

**Supplementary Table S10.** List of the seven published studies used in the performance evaluation of 9 known essential genes using shRNA libraries. KRAS-mu indicates cell lines harboring a KRAS mutation; KRAS-wt indicates cell lines with wild type KRAS

Study	Library	Library coverage	# of hits	Cell lines screened	Row #	H score			
This study	TRC, arrayed	16,039 genes (80,598 hairpins)	1,252	HeLa	1	✓			
			244	A549	9	✓			
			242	H1650	10	✓			
			215	H187	11	✓			
			233	H1975	12	✓			
			234	H82	13	✓			
			254	HCC827	14	✓			
			247	JURKAT	15	✓			
			245	K562	16	✓			
			250	LN299	17	✓			
Luo et al. <sup>61</sup>	TRC, pooled	9,500 genes (45,000 hairpins)	251	REH	18	✓			
			250	SUPT1	19	✓			
			242	U2L	20	✓			
			8	NOMO-1, Fibroblast, HMEC, THP-1	28	X			
			Barbie et al. <sup>3</sup>	TRC, arrayed	957 genes (5,002 hairpins)	45	786-O, A549, DLD-1, Fibroblast, HCT-116, HMEC-TERT, LN-229, LNCaP, MCF7, MDA-MB-231, MDA-MB-453, NOMO-1, OVCAR-8, PC-3, RPMI-8226, T47D, THP-1, TOV-21G, U87-MG	21	X
						582	25 Ovarian cell lines (A2780, Caov-3, Caov-4, COLO-704, COV362, COV434, COV504, EFO-21, EFO-27, Hey-A8, IGROV1, JHOC-5, KURAMOCHI, NIH:OVCAR-3, OV-90, OVCAR-4, OVCAR-8, OVISe, OVMANA, RKN, RMG-I, SNU-840, TOV-112D, TOV-21G, TYK-nu)	22	X
567	18 Colon cell lines (C2BBE1, COLO-205, DLD-1, GP2d, HT-29, HT-55, HuTu80, KM12, LoVo, LS411N, LS513, NCI-H508, RKO, SK-CO-1, SNU-C1, SNU-C2A, SW48, SW480)	23				X			
Cheung et al. <sup>11</sup>	TRC, pooled	11,194 genes (54,020 hairpins)	588	13 Pancreas cell lines (AsPC-1, BxPC-3, CFPAC-1, HPAC, KP-1NL, KP4, L3.3, MIA PaCa-2, Panc 03.27, Panc 08.13, Panc 10.05, QGP-1, SU.86.86)	24	X			

			594	8 NSCLC cell lines (A549, HCC2814, HCC364, HCC827, NCI-H1650, NCI-H1975, NCI-H2122, NCI-H661)	25	X
			578	7 Esophageal Squamous cell lines (KYSE-150, KYSE-30, KYSE-450, KYSE-510, T.T, TE-15, TE-9)	26	X
			584	6 GBM cell lines (LN-215, LN-229, LN-319, LN-464, SF767, U-251 MG)	27	X
Silva et al. <sup>54</sup>	Elledge-Hannon, pooled	6,000 hairpins	535	MCF-10A, MDA-MB-435	2	✓
			87	DLD-1	3	✓
Schlabach et al. <sup>53</sup>	Elledge-Hannon, pooled	2,294 genes (8,203 hairpins)	155	HCC1954	4	✓
			147	HCT116	5	✓
			671	HMEC	6	✓
Luo et al. <sup>52</sup>	Elledge-Hannon, pooled	32,293 transcripts (74,905 hairpins)	366	DLD-1 (KRAS-mut)	7	✓
				DLD-1 (KRAS-wt)	8	✓