' (CTG). Summary of all scored 'hits' from negative control-independent and negative control-dependent statistical analysis on absolute viability at day 4.5 post-transfection.

Table S15. HT caspase 3/7-dependent apoptosis AUC analysis (Apotox) N=12. AUC estimates of caspase-dependent apoptosis were calculated utilizing all three data points (1.5 day, 3 day, 4.5 day) for all kinase targets and all 12 data points from three separate siRNAs per gene plus a pool of all three siRNAs each in triplicate.

Table S16. HT caspase 3/7-dependent apoptosis AUC analysis (Apotox) N=3 pooled. AUC estimates of caspase-dependent apoptosis were calculated utilizing all three data points (1.5 day, 3 day, 4.5 day) for all kinase targets utilizing pool of all three siRNAs each in triplicate.

Table S17. Statistical analysis summary for caspase 3/7 dependent apoptosis (Apotox). Statistically significant differences in AUC estimates of caspase-dependent apoptosis resulting from RNAi mediated knockdown of kinase targets using N=12 and N=3 pooled siRNA data evaluated versus the universal negative control siRNA using one-way ANOVA with Dunnetts post-test for multiple comparisons, $P<0.05$ as significant.

Table S18. Secondary validation assay statistical analysis (absolute viability). Statistically significant differences in absolute viability (day 4.5) resulting from RNAi mediated knockdown of kinase targets of pooled siRNAs in triplicate evaluated versus the siRNA negative control (SINC) using one-way ANOVA with Dunnetts post-test for multiple comparisons, $P<0.05$ as significant.

Table S19. Differential viability and caspase 3/7 dependent apoptosis AUC analysis of secondary validation assay. Differential viability calculated using mean of cell viability measures at day 4.5 and day 1.5 (d4.5-d1.5) for all 20 kinase targets utilizing pool of all three siRNAs each in triplicate. AUC estimates of caspase-dependent apoptosis calculated utilizing all three data points (1.5 day, 3 day, 4.5 day) for all kinase targets utilizing pool of all three siRNAs each in triplicate.

Table S20. Statistical analysis summary of differential viability and caspase 3/7 dependent apoptosis. Statistically significant differences in differential viability and caspase-dependent apoptosis ($AUC_{estimate}$) resulting from RNAi mediated knockdown of 20 kinase targets on pooled siRNAs in triplicate evaluated versus the siRNA negative control (SINC) using one-way ANOVA with Dunnetts post-test for multiple comparisons, $P<0.05$ as significant.

Table S21. Drug sensitivity and TP53 mutational status data on squamous cell carcinoma cell lines from COSMIC on Wee1/Chk1 Inhibitor (681460). Table outlining TP53 gene mutational status (TP53 specific mutation, disruptive status, squamous cell origin) from the Sanger Cancer Cell Line Project on 820 cell lines and cross-referenced with the Catalogue of Somatic Mutations in Cancer (COSMIC) drug sensitivity data (Release 2 July 2012) on 541 cancer cell lines treated with a WEE1/CHK1 inhibitor, 681640. IC_{50} values presented as natural log (μM).