Table S3: Proteins that are predicted to be involved in 'double switches' based on experimental protein-protein interaction data

SH2 motifs	Class I WW	SH3-1
Grb2	CASL_HUMAN • O75815 (SH2) • P16333 (SH2) • P07948 (SH2) • P46108 (SH2) • P46109 (SH2) • P06239 (SH2) • Q96J02 (WW) JUN_HUMAN • P40763 (SH2) • P42224 (SH2) • Q14765 (SH2) • Q13526 (WW)	IRS2_HUMAN • Q5T4P3 (SH2) • O15524 (SH2) • Q06124 (SH2) • P19174 (SH2, SH3-1)
Ptp2	DAG1_HUMAN • P06241 (SH2) • P62993 (SH2) • P16333 (SH2) • P12931 (SH2) • P27986 (SH2) • P11532 (WW) • P46939 (WW)	
Src	EZRI_HUMAN • P27986 (SH2) • P07332 (SH2) • P43405 (SH2) • P07332 (SH2) • P46940 (WW)	CD3E_HUMAN • P43405 (SH2) • P43403 (SH2) • P27986 (SH2, SH3-2) • P16333 (SH2, SH3-1) • O43639 (SH2, SH3-1) • Q8TE68 (SH3-1) • Q8TE67 (SH3-1) • Q12929 (SH3-1) • Q9H6S3 (SH3-1) HCLS1_HUMAN • Q9H788 (SH2) • P62993 (SH2, SH3-1) • P090769 (SH2, SH3-1) • P07948 (SH2, SH3-1) PTN6_HUMAN • O60674 (SH2) • P43403 (SH2) • P51692 (SH2) • P43405 (SH2) • Q13094 (SH2) • Q8WV28 (SH2) • P27986 (SH2, SH3-2) • P62993 (SH2, SH3-1) • P07948 (SH2, SH3-1) • P15498 (SH2, SH3-1) • P06239 (SH2, SH3-1) PTN11_HUMAN • P40763 (SH2) • O60674 (SH2) • O14543 (SH2) • Q92835 (SH2) • P51692 (SH2) • P42229 (SH2) • Q14451 (SH2) • O00459 (SH2) • P27986 (SH2, SH3-2) • P46109 (SH2, SH3-1, SH3-2) • P62993 (SH2, SH3-1) • P16885 (SH2, SH3-1) • P56945 (SH3-1)

Stat5	SYNPO_HUMAN • P62993 (SH2) • Q96QZ7 (WW) ERBB4_HUMAN • O43639 (SH2) • P42684 (SH2) • P20936 (SH2) • P46108 (SH2) • P46109 (SH2) • P62993 (SH2) • P16333 (SH2) • P00519 (SH2) • Q06124 (SH2) • P29353 (SH2) • P51692 (SH2) • P42229 (SH2) • P43405 (SH2) • O00459 (SH2) • P46937 (WW) • Q96J02 (WW)	OCLN_HUMAN • P07947 (SH2, SH3-1) • A2A3H9 (SH3-2) • Q07157 (SH3-2) LYN_HUMAN • P29350 (SH2) • O60674 (SH2) • Q92835 (SH2) • P29353 (SH2) • P43405 (SH2) • Q13094 (SH2) • P12931 (SH2, SH3-1) • P16885 (SH2, SH3-1) • P07948 (SH2, SH3-1) • P42680 (SH2, SH3-1) • P56945 (SH3-1) • A4D174 (SH3-1) • P14317 (SH3-1) • P78352 (SH3-1) • Q14511 (SH3-1) • Q15642 (SH3-1) • O75563 (SH3-1) • Q86WV1 (SH3-1)
Crk	WIPF2_HUMAN • O43639 (SH2) • Q9NZC7 (WW)	NCK1_HUMAN • O60674 (SH2) • O15524 (SH2) • O14512 (SH2) • P52757 (SH2) • Q13094 (SH2) • Q8WV28 (SH2) • P06241 (SH2, SH3-1) • P46108 (SH2, SH3-1, SH3-2) • P42684 (SH2, SH3-1) • P20936 (SH2, SH3-1) • P00519 (SH2, SH3-1) • O43281 (SH3-1) • Q14511 (SH3-1) • A7KAX9 (SH3-1) • Q9NZQ3 (SH3-1) • Q14185 (SH3-1) • P56945 (SH3-1) • Q9ULH1 (SH3-1) • Q8IZP0 (SH3-1) • O43150 (SH3-1) • Q8IZD9 (SH3-2) • Q9UPZ8 (SH3-2) • Q9UPX8 (SH3-2) • O94885 (SH3-2) • O15117 (SH3-2) • Q9BYB0 (SH3-2)

Table row titles list five different SH2 motifs: $SH2^{Grb2}$, $SH2^{Ptp2}$, $SH2^{Src}$, $SH2^{Stat5}$ and $SH2^{Crk}$. Table columns list Class I WW and SH3 motifs. Each table cell includes potential double switches: The proteins that include the two motifs are shown in capital letters of their Swissprot ID (these proteins originate in Table S2). Each of these motif-containing proteins is documented to interact with human proteins that include WW/SH2/SH3 domains (bullets; shown as Swissprot accessions). Domain content of the latter proteins is brought in parentheses. For instance, the first table entry details CASL_HUMAN as having both $SH2^{Grb2}$ and Class I WW motifs. This protein is also documented as interacting with O75815 (that includes an SH2 domain) and with Q96J02 (that includes a WW domain). Domain assignment was done using Pfam definitions [1].

1. Finn RD, Mistry J, Tate J, Coggill P, Heger A, et al. (2010) The Pfam protein families database. Nucleic Acids Res 38: D211-222.