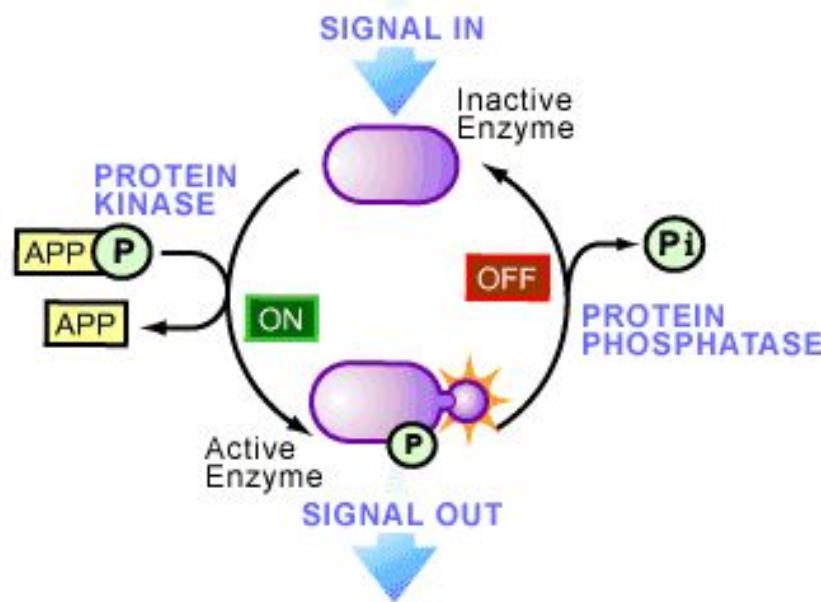


Cell Type Deconvolution by Phosphoproteomics

Bridget Li, Cameron Flower, Angela Ahn, Dr. Forest White

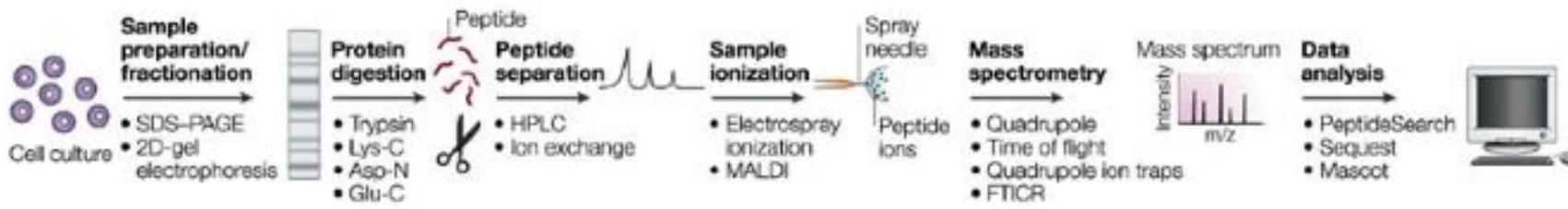
Background

- Signal transduction
- Protein phosphorylation
 - Kinases
 - Phosphatases
 - Adapter proteins
- Cancer



Background

- Phosphoproteomics
- Mass spectrometry



Project Overview

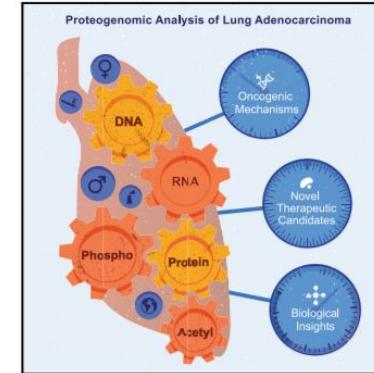
- Identify cell types in tumor tissue samples based on bulk phosphoproteomic data
- Data from a 2020 study in *Cell*
- Started by doing correlation analysis

Cell

Resource

Proteogenomic Characterization Reveals Therapeutic Vulnerabilities in Lung Adenocarcinoma

Graphical Abstract



Authors

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Correspondence

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In Brief

Comprehensive proteogenomic characterization of lung adenocarcinomas and paired normal adjacent tissues from patients of diverse smoking status and country of origin yields insights into cancer taxonomy, oncogenesis, and immune response; offers novel candidate biomarkers and therapeutic targets; and provides a community resource for further discovery.

Highlights

- Comprehensive LUAD proteogenomics exposes multi-omic clusters and immune subtypes
- Phosphoproteomics identifies candidate ALK-fusion diagnostic markers and targets
- Candidate drug targets: PTPN11 (EGFR), SOS1 (KRAS), neutrophil degranulation (ST7K11)
- Phospho and acetyl modifications denote tumor-specific markers and druggable proteins

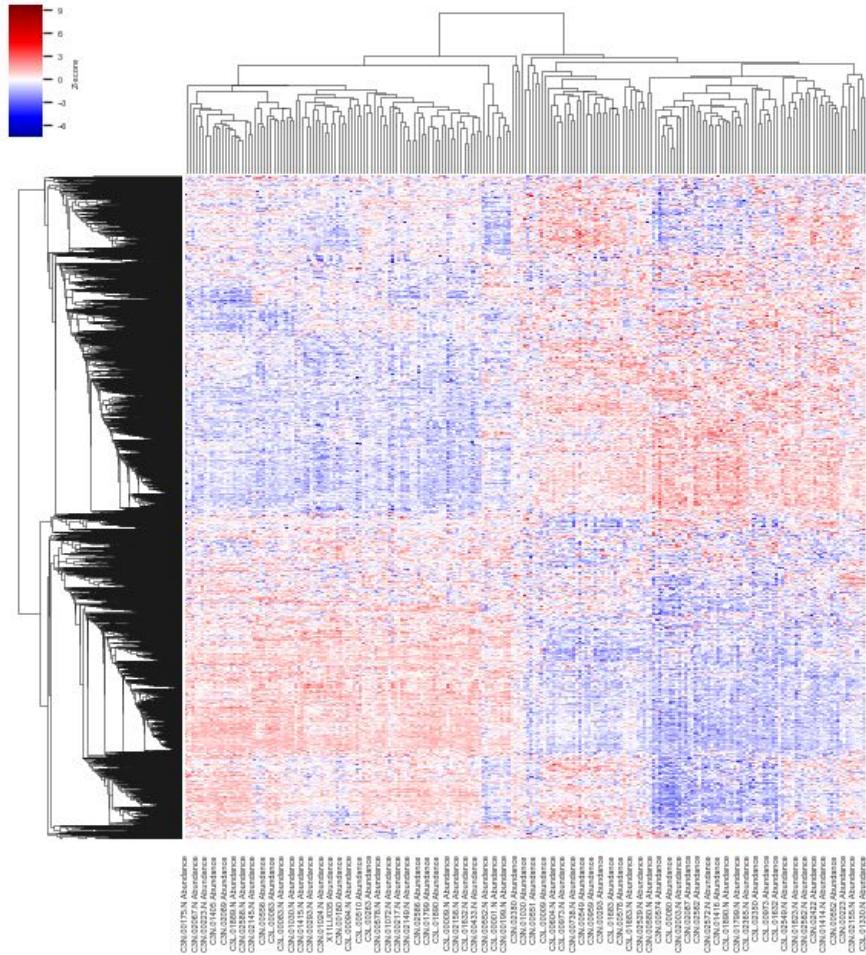


Gillette et al., 2020, Cell 182, 200-225
July 9, 2020 © 2020 Elsevier Inc.
<https://doi.org/10.1016/j.cell.2020.06.013>

CellPress

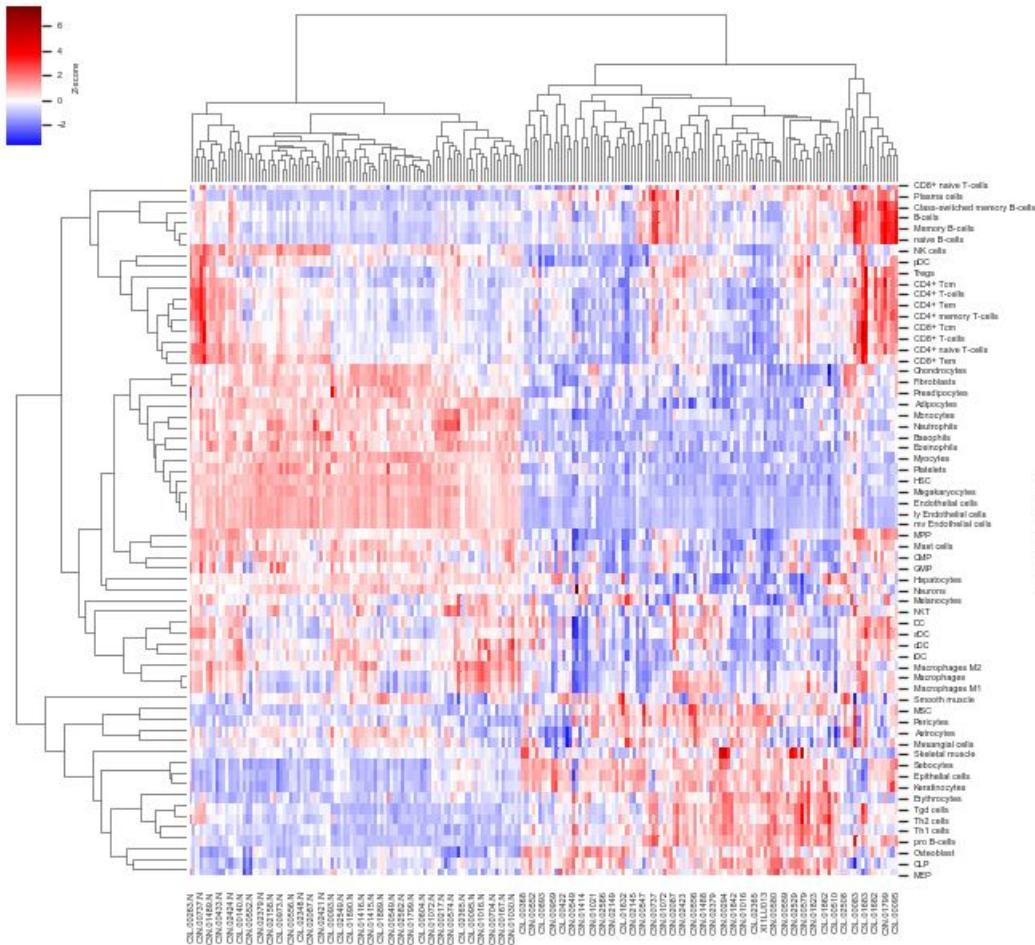
Phosphopeptide vs. Sample Heatmap

- 5256 peptides
- 211 samples

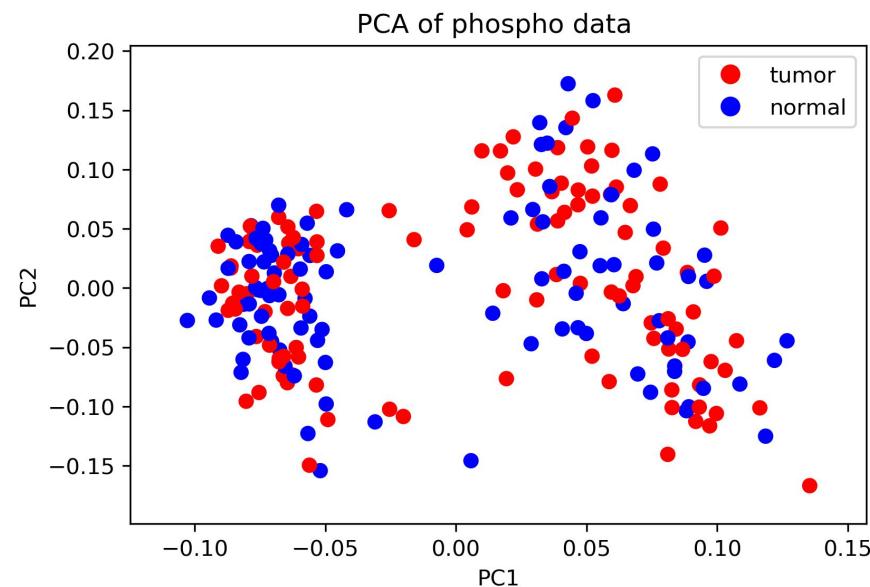
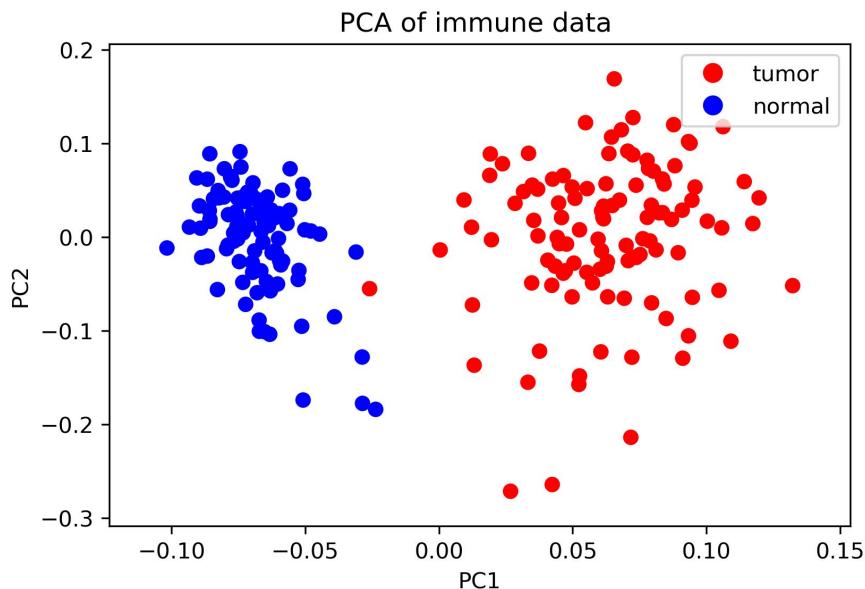


Immune Cell vs. Sample Heatmap

- 64 immune cells
- 211 samples

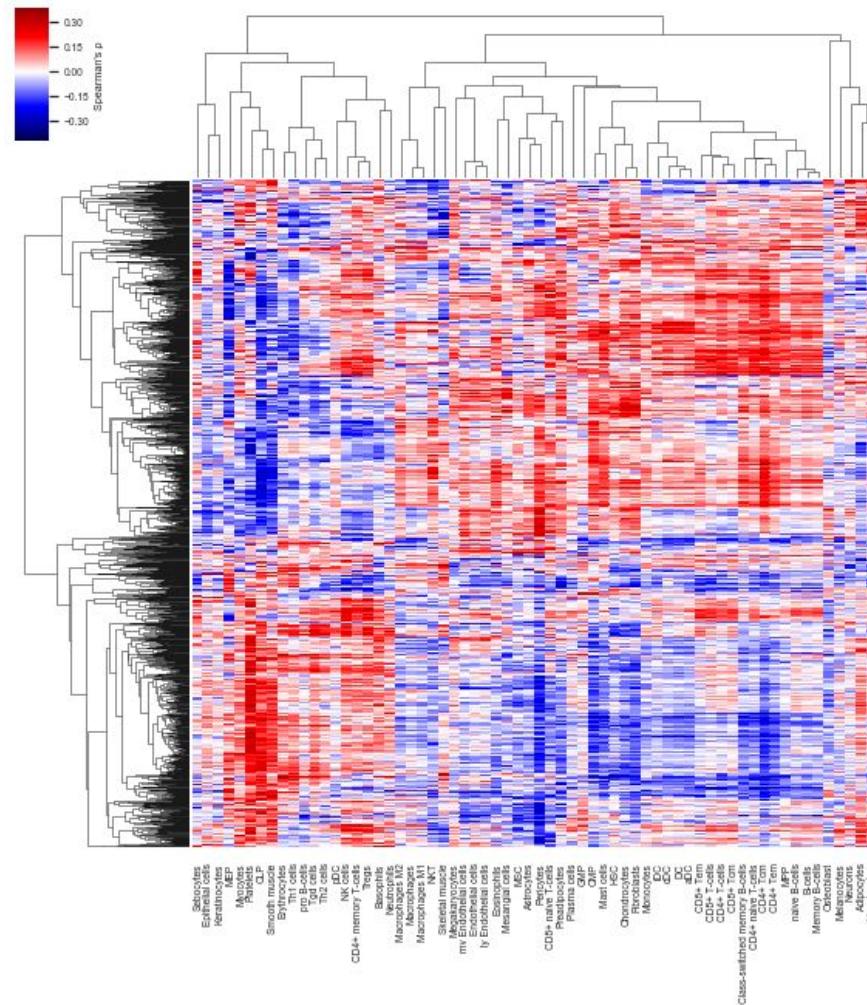


Principal Component Analysis (PCA)

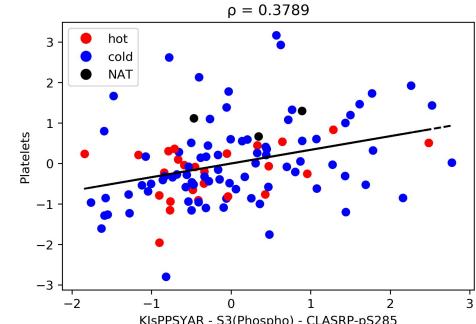
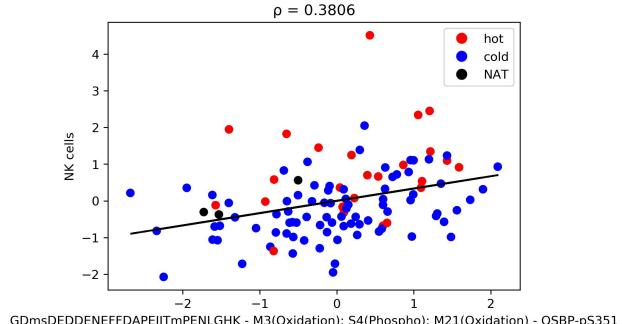
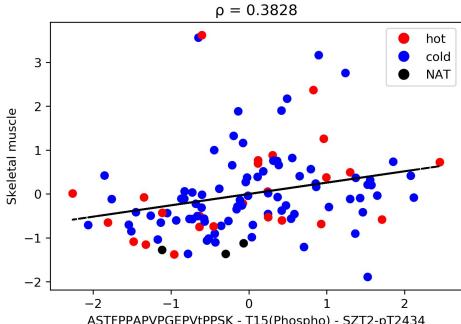
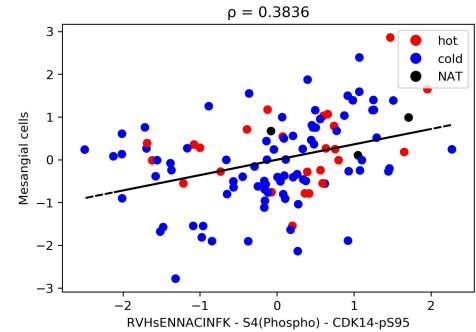
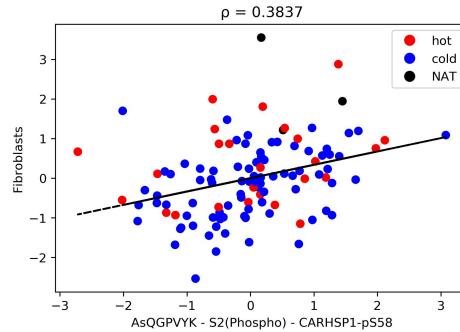
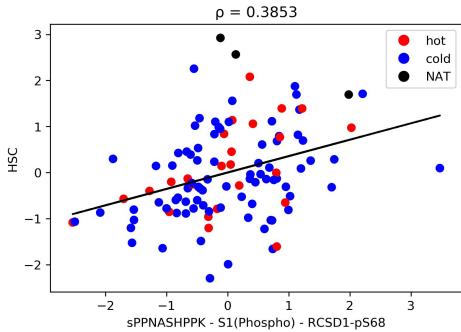


Phosphopeptide vs. Immune Cell Heatmap

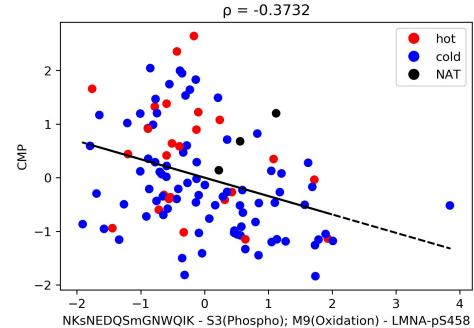
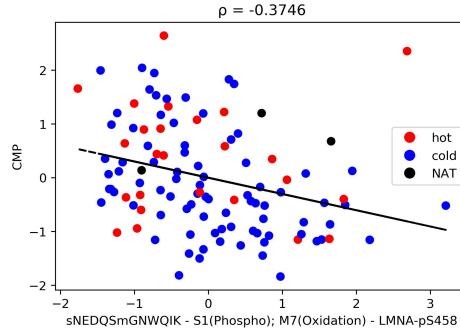
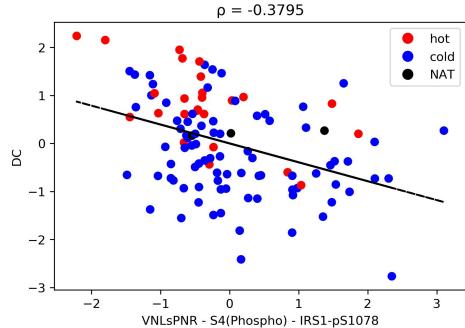
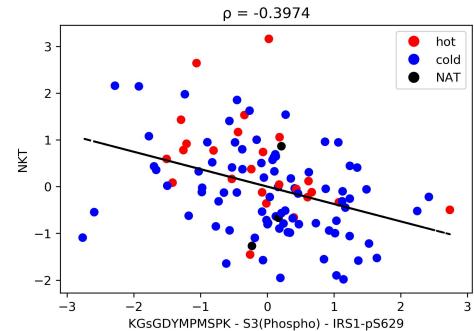
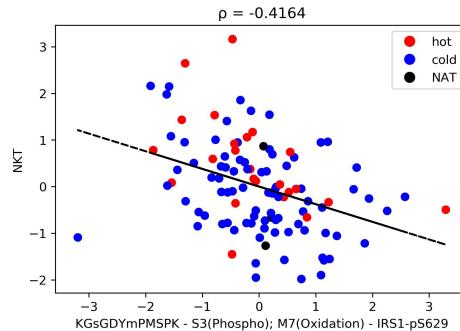
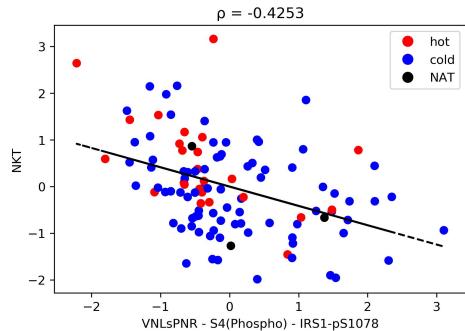
- 1584 peptides
 - 64 immune cells



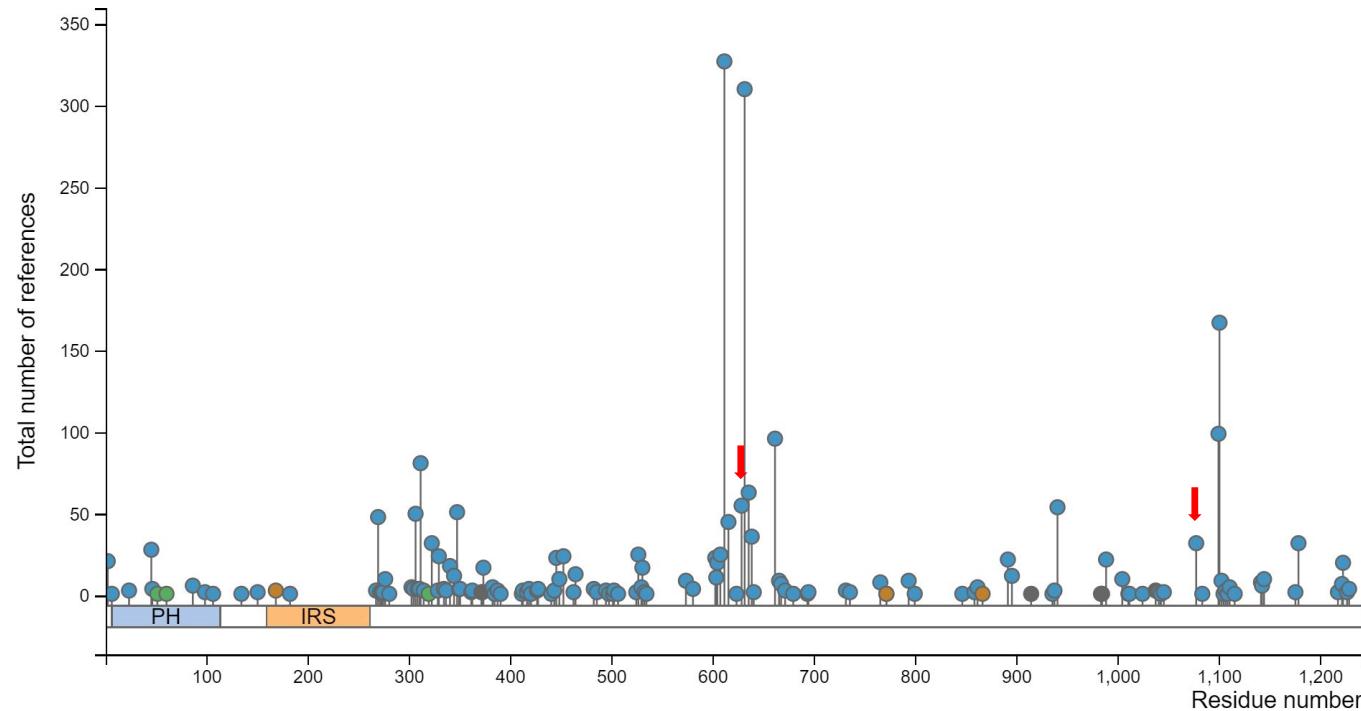
Most Correlated Peptides and Immune Cells



Least Correlated Peptides and Immune Cells



Insulin Receptor Substrate 1 (IRS1)



Future Work

- Biomarker analysis
 - Found matches between sample peptides and biomarkers
 - ['NES', 'VIM', 'NRP1', 'SPN', 'RORA', 'S100A9', 'NFKB1', 'STAT1', 'C5AR1', 'CD44', 'GP1BB', 'KIT', 'STAT3', 'RUNX1', 'ALDOC', 'PECAM1', 'PTPRC', 'AQP4', 'PEA15', 'ITGA4', 'FOXO1', 'NDRG2', 'MSR1', 'VPS54']
- Predictions based on signatures
- Other datasets

immune_cell

A	B	C	D	E	F	G	H	I	J	K	L	M	N	O
1	gene	Uniprot or Protein.ncbi Alias(es)	localizatio	cells	.1	cells.2	cells.3	cells.4		cells.5	cells.6	cells.7	cells.8	cells.9
2	AHR	P35869	Aryl hydro AHR	BHLH-intracellu	LT1	Th22	NCR+ ILC3	NCR-ILC3	Th17	ILC3				
3	ALDH1L1	Q75891	Cytosolic 1ALDH1L1	FTHFD	astrocyte									
4	ARG1	P05089	Arginase-1ARG1	intracellu	m2c	micro	macropha	ILC2						
5	AXL	P30530	Tyrosine-pAXL	UFO	extracellu	tissue	associated	Mac						
6	BACH2	Q9BYV9	Transcript	BACH2	intracellu	germinal	center	B						
7	BATF	Q16520	Basic leuci	BATF	intracellu	fTh	Th22	Th2	Th17					
8	BATF3	Q9NR55	Basic leuci	BATF3	SNI	intracellu	classical	D	Th17					
9	BTLA	Q72649	B- and T-ly	BTLA	extracellu	follicular	Th							
10	CCL1	P22362	C-C motif	(C)CCL1	SCYA	secreted	M2a	M2b						
11	CCL11	P51671	Eotaxin	(C)CCL11	SCY	secreted	M1	m1	microglia					
12	CCL14	Q16627	C-C motif	(C)CCL14	NCC	secreted	M2a							
13	CCL15	Q16665	C-C motif	(C)CCL15	Mif	secreted	M1	m1	microglia					
14	CCL16	Q15467	C-C motif	(C)CCL16	ILN	secreted	M2c	m2c	microglia					
15	CCL17	Q95853	C-C motif	(C)CCL17	SCY	secreted	M2a							
16	CCL18	P55774	C-C motif	(C)CCL18	AM	secreted	M2a	m2c	micro	M2c				
17	CCL19	Q99731	C-C motif	(C)CCL19	ELC	secreted	M1	m1	microglia					
18	CCL2	P13500	C-C motif	(C)CCL2	MCP	secreted	M1	M2a	m1	microglia				
19	CCL20	P78556	C-C motif	(C)CCL20	LAR	secreted	M1	M2b	m1	microglia				
20	CCL22	P00626	C-C motif	(C)CCL22	MD	secreted	M2a							
21	CCL23	P55773	C-C motif	(C)CCL23	Mif	secreted	M2a							
22	CCL24	P000175	C-C motif	(C)CCL24	MIF	secreted	M2a							
23	CCL26	Q9Y256	C-C motif	(C)CCL26	SCY	secreted	M2a							
24	CCR3	P10147	C-C motif	(C)CCL3	GOS	secreted	M1	m1	micro	effector	C1	basophil	ILC1	
25	CCR4	P13236	C-C motif	(C)CCL4	LAG1	secreted	M1	m1	micro	effector	CD8	T		
26	CCR5	P13501	C-C motif	(C)CCL5	D17	secreted	M1	m1	micro	M2d	effector	CD8	T	
27	CCR8	P80075	C-C motif	(C)CCL8	MCP	secreted	M1	m1	microglia					
28	CCR1	P32246	C-C chemic	CCR1	CMK	extracellu	Th1							
29	CCR10	P46092	C-C chemic	CCR10	GP	extracellu	Th22							
30	CCR2	P41597	C-C chemic	CCR2	CMK	extracellu	M2c							
31	CCR3	P51677	C-C chemic	CCR3	CMK	extracellu	basophil							
32	CCR4	P51679	C-C chemic	CCR4	CMK	extracellu	Th2	Th17	Th22					
33	CCR5	P51681	C-C chemic	CCR5	CMK	extracellu	Th1							
34	CCR6	P51684	C-C chemic	CCR6	CKR1	extracellu	Th17	Th22	Lti					
35	CCR7	P32248	C-C chemic	CCR7	CMK	extracellu	classical	D	Lti					
36	CCR8	P51685	C-C chemic	CCR8	CKR1	extracellu	Th2							
37	CCR9	P51686	C-C chemic	CCR9	GP	extracellu	ILC2							
38	CD101	Q93033	Immunogl	(CD101	EV	extracellu	Treg							
39	CD14	P08571	Monocyte	CD14		extracellu	monocytic	intermedi	classical	m	classical	D	inflammat	macropha
40	CD151	P48509	CD151	ant	CD151	T5f	extracellu	platelet						
41	CD160	Q05971	CD160	ant	CD160	BY	extracellu	NKT						
42	CD163	Q86VB7	Scavenger	CD163	M1	extracellu	m2c	micro	macropha	M2a	M2c			
43	CD164	Q04908	Sialomucir	CD164		extracellu	stem	cells						
44	CD177	Q8N603	CD177	ant	CD177	NB	extracellu	neutrophil						
45	CD180	Q99467	CD180	ant	CD180	LYF	extracellu	Marginal	Zone	B				
46	CD19	P15391	B-lymphoc	CD19		extracellu	B	Marginal	memory	B	regulatory	B		

immune_cell_markers_final

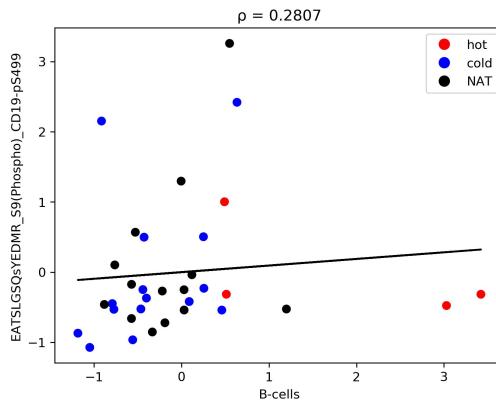
Spring 2021

- Fall 2020
 - Kept peptides that were present in every sample
 - Performed overall correlations between peptides and immune cells
 - Tumor samples only
- Spring 2021
 - Keep every peptide observed
 - Remove samples that have missing values for a given peptide
 - Focus on peptides of interest
 - Performed correlations between specific pairs of peptides
 - Performed correlations between specific peptides and immune cells

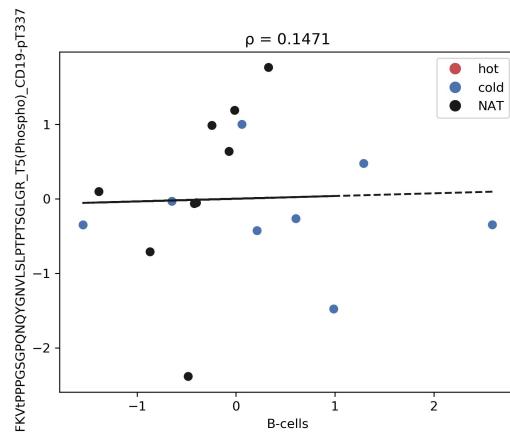
CD19

CD19 and B-Cells

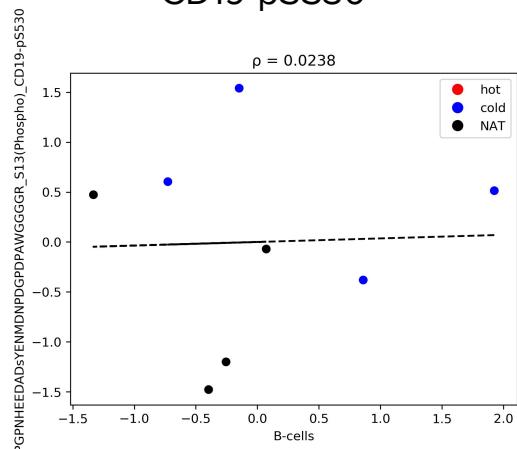
CD19-pS499



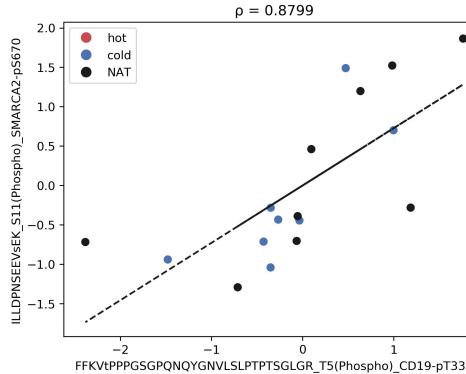
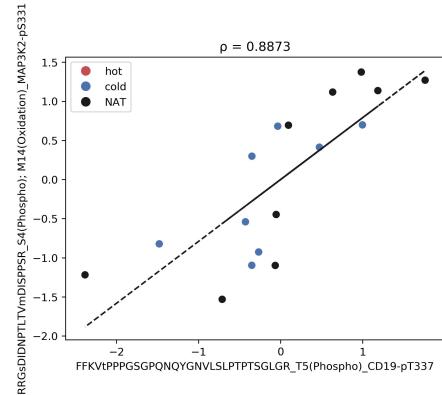
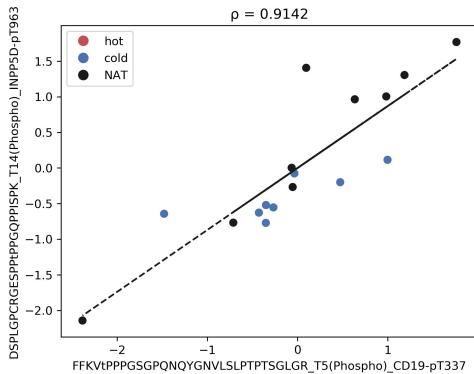
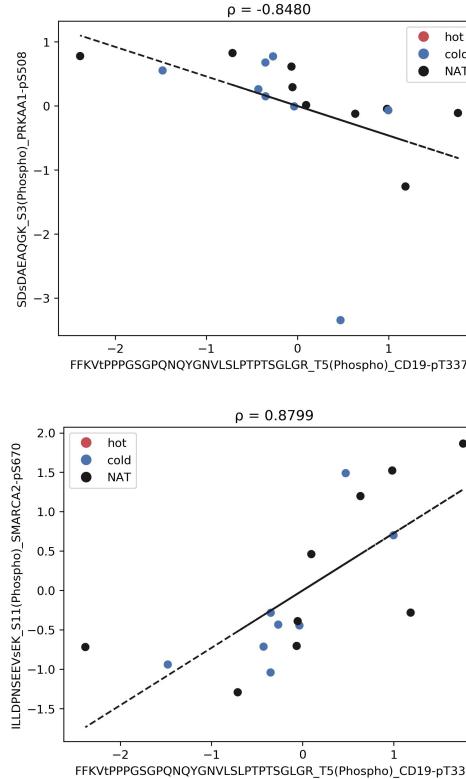
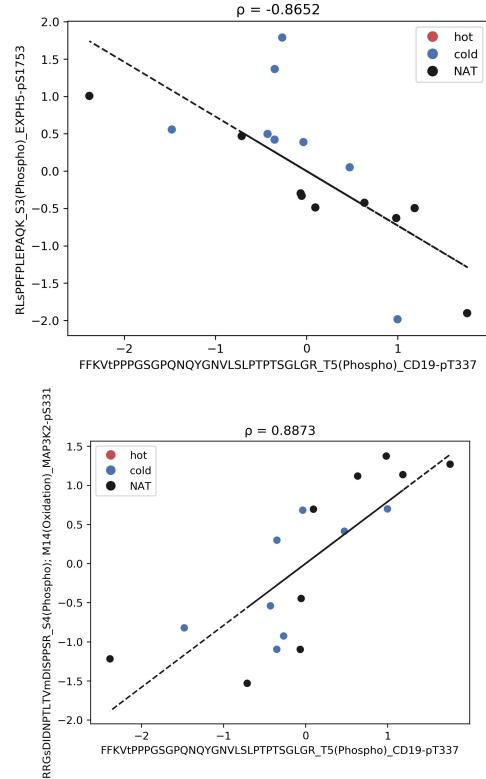
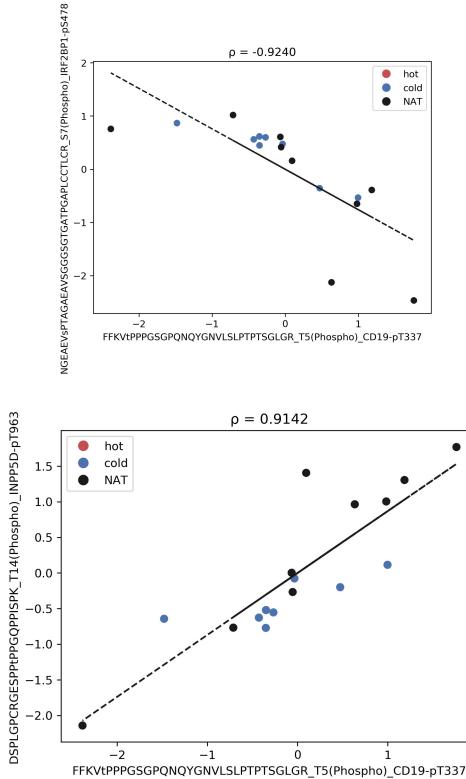
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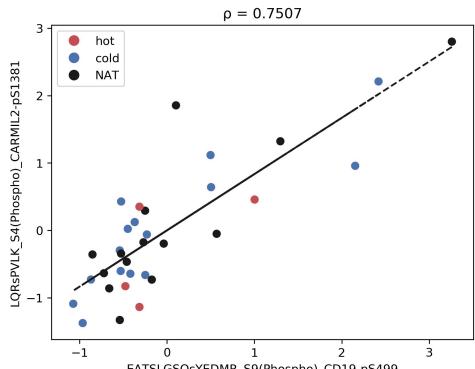
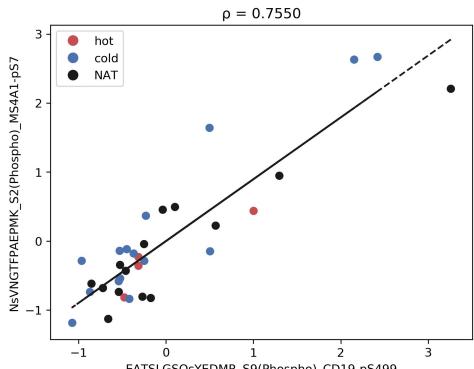
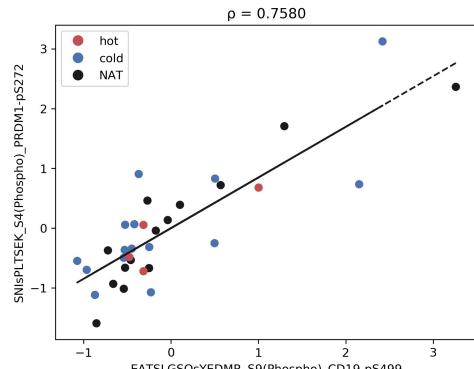
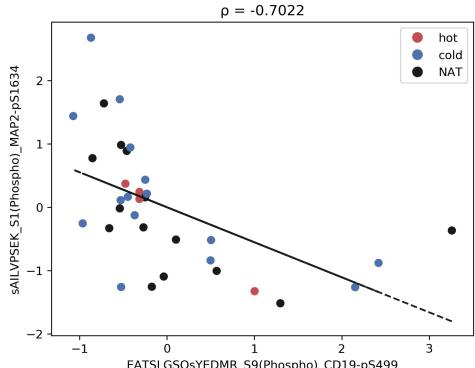
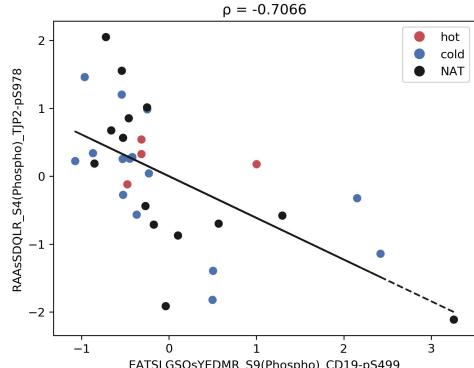
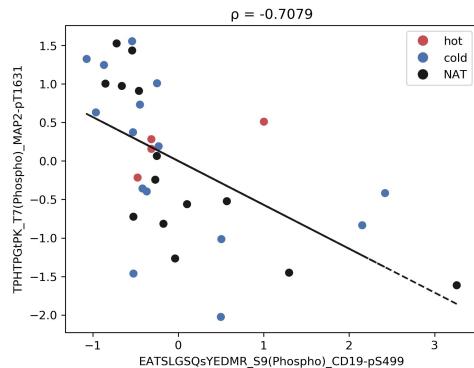
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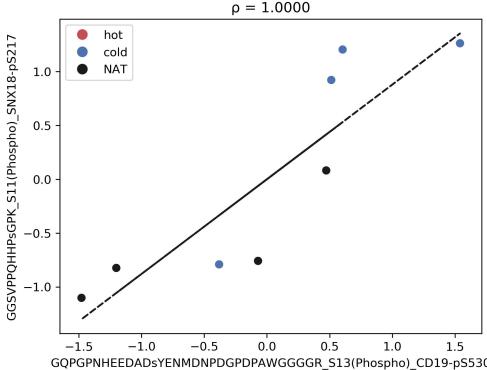
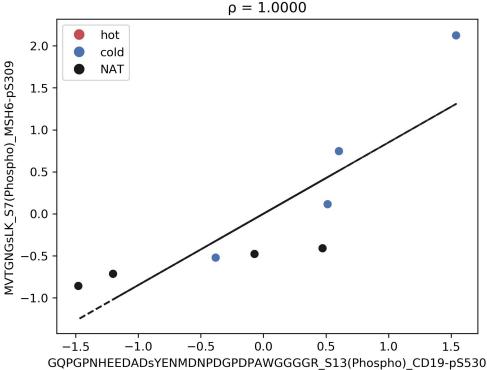
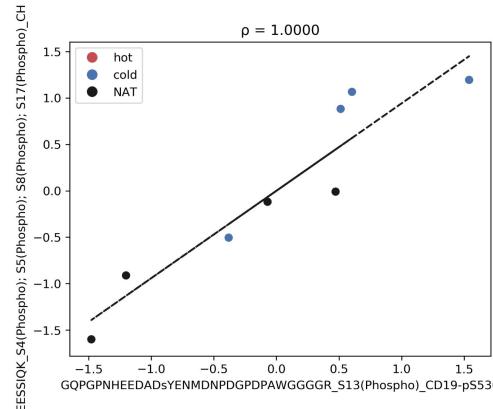
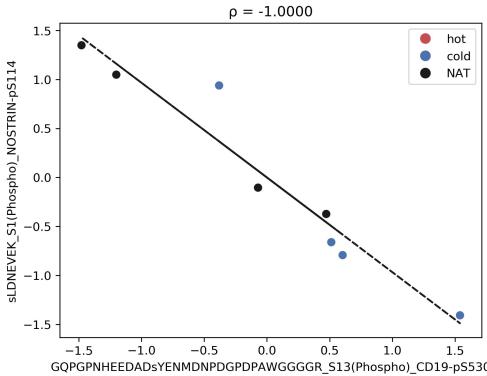
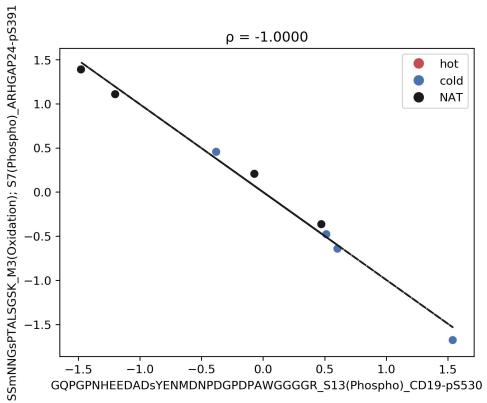
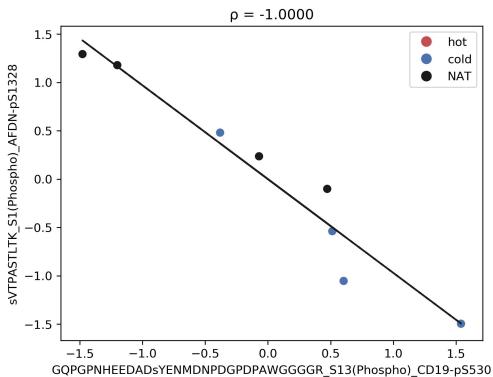
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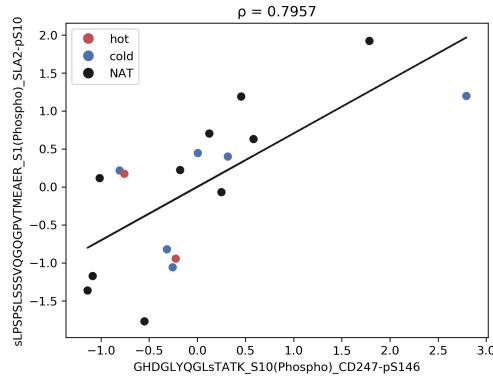
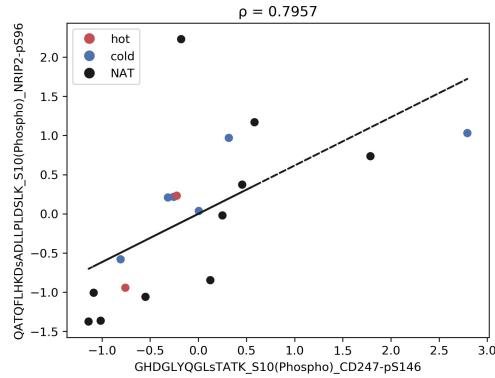
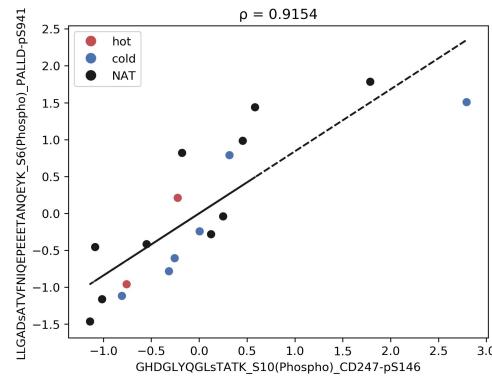
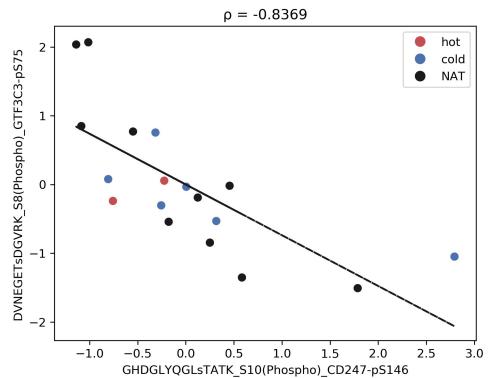
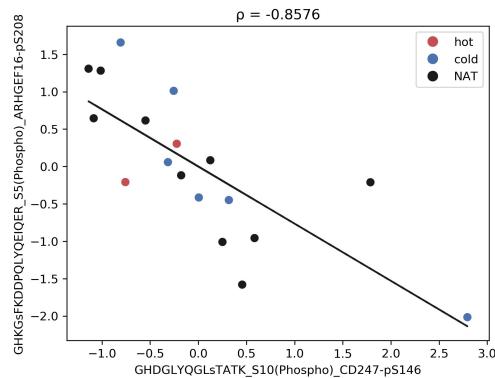
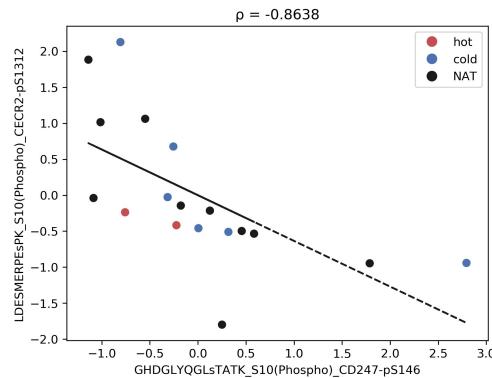


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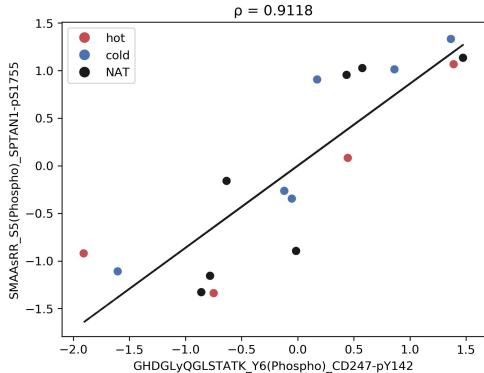
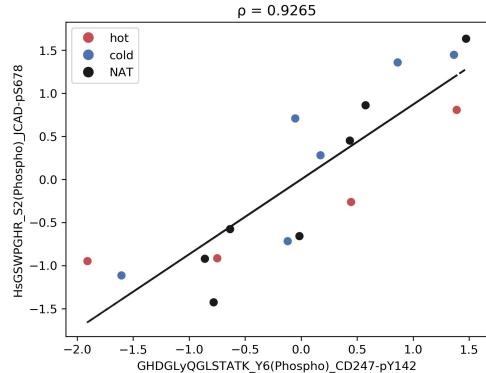
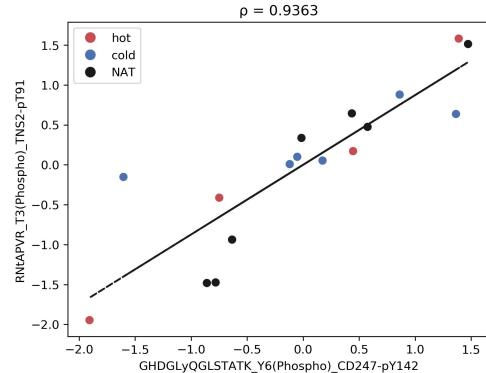
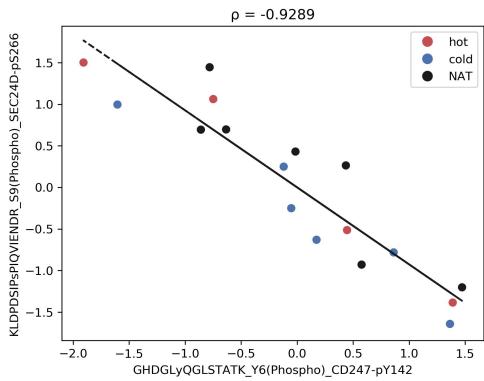
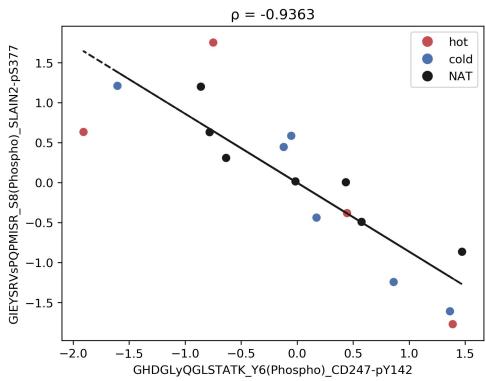
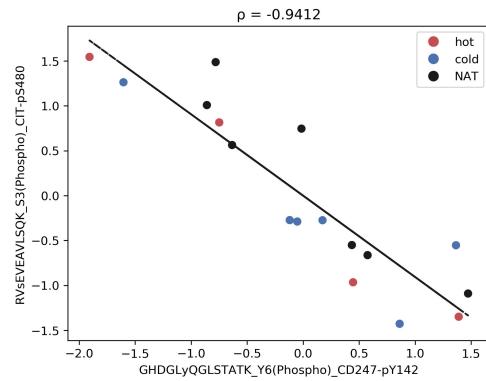


CD247

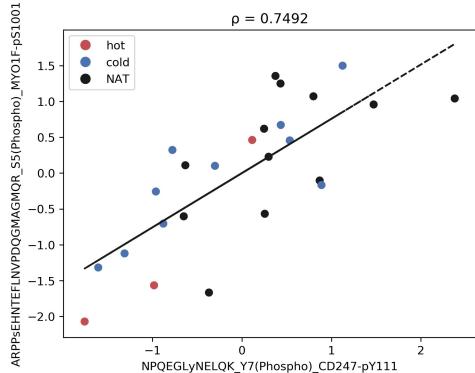
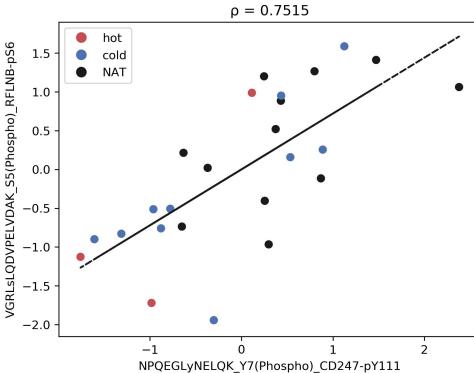
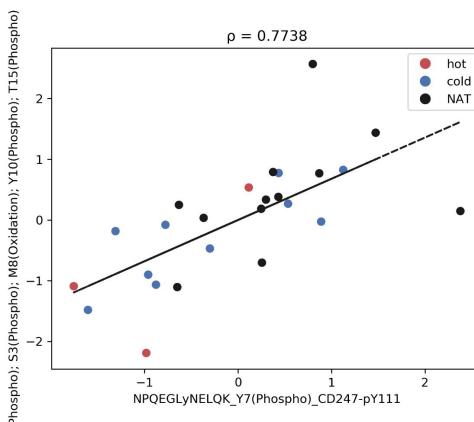
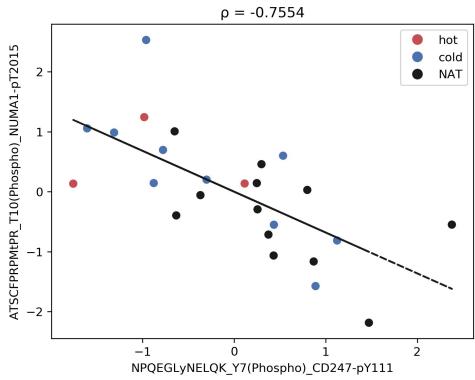
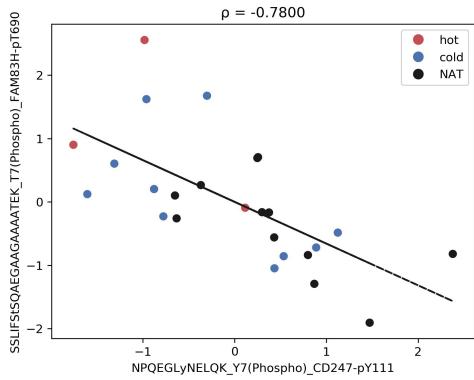
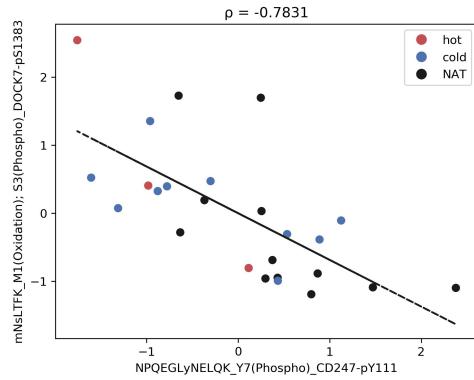
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CD247-pY142

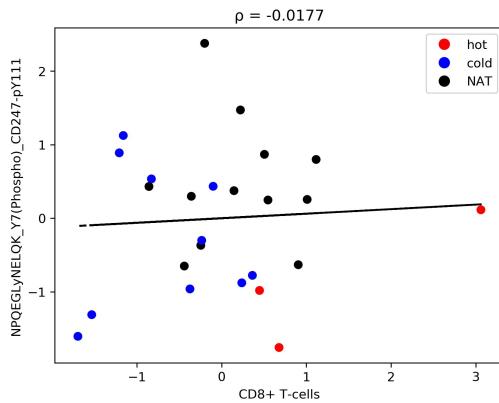


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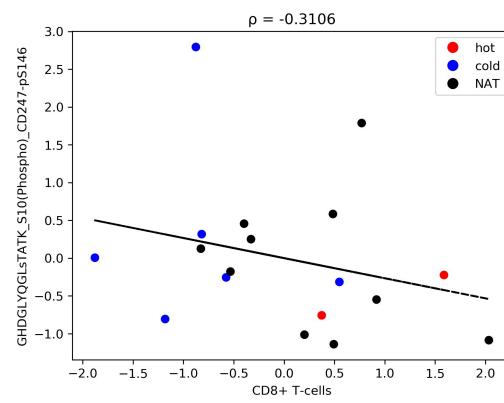


CD247 and CD8+ T-Cells

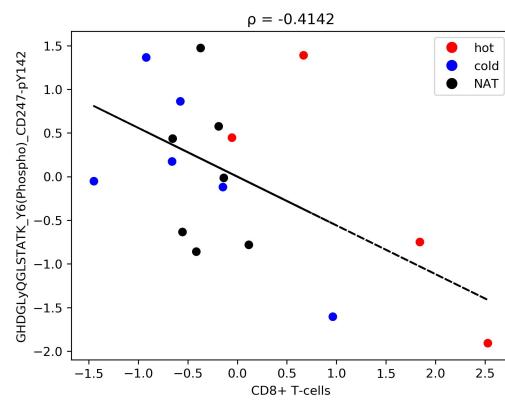
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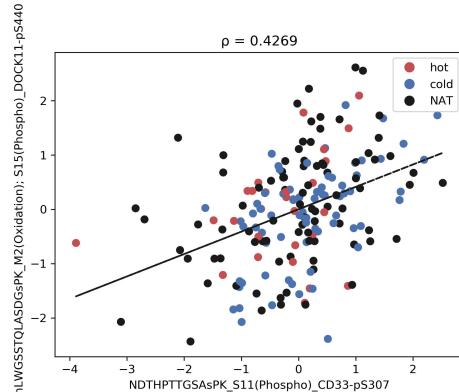
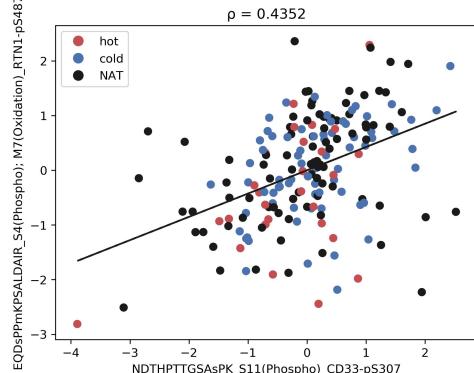
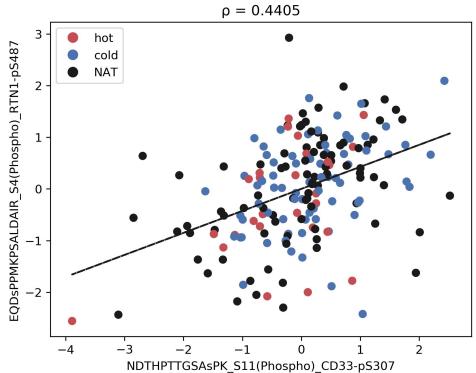
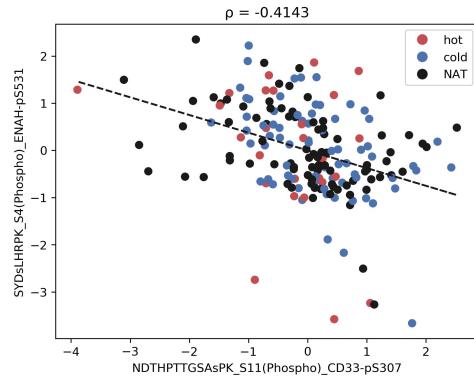
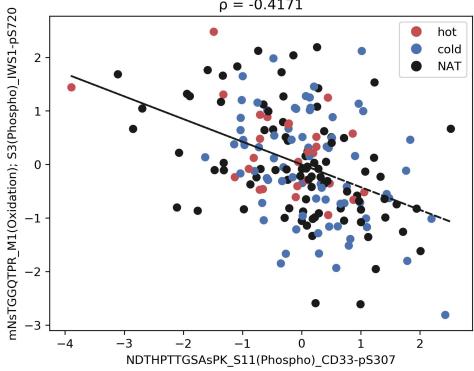
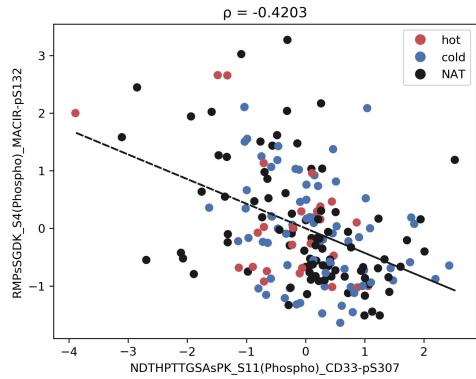


CD247-pY142

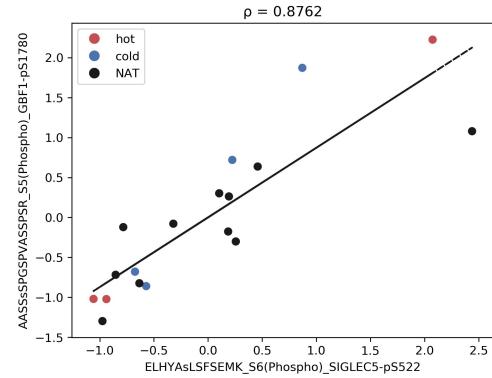
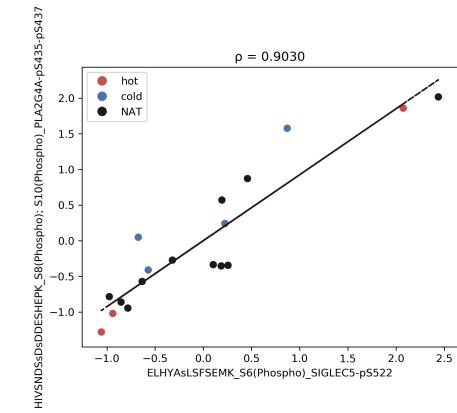
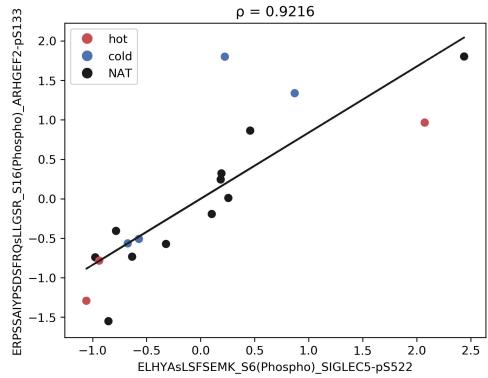
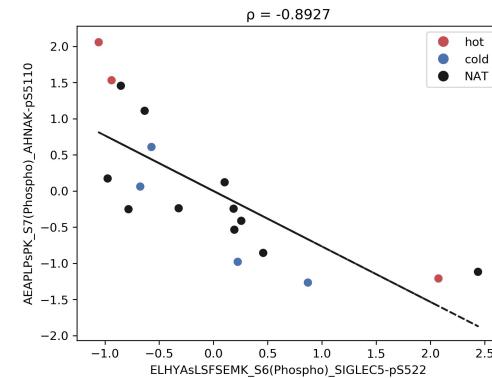
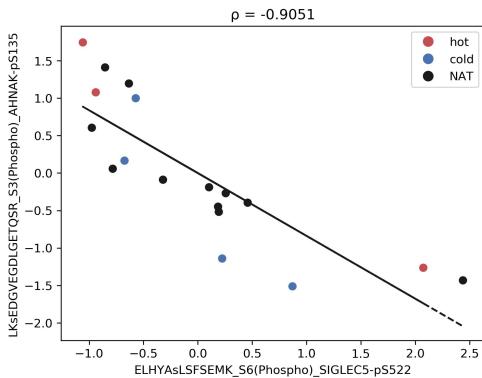
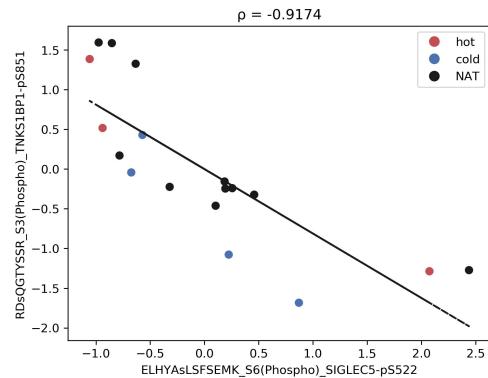


SIGLECs

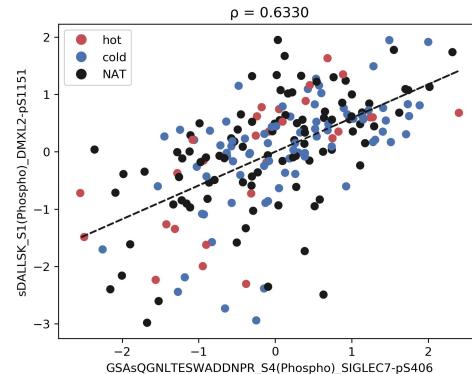
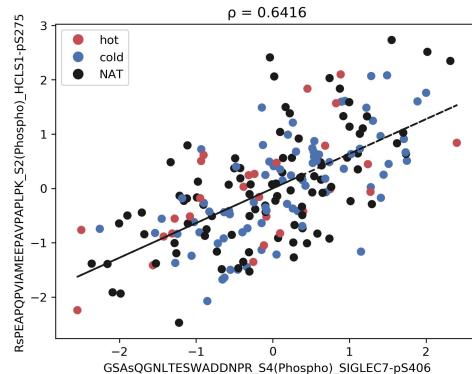
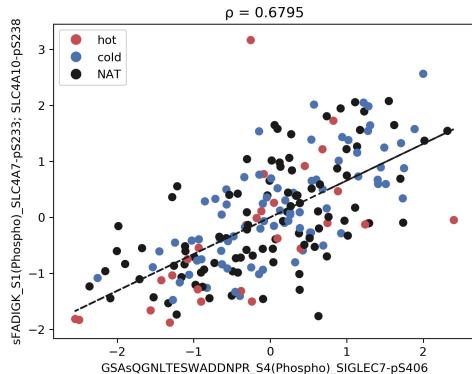
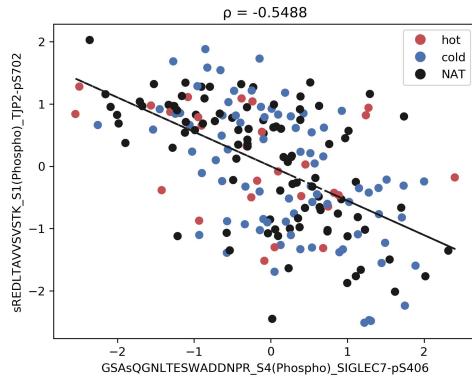
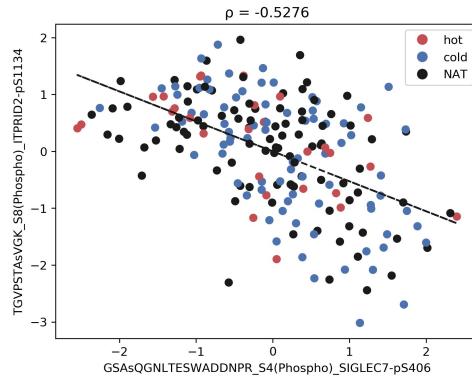
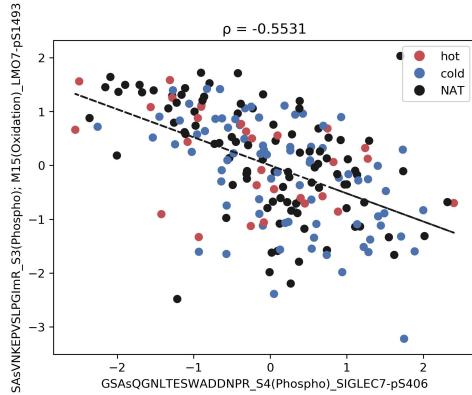
CD33-pS307



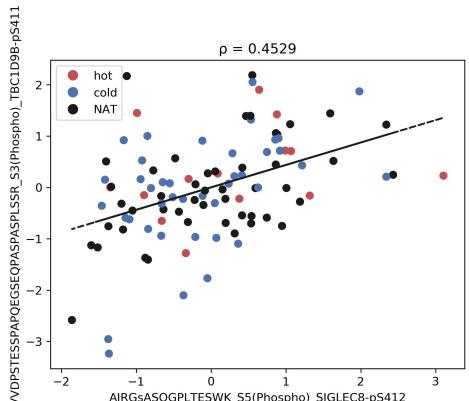
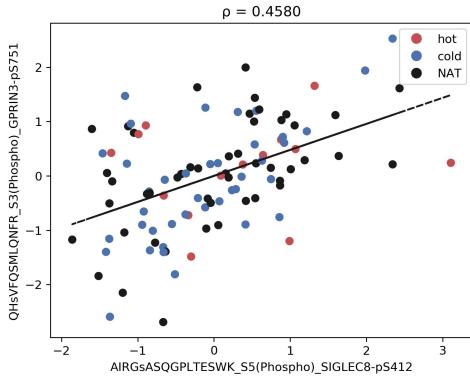
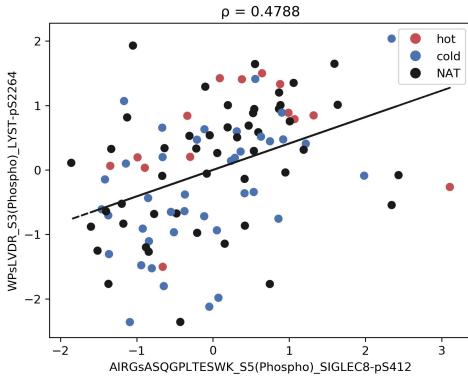
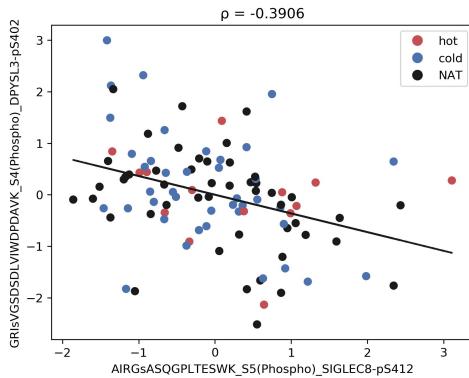
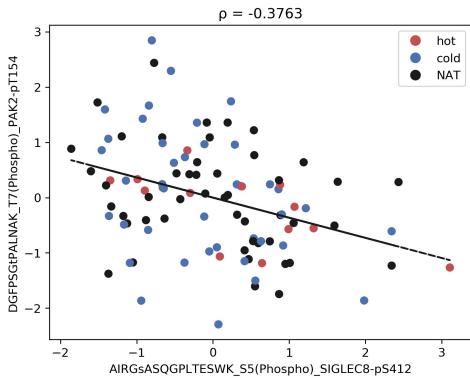
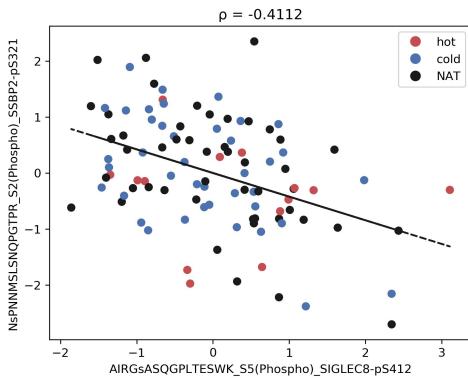
SIGLEC5-pS522



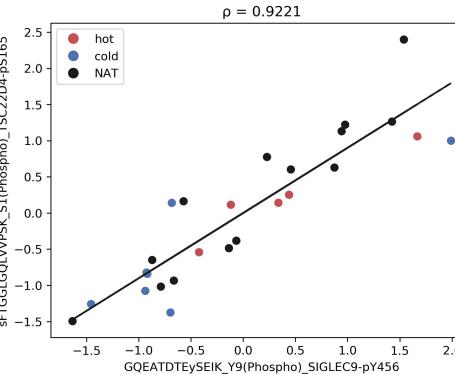
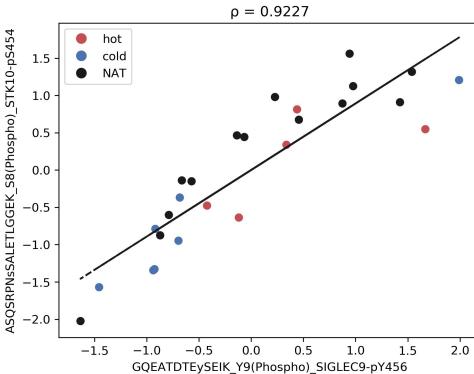
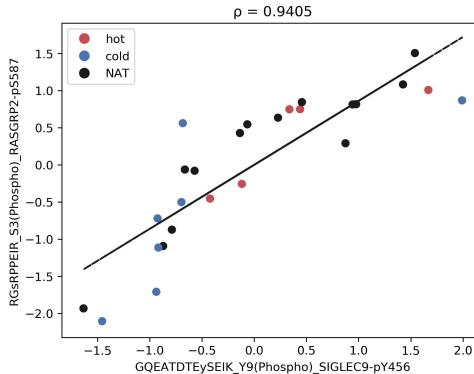
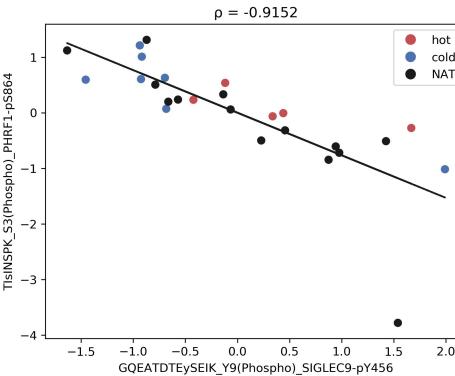
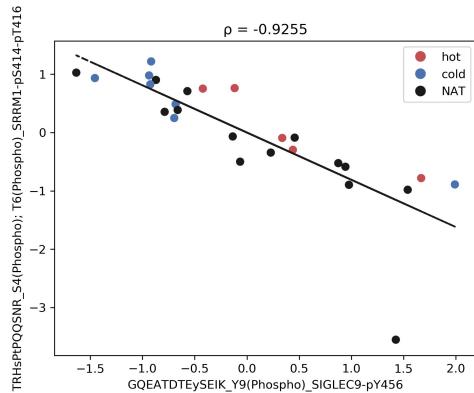
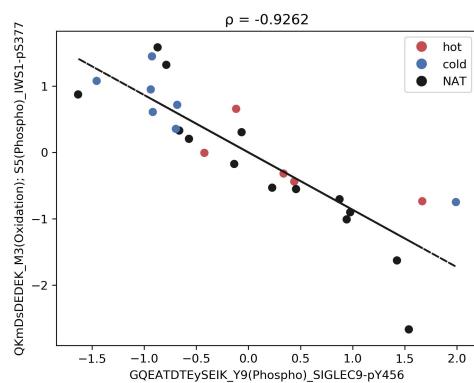
SIGLEC7-pS406



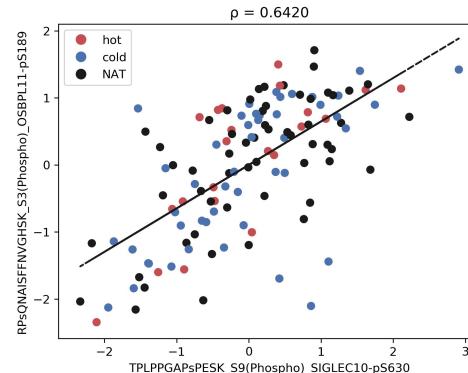
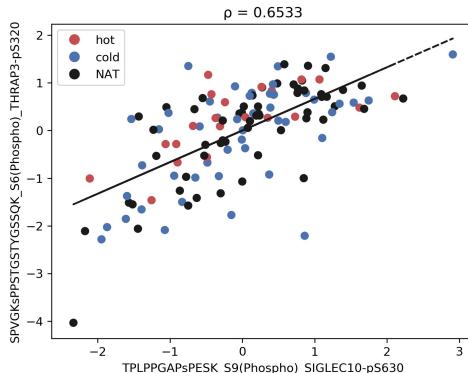
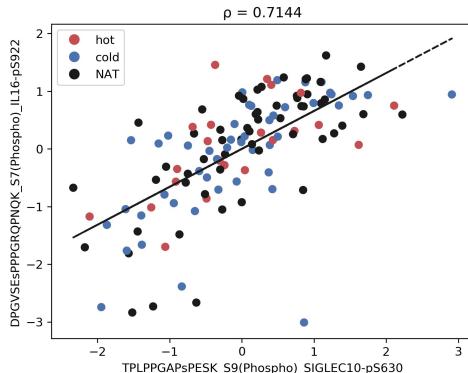
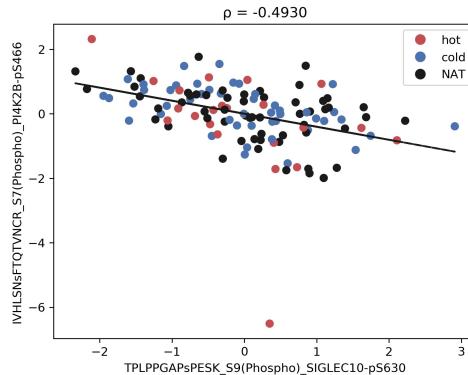
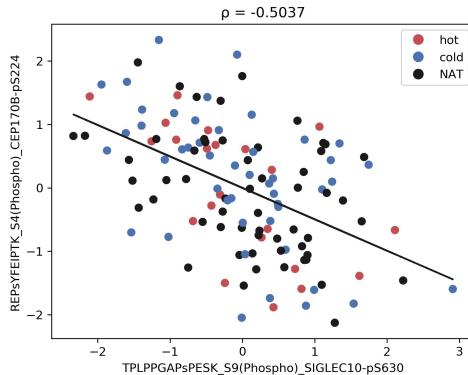
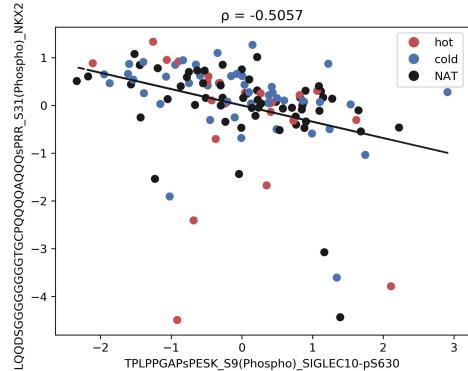
SIGLEC8-pS412



SIGLEC9-pY456

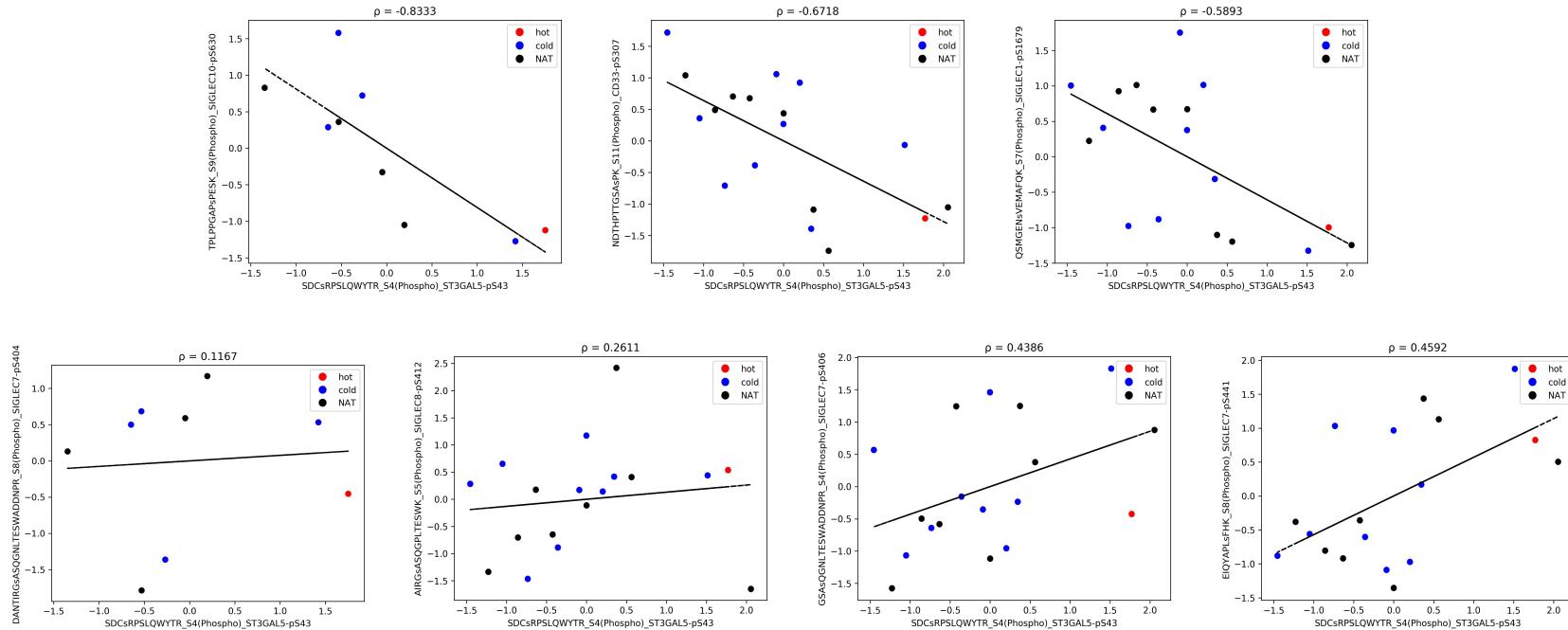


SIGLEC10-pS630

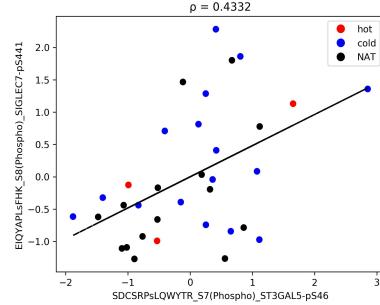
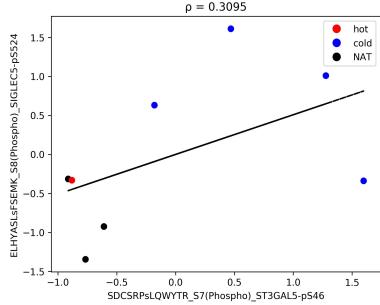
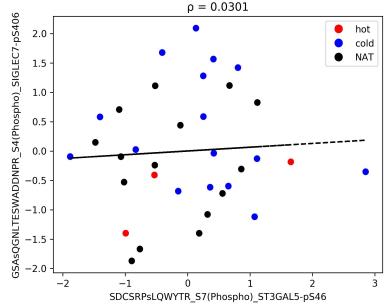
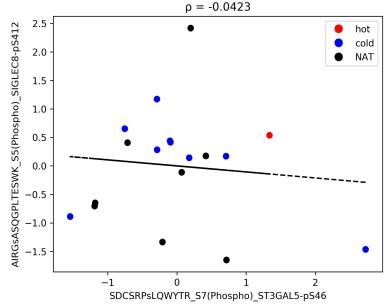
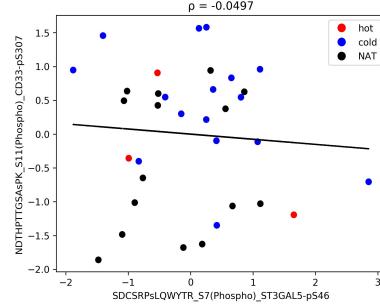
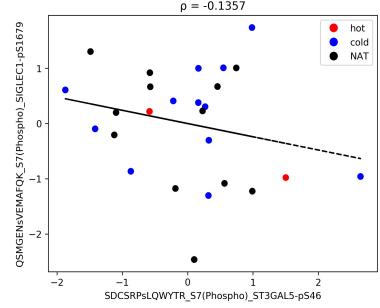
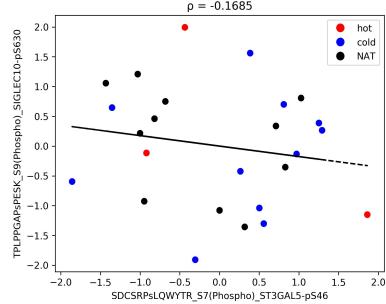
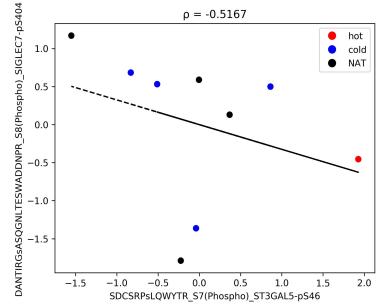


SIGLEC-Sialyltransferase Correlations

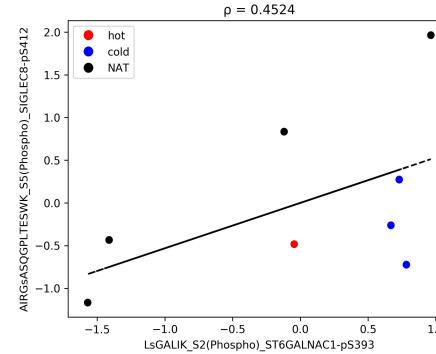
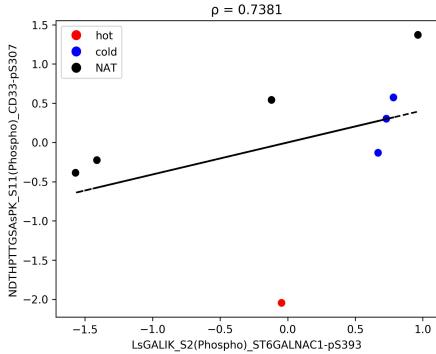
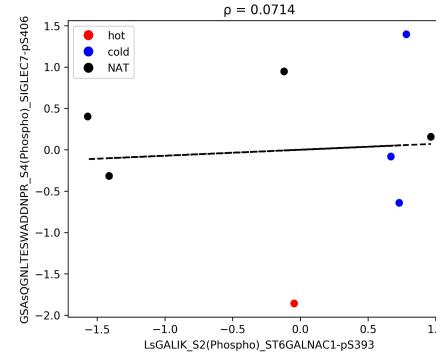
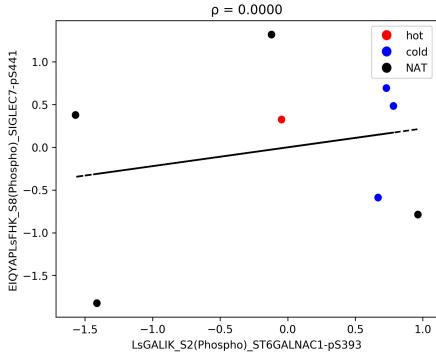
ST3GAL5-pS43 and SIGLECs



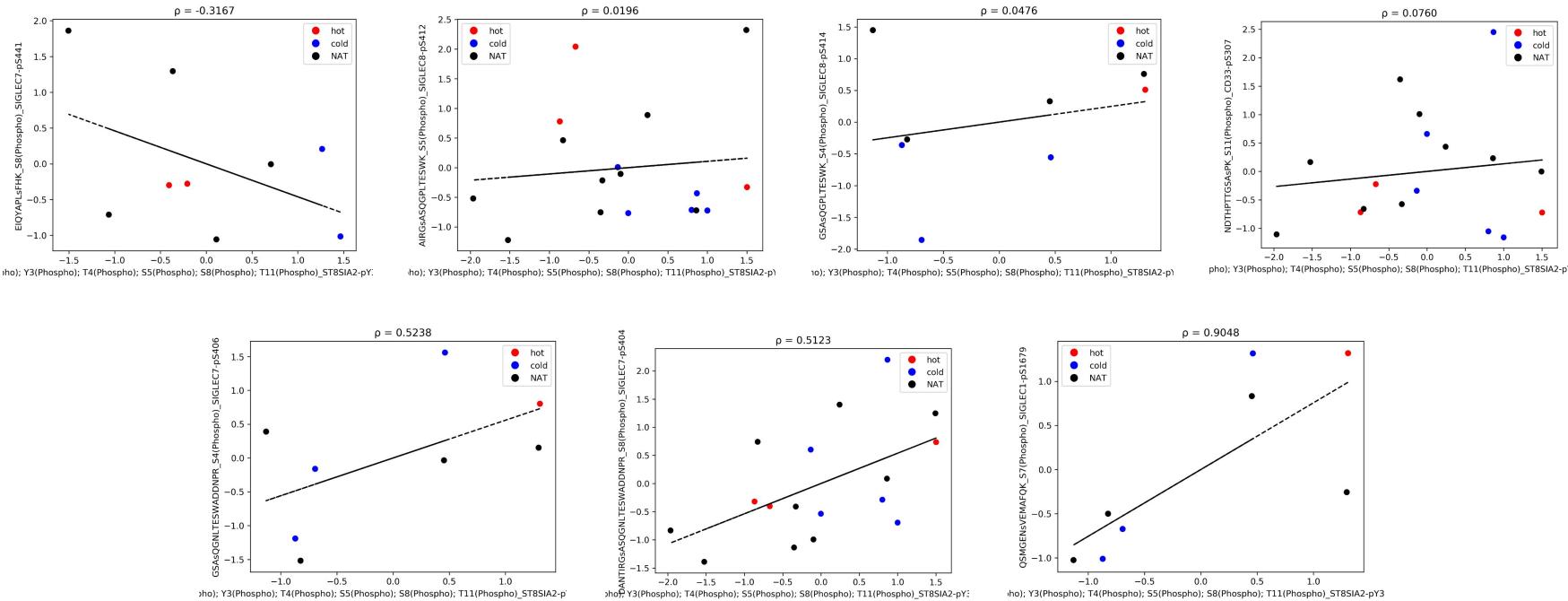
ST3GAL5-pS46 and SIGLECs



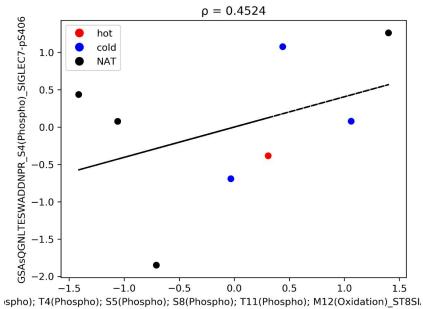
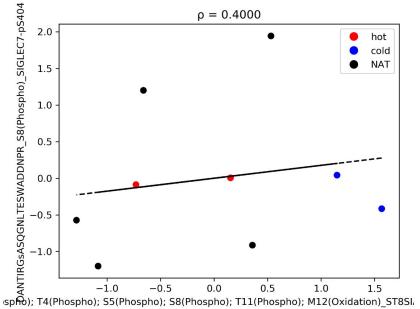
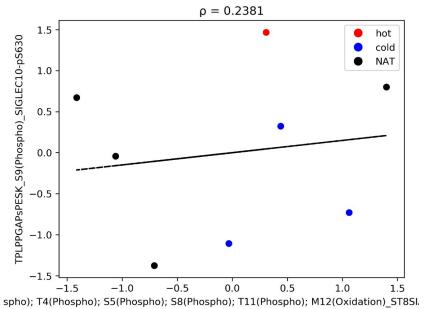
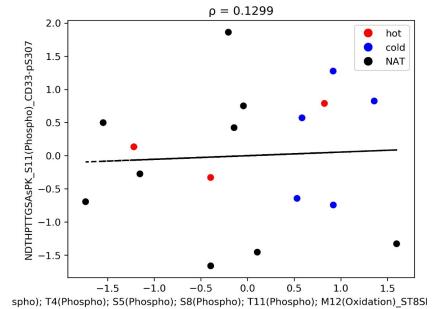
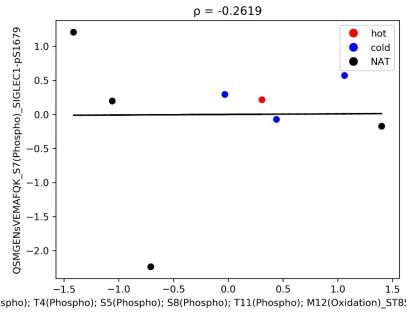
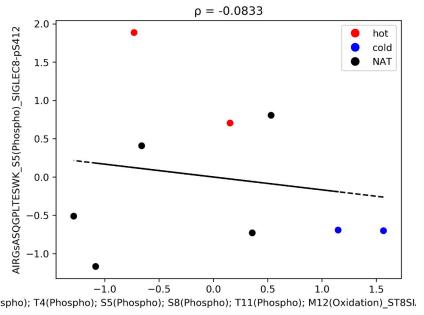
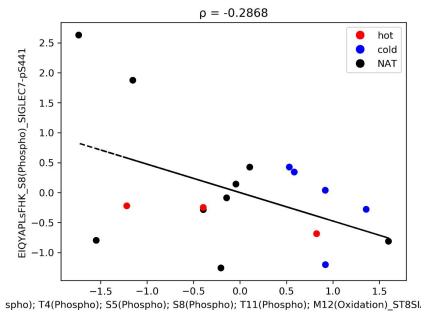
ST6GALNAC1-pS393 and SIGLECs



ST8SIA2-pY337 and SIGLECs



ST8SIA2-pY339 and SIGLECs



Future Work

- Lung cancer-specific biomarkers
- Peptides that aren't well characterized
- Other datasets