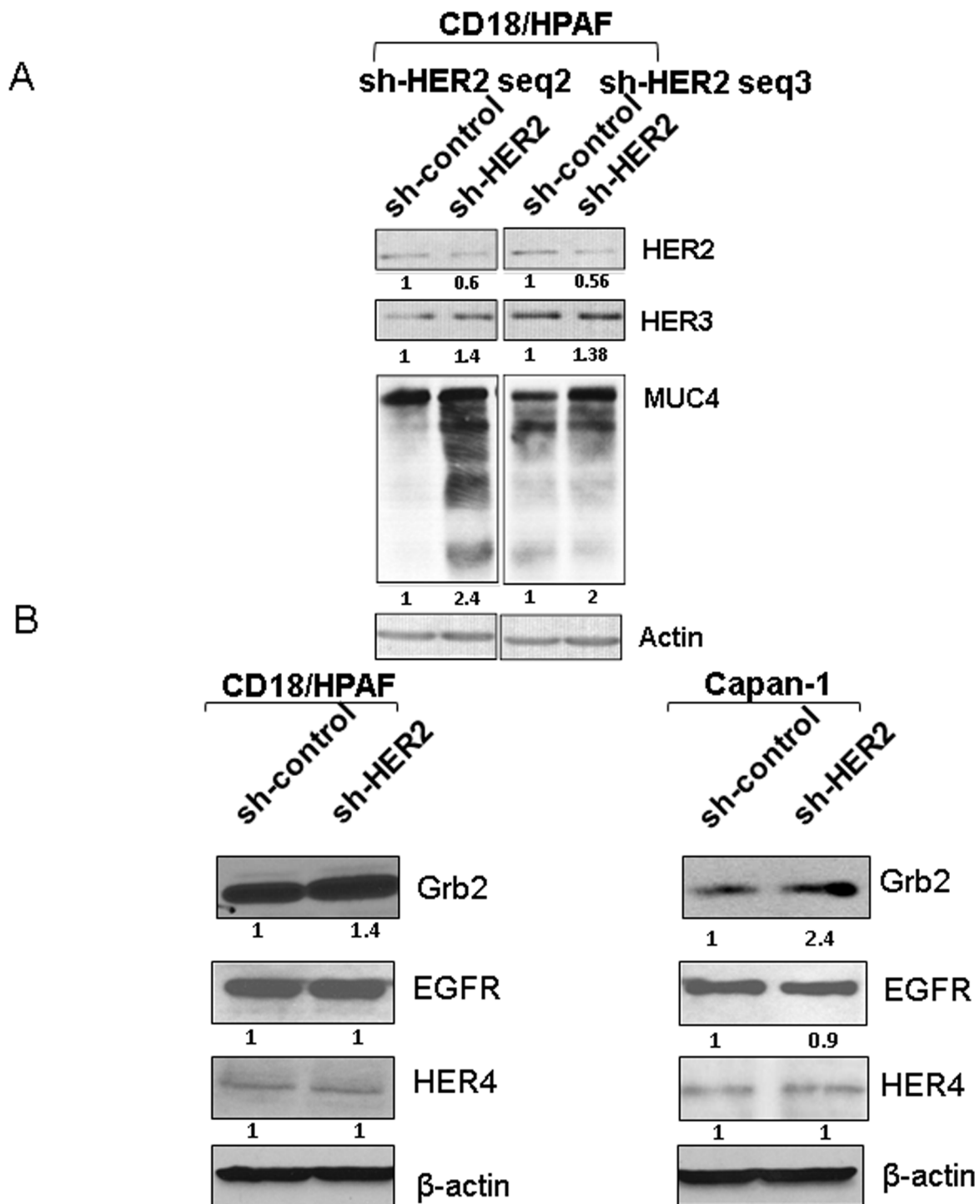


SUPPLEMENTARY FIGURES



Supplementary Figure S1: Effect of HER2 knockdown on expression of Grb2, EGFR and HER4. A. Represents upregulation of MUC4 and HER3 in HER2 knockdown (sh-HER2 seq-2 and Seq-3) pancreatic cancer cells CD18/HPAF. B. As a result of HER2 silencing, Grb2 levels significantly increased as shown in immunoblot studies using two stable knockdown (~40%) pancreatic cancer cells (CD18/HPAF and Capan-1) when compared to scrambled control cells. There was no change in EGFR and HER4 levels in both the pancreatic cancer cells.

Range 1: 22 to 997 Graphics		▼ Next Match ▲ Previous Match		
Score	Expect Method	Identities	Positives	Gaps
900 bits(2327)	0.0 Compositional matrix adjust.	465/983(47%)	621/983(63%)	29/983(2%)
Query 25	SQAVCPGTLNGLSVTGAENQYQTLTKLYKERCEVVMGNLEIVLTGHNADLSFLQWIREVT			84
Sbjct 22	S VC GT L + E L LY+ C+VV GNLE+ NA LSFLQ I+EV			81
Query 85	GYVLVAMNEFSTLPLPNLRVVRGTQVYDQKFAIFVM-----LNYNTNSSHA----LRQLR			135
Sbjct 82	GYVL+A N+ +PL LR+VRGTQ+++ +A+ V+ LN T + A LR+L+			141
Query 136	LTQLTEILSGGVYIEKNDKLCHEMDTIDWRDIVRDRDA---EIVVKDNGRSCPPCHEVCKG			192
Sbjct 142	L LTEIL GGV I++N +LC+ DTI W+DI + ++ + R+C PC +CKG			201
Query 193	-RCWGPGESEDCQTLTKTICAPQCNGHCFGNPNQCCHDECAGGCSGPQDTCDFACRHFND			251
Sbjct 202	RCWG SEDCQ+LT+T+CA C C GP P CCH++CA GC+GP+ +DC AC HFN			260
Query 252	SGACVPRCPQPLVYNKLTQLEPNPHTKYQYGGVCVASCPHNFV-VDQTSVVRACPPDKM			310
Sbjct 261	SG C CP + YN TF+ PNP +Y +G CV +CP+N++ D SC CP			320
Query 311	EVD-KNGLKMCPECGGLCPKACEGTGSG--SRFQTVDSNIDGFVNCTKILGNLDFLITG			367
Sbjct 321	EV ++G + CE C C + C G G + V S+NI F C KI G+L FL			380
Query 368	LNGDPWHKIPALDPEKLVNVRTVREITGYLNIQSWPPHMHNFVSNLTTIGGRSLYNRG			427
Sbjct 381	+GDP L PE+L VF T+ EITGYL I +WP + + SVF NL I GR L+N			440
Query 428	FSLIMKLNVTSLGFRSLKEISAGRIYISANRQLCYHHSLNWTKVLRGPTERLDIKHN			487
Sbjct 441	+SL ++ L ++ LG RSL+E+ +G I N LC+ H++ W ++ R P + L N			498
Query 488	RPRRDCVAEGKVCPLCSSGGCWGPGQCLSCRNYSRGGVCVTHCNFLNGEPREFAHEA			547
Sbjct 499	RP +CV EG C LC+ G CWGPGP QC++C + RG CV C L G PRE+ +			558
Query 548	ECFSCHPECQPMEGTATCNGSGSDTCAQCAHFRDGPVSSCPHGVLG--AKGPIYKYPD			605
Sbjct 559	C CHPECQ G+ TC G +D C CAH++D P CV+ CP GV + PI+K+PD			618
Query 606	VQNECRPCHENCTQGCKGPELQDCLGQTLVLIGKTHLTMALTVIAGLVVIFMMLGGTFLY			665
Sbjct 619	+ C+PC NCT C + + C + + LT ++ + G++++ ++ +			674
Query 666	WRGRRIQ-NKRAMRRYLERGESIEPLDPS-EKANKVLARIFKETELRKLKVLGSGVFGTV			723
Sbjct 675	+ R+ + K MRR L+ E +EPL PS N+ RI KETELRK+KVLGSG FGTV			734
Query 724	IKRRQKIRKTYMRRLLQETELVEPLTPSGAMPNQAQMRILKETELRKKVVLGSGAFGTV			734
Query 724	HKGWVWIPGESIKIPVCIKVEDKSGRQSFQAVTDHMLAIGSLDHAHIVRLLGLCPGSSL			783
Sbjct 735	+KG+WIP+GE++KIPV IKV+ + + ++ + + D + + ++ RLLG+C S++			794
Query 784	YKGIWIPDGENVKIPVAIKVLENTSPKANKEILDEAYVMAGVGSPIVSRLLGICLTSTV			794
Query 784	QLVTOYLPGLSLLDHVRQHRGALGPQLLNWGVQIAKGMYYLEEHGMVHRNLAARNVLLK			843
Sbjct 795	QLVTQ +P G LLDHVR++RG LG Q LLNW +QIAKGM YLE+ +VHR+LAARNVL+K			854
Query 844	QLVTQLMPYGCLLDHVRENRRGLGSQDLLNWCMIKAGMSYLEDVRLVHRDLAARNVLVK			854
Query 844	SPSQVQVADFGVADLLPDDKQLLYSEAKTPIKWMALSIHFGKYTHQSDVWSYGVTWVE			903
Sbjct 855	SP+ V++ DFG+A LL D+ + K PIKWMALSI ++THQSDVWSYGVTWVE			914
Query 904	SPNHVKITDFGLARLLDIDETEHADGKVPKWMALSIILRRRFTHQSDVWSYGVTWVE			914
Query 904	LMTFGAEPYAGRLAEVDPDLEKGERLAQPQICTIDVYVMVKCWMIDENIRPTFKELAN			963
Sbjct 915	LMTFGA+PY G+ E+PDLEKGERL QP ICTIDVYM+MVKCWMID RP F+EL +			974
Query 964	LMTFGAKPYDGPAREIPDLEKGERLPQPPICTIDVYIMVKCWMIDSECRPRFRELVS			974
Query 964	EFTRMARDPPRYLVIKRES-GPG 985			
Sbjct 975	EF+RMARDP R++VI+ E GP 997			

HER2

Sequence search results

[Show](#) the detailed description of this results page.

We found **6** Pfam-A matches to your search sequence (**5** significant and **1** insignificant). You did not choose to search for Pfam-B matches.



[Show](#) the search options and sequence that you submitted.

[Return](#) to the search form to look for Pfam domains on a new sequence.

HER3

Sequence search results

[Show](#) the detailed description of this results page.

We found **5** Pfam-A matches to your search sequence (**all** significant). You did not choose to search for Pfam-B matches.



[Show](#) the search options and sequence that you submitted.

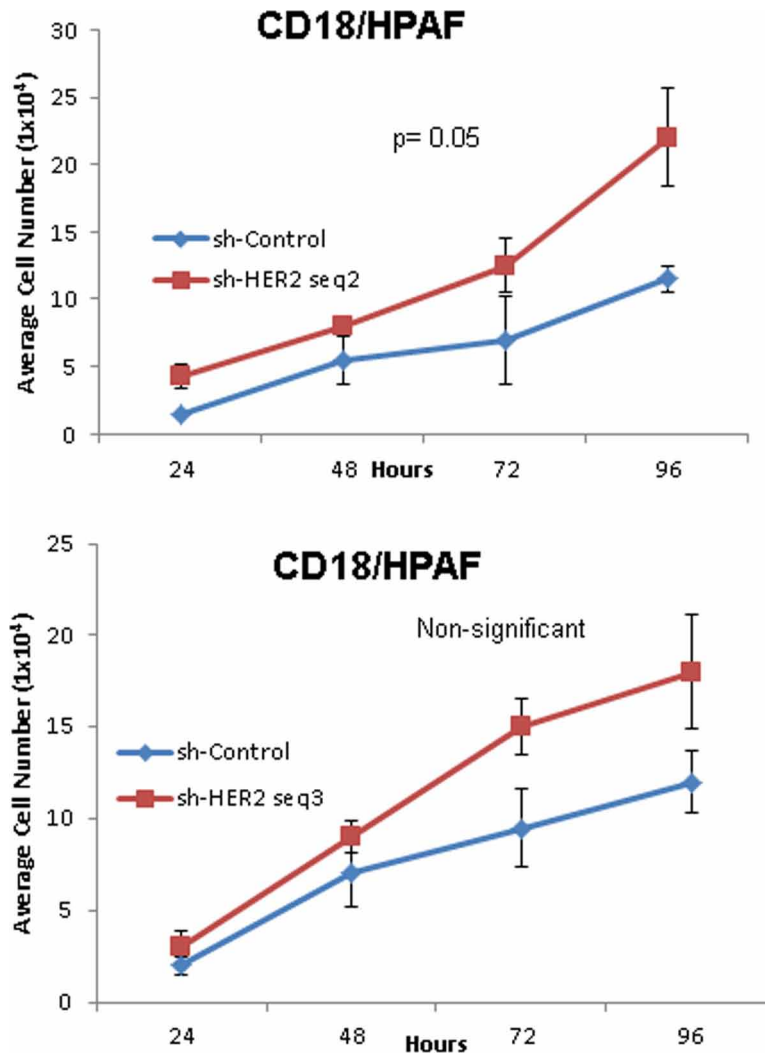
[Return](#) to the search form to look for Pfam domains on a new sequence.

Significant Pfam-A Matches

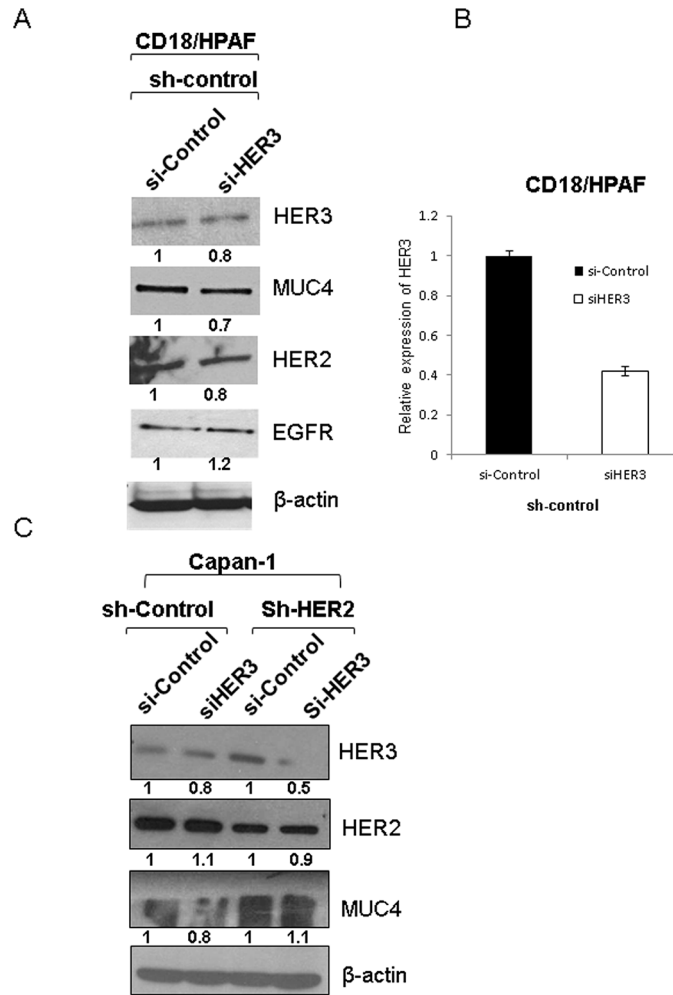
[Show](#) or [hide](#) all alignments.

Family	Description	Entry type	Clan	Envelope		Alignment		HMM		HMM length	Bit score	E-value	Predicted active sites	Show/hide alignment
				Start	End	Start	End	From	To					
Recep_L_domain	Receptor L domain	Domain	n/a	55	167	56	166	2	111	112	104.3	3.4e-30	n/a	Show
Furin-like	Furin-like cysteine rich region	Domain	CL0547	169	332	182	332	11	149	149	108.0	3e-31	n/a	Show
Recep_L_domain	Receptor L domain	Domain	n/a	353	474	353	472	1	110	112	102.4	1.3e-29	n/a	Show
GF_recep_IV	Growth factor receptor domain IV	Domain	CL0547	499	630	499	629	1	131	132	162.4	3.7e-48	n/a	Show
Pkinase_Tyr	Protein tyrosine kinase	Domain	CL0016	709	965	710	964	2	258	259	259.4	2.5e-77	n/a	Show

Supplementary Figure S2A and S2B: Bioinformatic prediction of MUC4 and HER3 interaction. **S2A.** Sequence alignment between Her2 and Her3 shows 47% identity and 63% positives suggesting a close relationship between these two sequences. **S2B.** Domain structure analysis of Her2 and Her3 also reveals almost identical structure indicating functional similarity between these two proteins.



Supplementary Figure S3A and S3B: Effect of HER2 knockdown (two other shHER2) on growth rate of pancreatic cancer cells. In order to validate the HER2 knockdown studies, we utilized the other two shHER2 sequence for growth kinetic assay. As a result of HER2 knockdown we also observed increased proliferation in HER2 knockdown cells in comparison to scramble control cells.



Supplementary Figure S4: Transient knockdown of HER3 in Capan-1 cells. The results show that the effect of HER3 knockdown on HER2 and MUC4 expression.