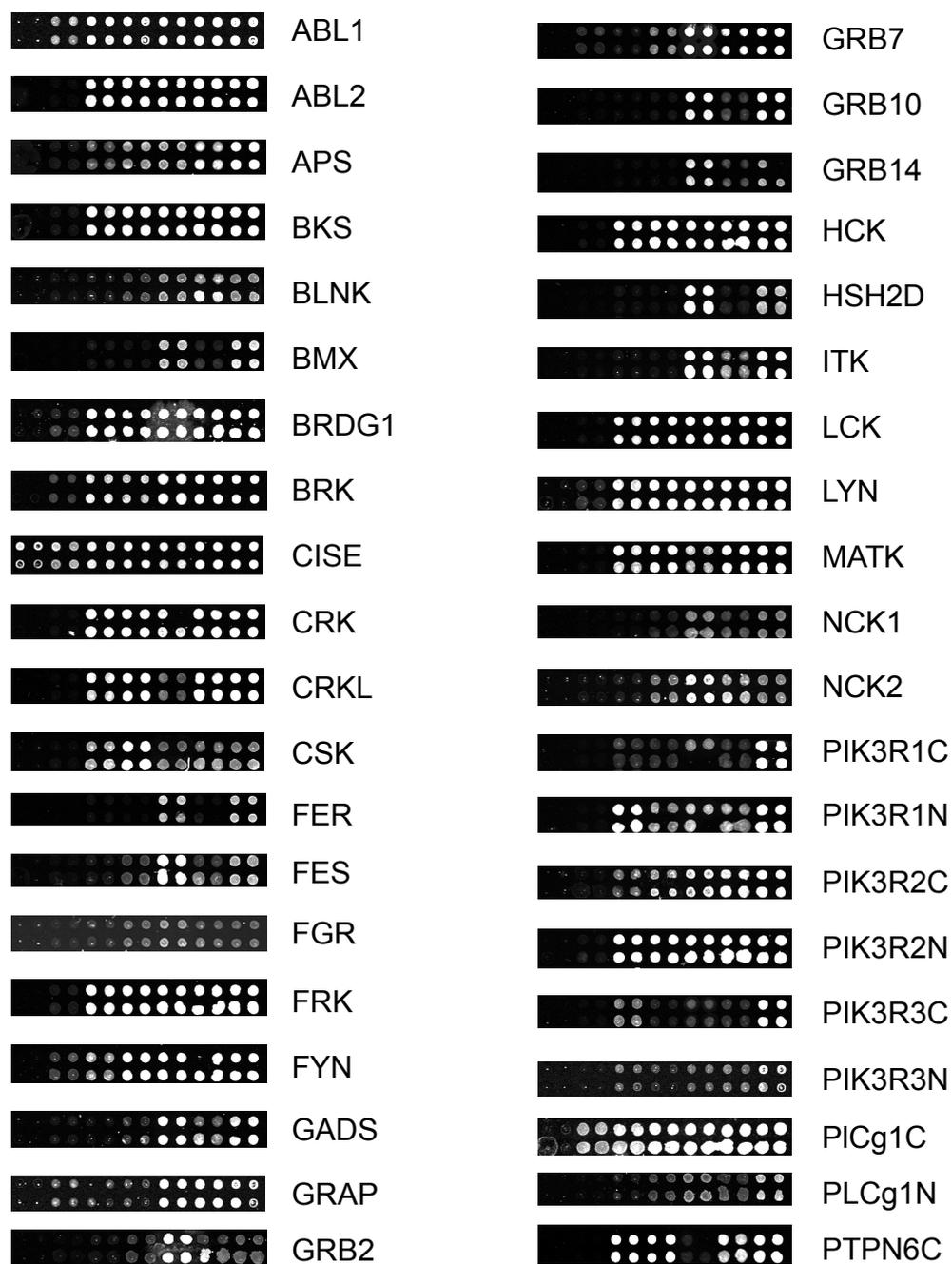


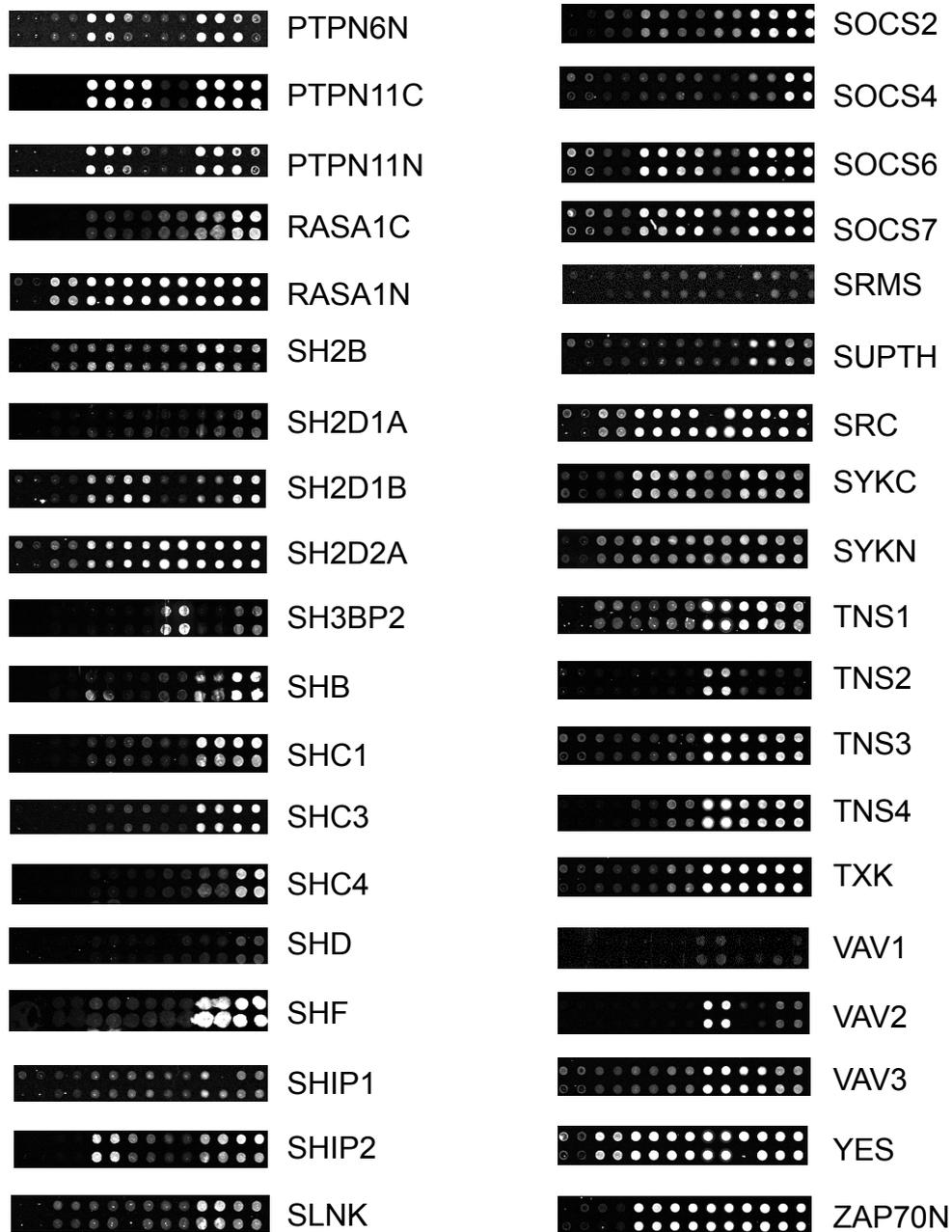
## **Supplementary Figures**

### **A Comprehensive Immunoreceptor Phosphotyrosine-based Signaling Network Revealed by Reciprocal Protein-Peptide Array Screening**

Huadong Liu, Lei Li, Courtney Voss, Feng Wang, Juewen Liu, and Shawn S-C. Li



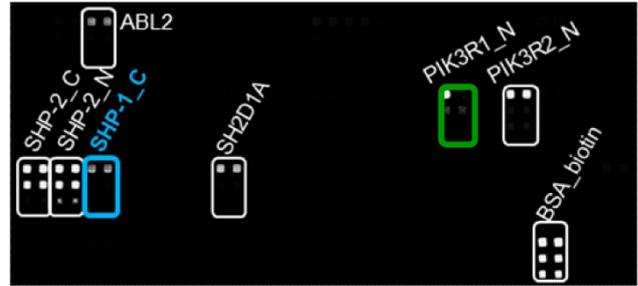
**Supplementary Figure 1a. Binding profiles of different SH2 domains on a CD22-pY peptide array.** The pY-containing peptide array representing the cytoplasmic Tyr phosphorylation sites in CD22 was probed for binding, respectively, to different human SH2 domains (in GST fusion). SH2 domains are identified on the right by the names of the corresponding proteins.



**Supplementary Figure 1b. Binding profiles of different SH2 domains on a CD22-pY peptide array (cont'd).**

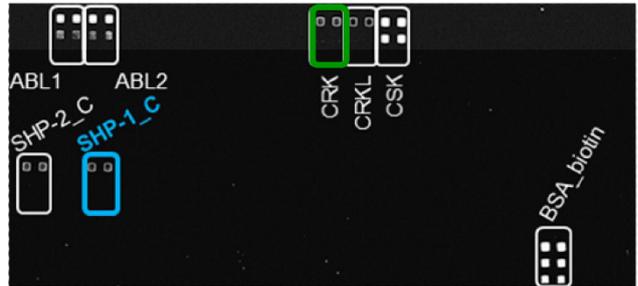
SLNK	PTPN11-C	GRB10	GST
SUPT6H	PTPN11-N	GRB14	ABL1
SYK-C	PTPN6-C	GRB2	ABL2
SYK-N	RASA1_N	GRB7	APS
SRC	RASA1_C	HCK	BLK
SRMS	SH2B	HSH2D	BLNK
TEC	SH2D1A	ITK	BMX
TNS1	SH2D1B	LCK	BRDG1
TNS2	SH2D2A	LYN	BRK
TNS4	SH3BP2	MATK	CRK
TXK	SHB	NCK1	CRKL
Vav1	SHC1	NCK2	CSK
VAV2	SHC3	PIK3R1_C	FER
VAV3	SHC4	PIK3R1_N	FES
YES	SHD	PIK3R2_C	FGR
ZAP70-N	SHE	PIK3R2_N	FRK
BSA-b	SHF	PIK3R3_C	FYN
GST	SHIP1	PIK3R3_N	GADS
Buffer	SHIP2	PLCg1-N	GRAP

pY762



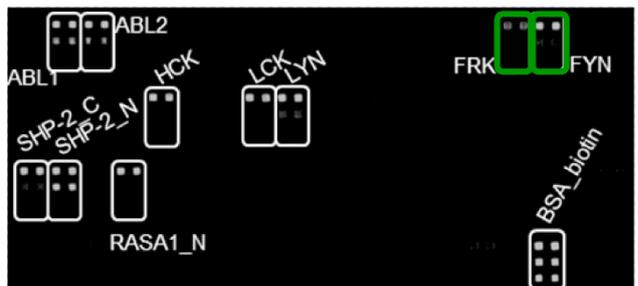
SLNK	PTPN11-C	GRB10	GST
SUPT6H	PTPN11-N	GRB14	ABL1
SYK-C	PTPN6-C	GRB2	ABL2
SYK-N	RASA1_N	GRB7	APS
SRC	RASA1_C	HCK	BLK
SRMS	SH2B	HSH2D	BLNK
TEC	SH2D1A	ITK	BMX
TNS1	SH2D1B	LCK	BRDG1
TNS2	SH2D2A	LYN	BRK
TNS4	SH3BP2	MATK	CRK
TXK	SHB	NCK1	CRKL
Vav1	SHC1	NCK2	CSK
VAV2	SHC3	PIK3R1_C	FER
VAV3	SHC4	PIK3R1_N	FES
YES	SHD	PIK3R2_C	FGR
ZAP70-N	SHE	PIK3R2_N	FRK
BSA-b	SHF	PIK3R3_C	FYN
GST	SHIP1	PIK3R3_N	GADS
Buffer	SHIP2	PLCg1-N	GRAP

pY796



SLNK	PTPN11-C	GRB10	GST
SUPT6H	PTPN11-N	GRB14	ABL1
SYK-C	PTPN6-C	GRB2	ABL2
SYK-N	RASA1_N	GRB7	APS
SRC	RASA1_C	HCK	BLK
SRMS	SH2B	HSH2D	BLNK
TEC	SH2D1A	ITK	BMX
TNS1	SH2D1B	LCK	BRDG1
TNS2	SH2D2A	LYN	BRK
TNS4	SH3BP2	MATK	CRK
TXK	SHB	NCK1	CRKL
Vav1	SHC1	NCK2	CSK
VAV2	SHC3	PIK3R1_C	FER
VAV3	SHC4	PIK3R1_N	FES
YES	SHD	PIK3R2_C	FGR
ZAP70-N	SHE	PIK3R2_N	FRK
BSA-b	SHF	PIK3R3_C	FYN
GST	SHIP1	PIK3R3_N	GADS
Buffer	SHIP2	PLCg1-N	GRAP

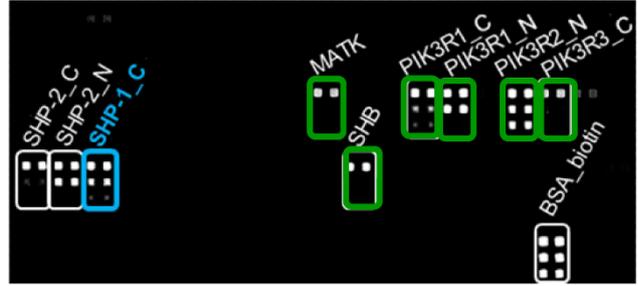
pY822



**Supplementary Figure 2a.** *SH2 domain arrays probed by different CD22-pY peptides.*  
This is a blown up version of data shown in Fig. 1 with the printing map shown on the left.

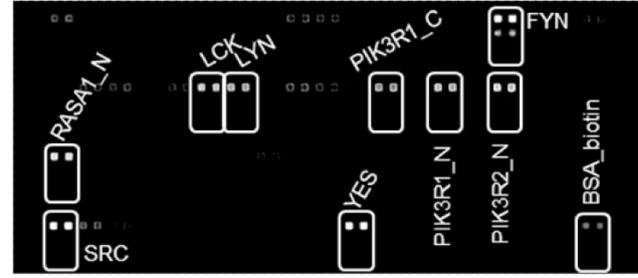
SLNK	PTPN11-C	GRB10	GST
SUPT6H	PTPN11-N	GRB14	ABL1
SYK-C	PTPNC-C	GRB2	ABL2
SYK-N	RASA1_N	GRB7	APS
SRC	RASA1_C	HCK	BLK
SRMS	SH2B	HSZD	BLNK
TEC	SH2D1A	ITK	BMX
TNS1	SH2D1B	LCK	BRDG1
TNS2	SH2D2A	LYN	BRK
TNS4	SHB2P2	MATK	CRK
TXK	SHB	NCK1	CRKL
Vav1	SHC1	NCK2	CSK
VAV2	SHC3	PIK3R1_C	FER
VAV3	SHC4	PIK3R1_N	FES
YES	SHD	PIK3R2_C	FGR
ZAP70-N	SHE	PIK3R2_N	FRK
BSA-b	SHF	PIK3R3_C	FYN
GST	SHIP1	PIK3R3_N	GADS
Buffer	SHIP2	PLCg1-N	GRAP

pY842



SYK-N	PTPNC-C	GRB14	GST
SRC	RASA1_N	GRB2	ABL1
SRMS	RASA1_C	GRB7	ABL2
TEC	SH2B	HCK	APS
TNS1	SH2D1A	HSZD	BLK
TNS2	SH2D1B	ITK	BLNK
TNS4	SH2D2A	LCK	BMX
TXK	SHB2P2	LYN	BRDG1
Vav1	SHB	MATK	BRK
VAV2	SHC1	NCK1	CRK
VAV3	SHC3	NCK2	CRKL
YES	SHC4	PIK3R1_C	CSK
ZAP70-N	SHD	PIK3R1_N	FER
SOC36	SHE	PIK3R2_C	FES
SOC52	SHF	PIK3R2_N	FGR
SOC54	SHIP1	PIK3R3_C	FRK
SOC57	SHIP2	PIK3R3_N	FYN
CIS-E	SLNK	PLCg1-N	GADS
GST	SUPT6H	PTPN11-C	GRAP
His-DAPP1	SYK-C	PTPN11-N	GRB10
His-SH2D3A	His-CSK	His-CBLB	His-ABL2
His-PTPN11-N	His-PLCG2N	His-PLCG2C	His-PLCG1C
BSA	His-PLCG1-C	His-ZAP70-T	His-SH2D4A

pY752

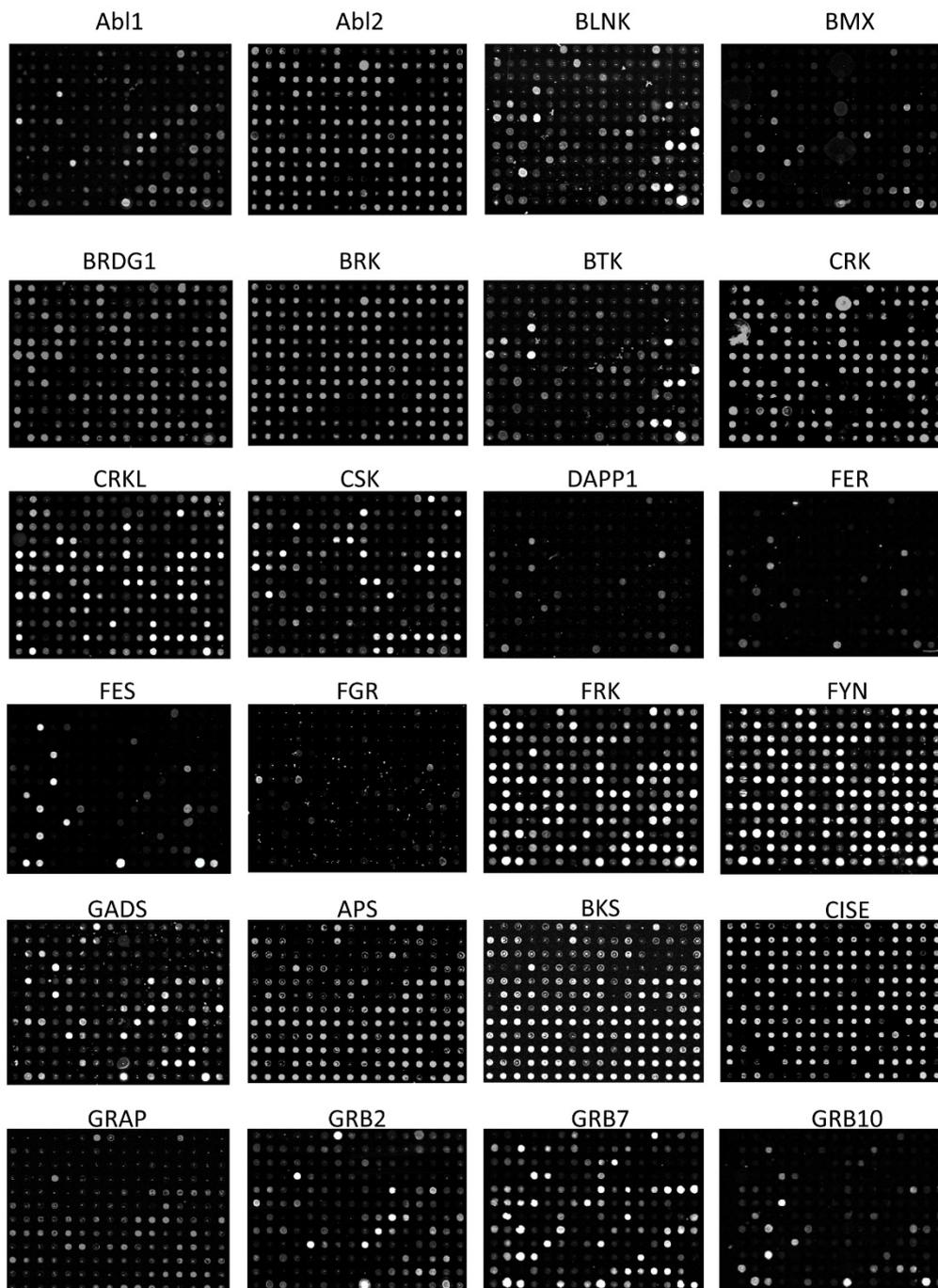


SYK-N	PTPNC-C	GRB14	BSA
SRC	RASA1_N	GRB2	ABL1
SRMS	RASA1_C	GRB7	ABL2
TEC	SH2B	HCK	APS
TNS1	SH2D1A	HSZD	BLK
TNS2	SH2D1B	ITK	BLNK
TNS4	SH2D2A	LCK	BMX
TXK	SHB2P2	LYN	BRDG1
Vav1	SHB	MATK	BRK
VAV2	SHC1	NCK1	CRK
VAV3	SHC3	NCK2	CRKL
YES	SHC4	PIK3R1_C	CSK
ZAP70-N	SHD	PIK3R1_N	FER
SOC36	SHE	PIK3R2_C	FES
SOC52	SHF	PIK3R2_N	FGR
SOC54	SHIP1	PIK3R3_C	FRK
SOC57	SHIP2	PIK3R3_N	FYN
CIS-E	SLNK	PLCg1-N	GADS
GST	SUPT6H	PTPN11-C	GRAP
BSA	SYK-C	PTPN11-N	GRB10

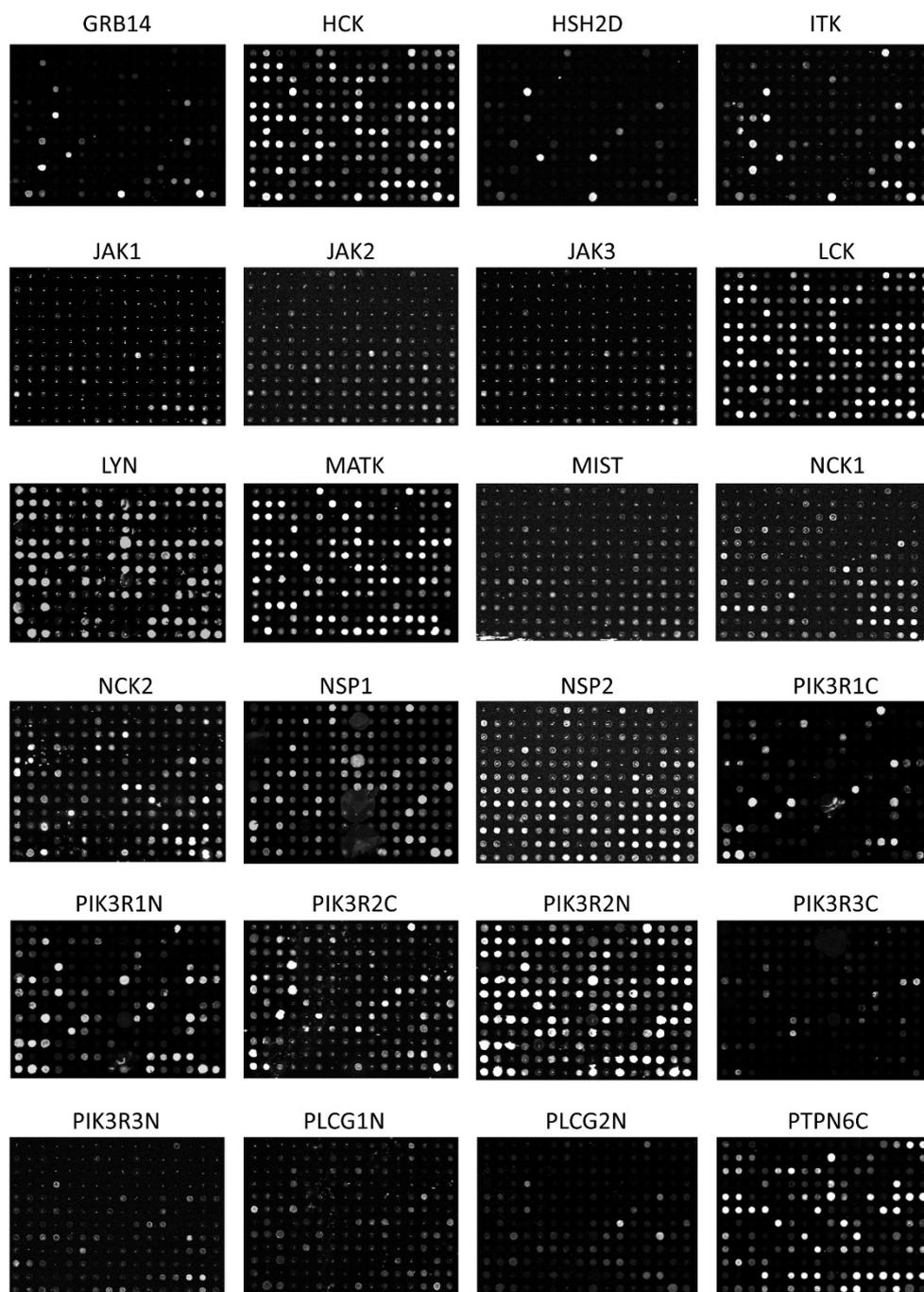
pY807



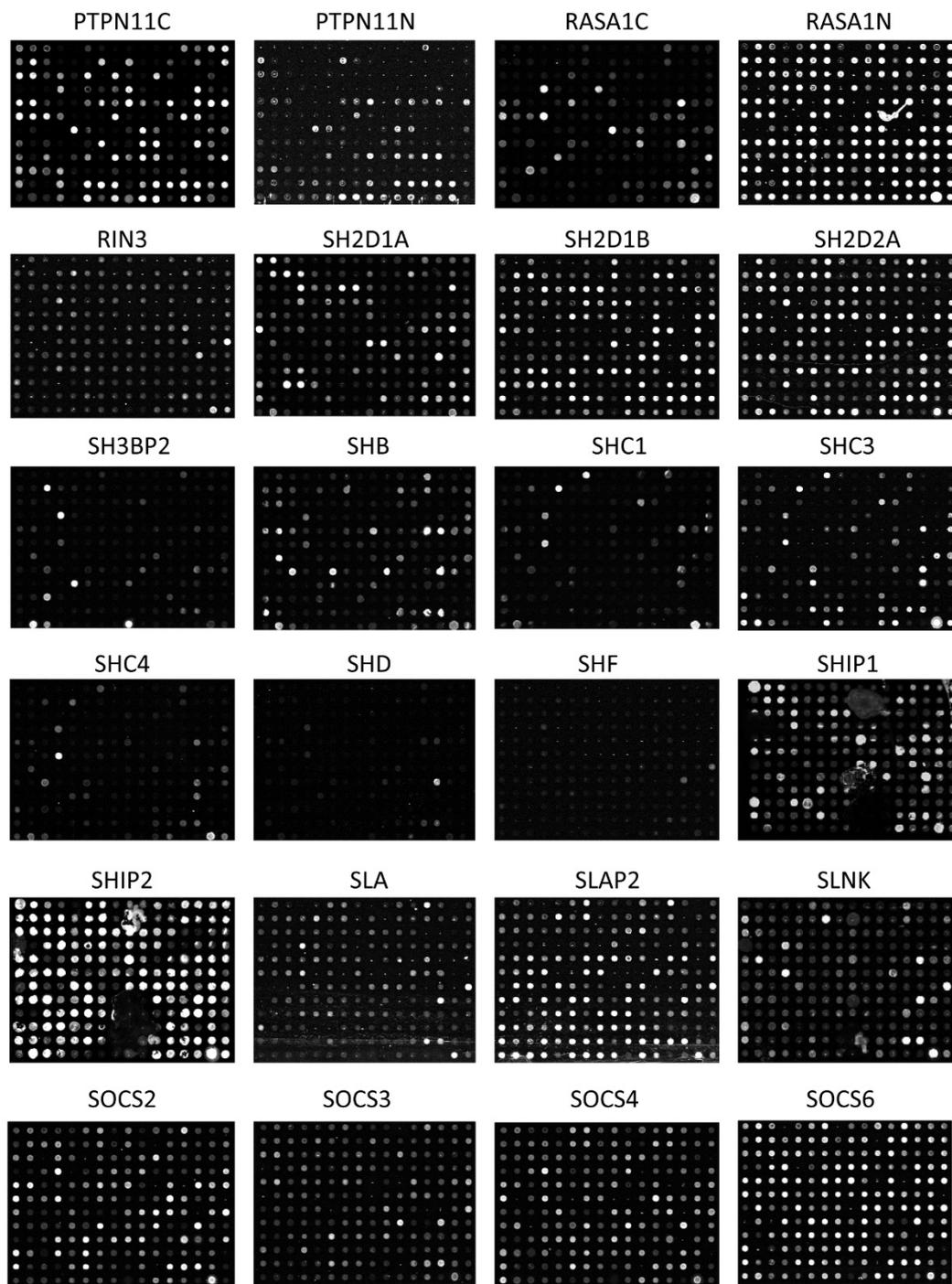
Supplementary Figure 2b. SH2 domain arrays probed by different CD22-pY peptides (cont'd).



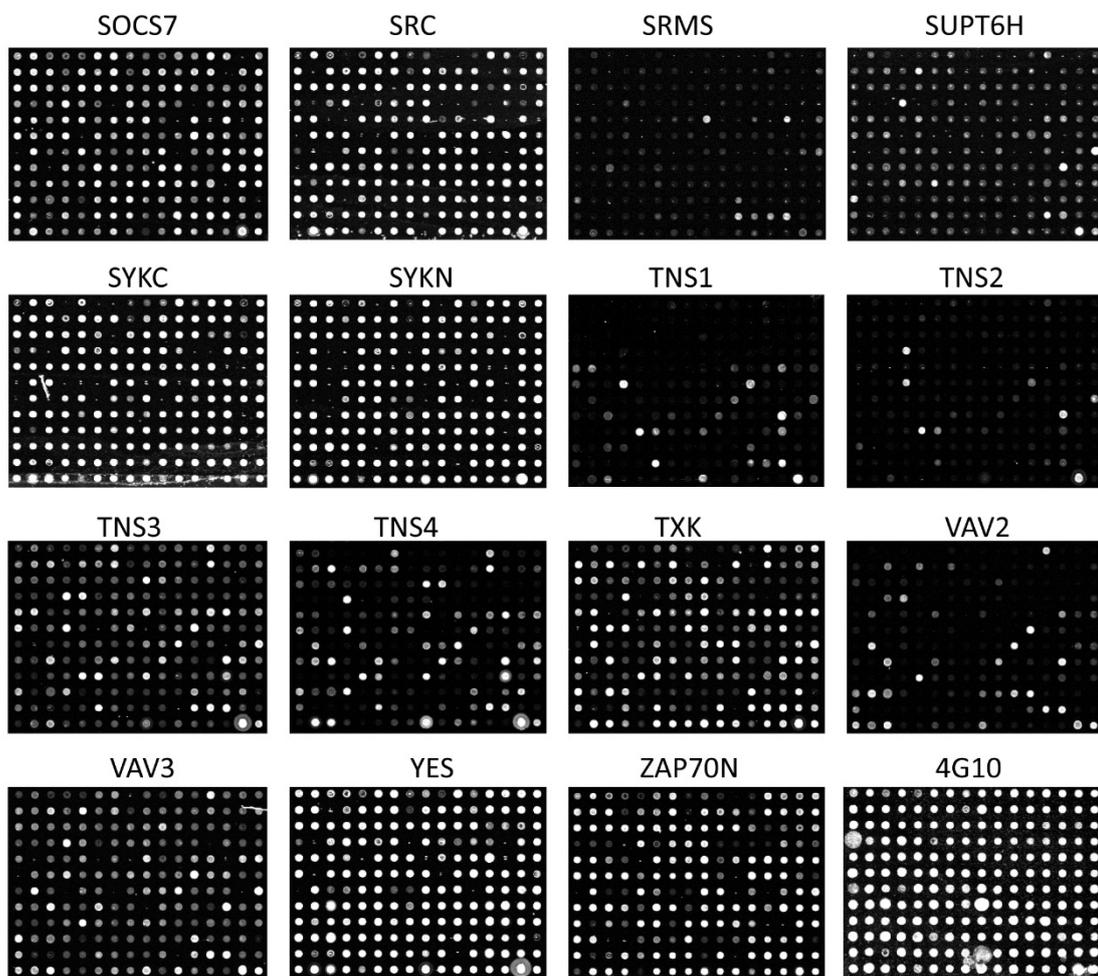
Supplementary Figure 3a. *Binding profiles of different SH2 domains on an ITRM peptide array.*



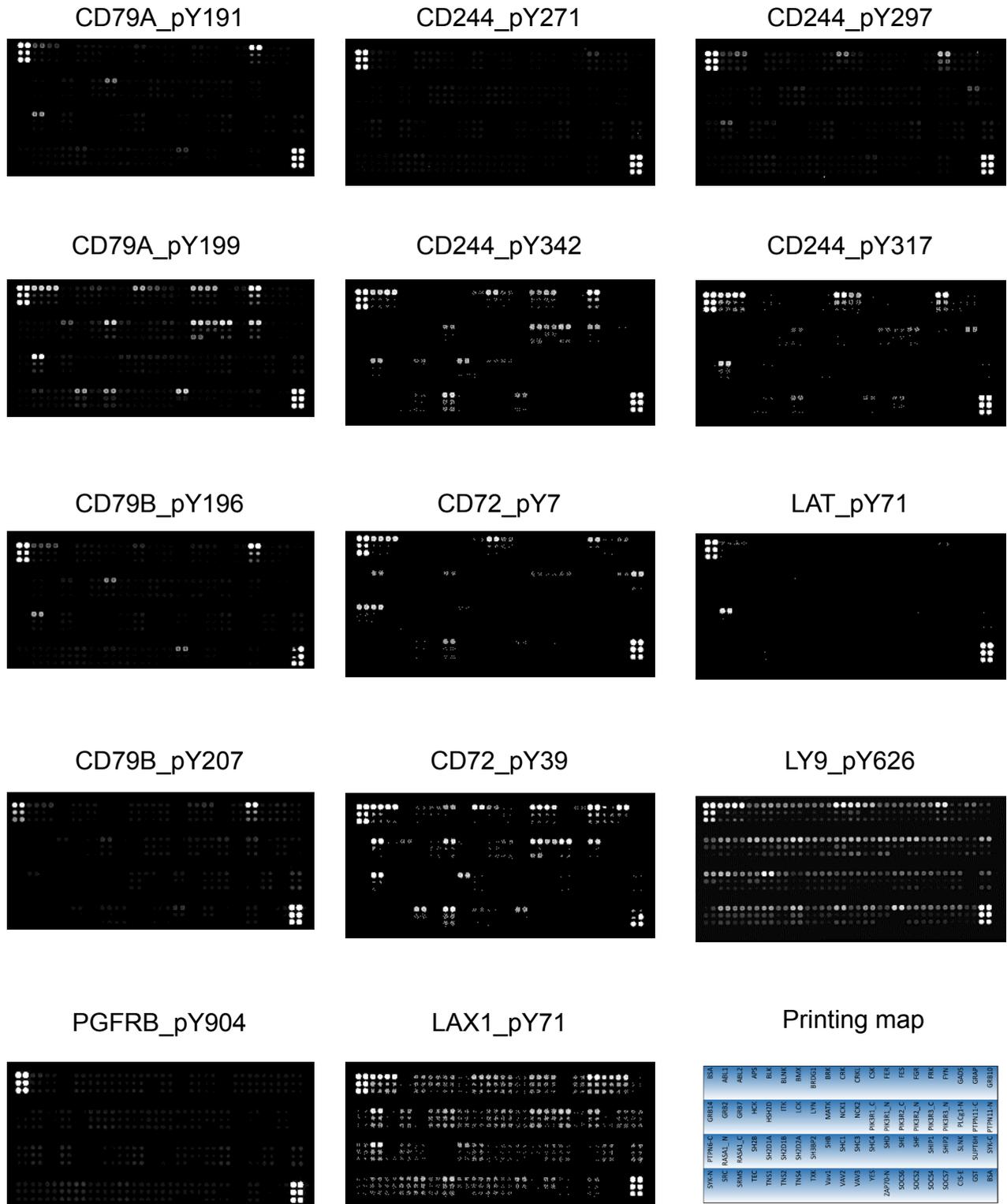
**Supplementary Figure 3b. Binding profiles of different SH2 domains on an ITRM peptide array (cont'd).**



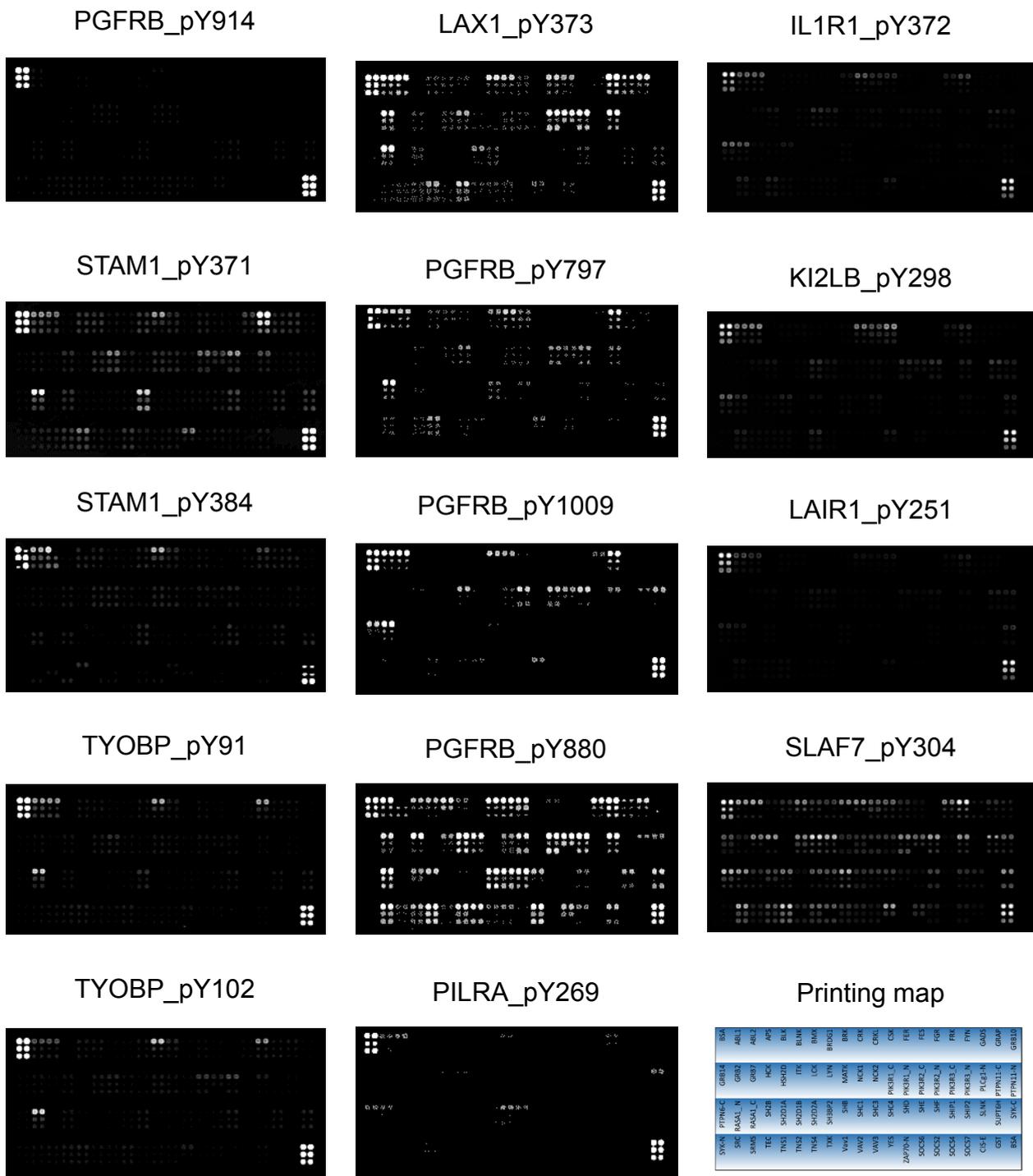
Supplementary Figure 3b. *Binding profiles of different SH2 domains on an ITRM peptide array (cont'd).*



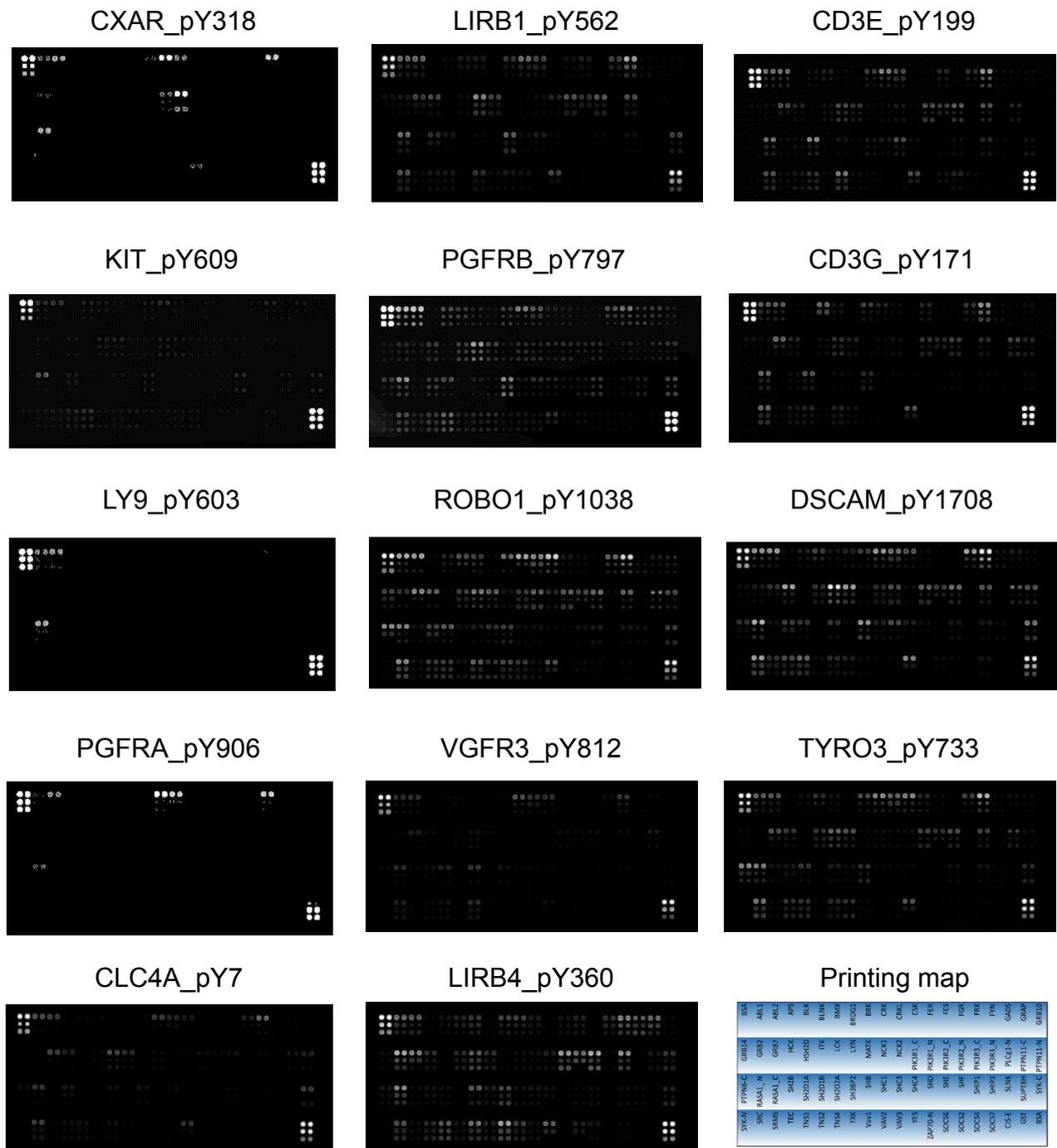
Supplementary Figure 3b. *Binding profiles of different SH2 domains on an ITRM peptide array (cont'd).*



Supplementary Figure 4a. *Binding profiles of different ITRM phosphopeptides on an SH2 domain array.*

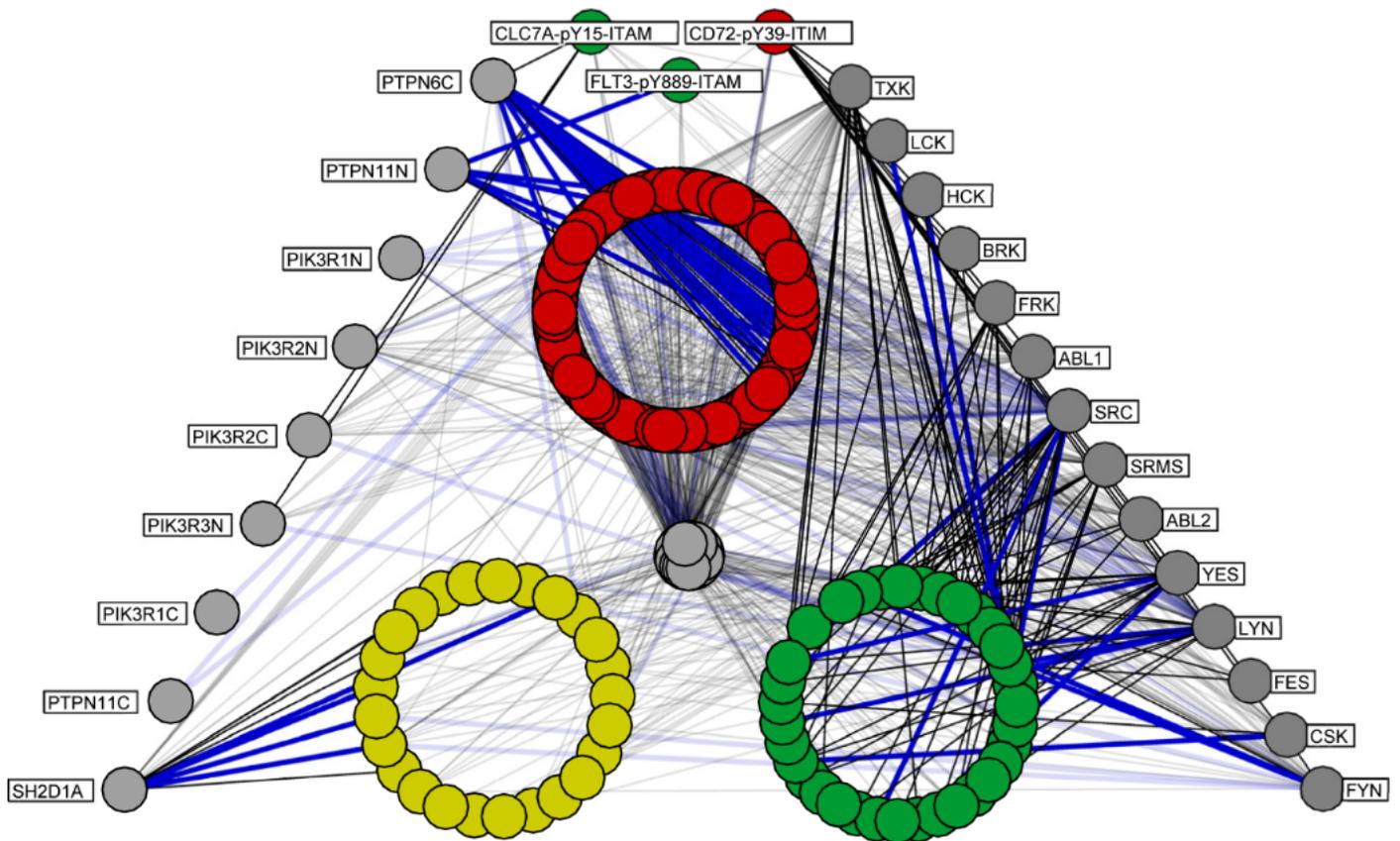


Supplementary Figure 3b. *Binding profiles of different SH2 domains on an ITRM peptide array (cont'd).*

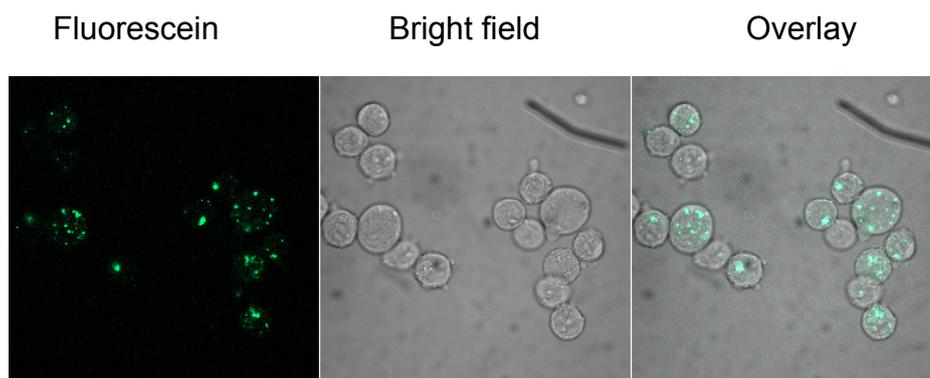


Supplementary Figure 3b. *Binding profiles of different SH2 domains on an ITRM peptide array (cont'd).*





**Supplementary Figure 6. Prediction of an immunoreceptor-SH2 domain signaling network based on data from bidirectional peptide-protein array screen.** ITRM-SH2 pairs in S1 were used as gold standards to rescue true-positive interactions buried in S2-4 (see also Supplementary Figure 5A). The resultant interactome contains interactions located within S1 as well as those “rescued” by the scheme described in the paper. Interactions annotated in the STRING database are marked blue. ITIMs are shown in red, ITAMs in green, and ITSMs in yellow. Three peptides on the top were shown as examples.



**Supplementary Figure 7. Microscopic images of cells transduced with fluorescein-labeled BSA- gold nanoparticles (AuNP) adducts.** YT cells were incubated with 10 nM AuNP-FITC-BSA for 4h at 37° C. Shown are fluorescent (left) and bright-field (middle) images of the cells with the overlaid image shown on the right.