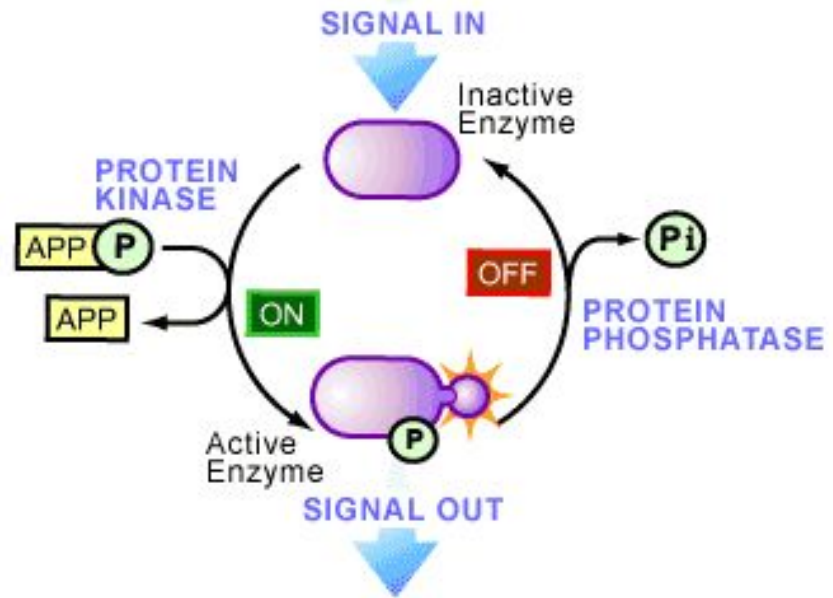


# Cell Type Deconvolution by Phosphoproteomics

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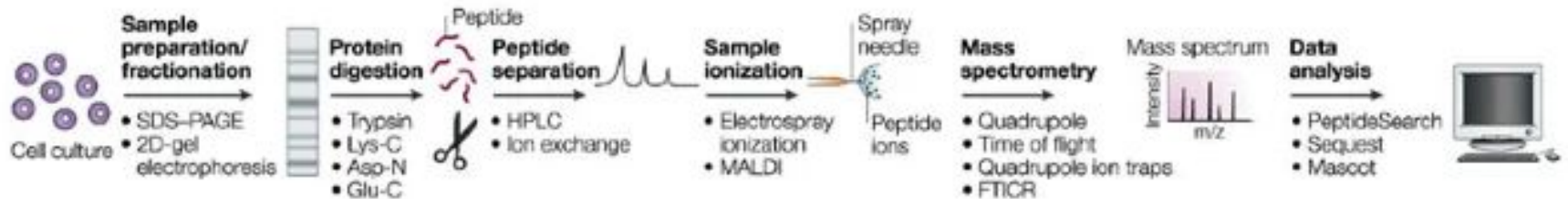
# Background

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



# Background

- Phosphoproteomics
- Mass spectrometry



# Project Overview

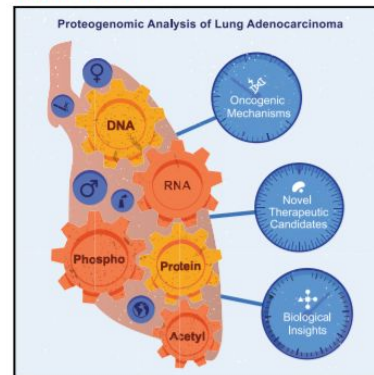
- Identify cell types in tumor tissue samples based on bulk phosphoproteomic data
- Data from a 2020 study in *Cell*
- Started by doing correlation analysis

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 (*STK11*)
- Phospho and acetyl modifications denote tumor-specific markers and druggable proteins

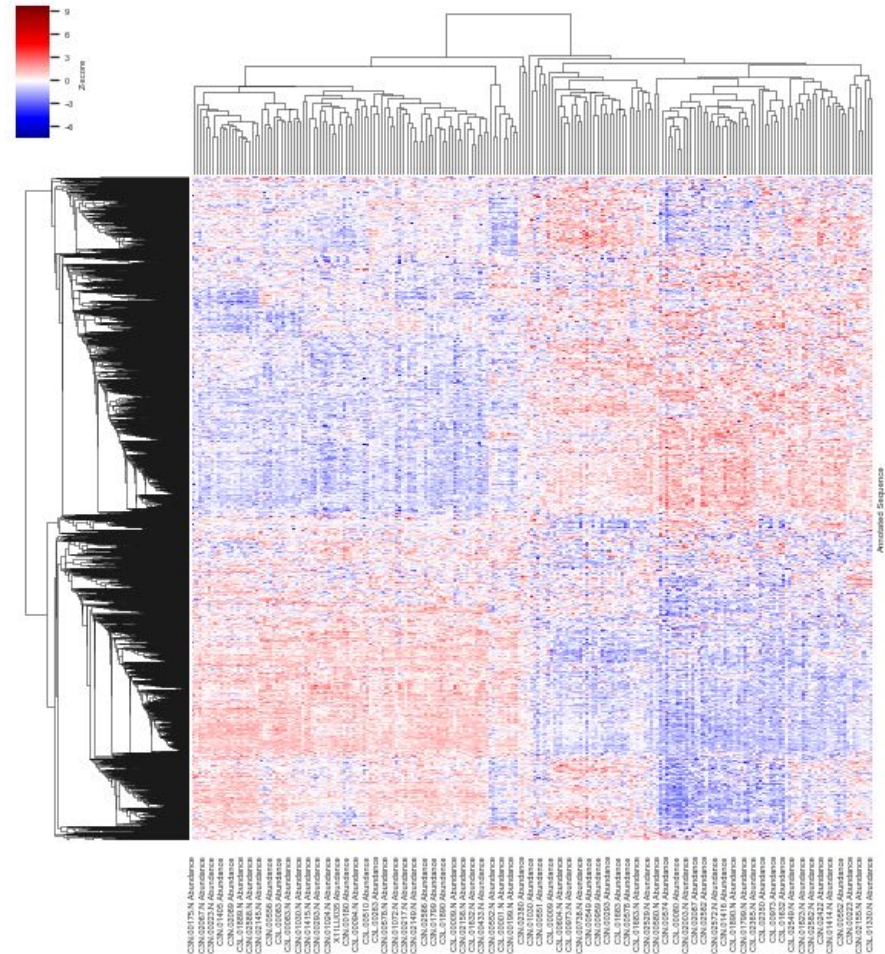


Gillette et al., 2020, Cell 182, 200–225  
July 9, 2020 © 2020 Elsevier Inc.  
<https://doi.org/10.1016/j.cell.2020.06.013>

CellPress

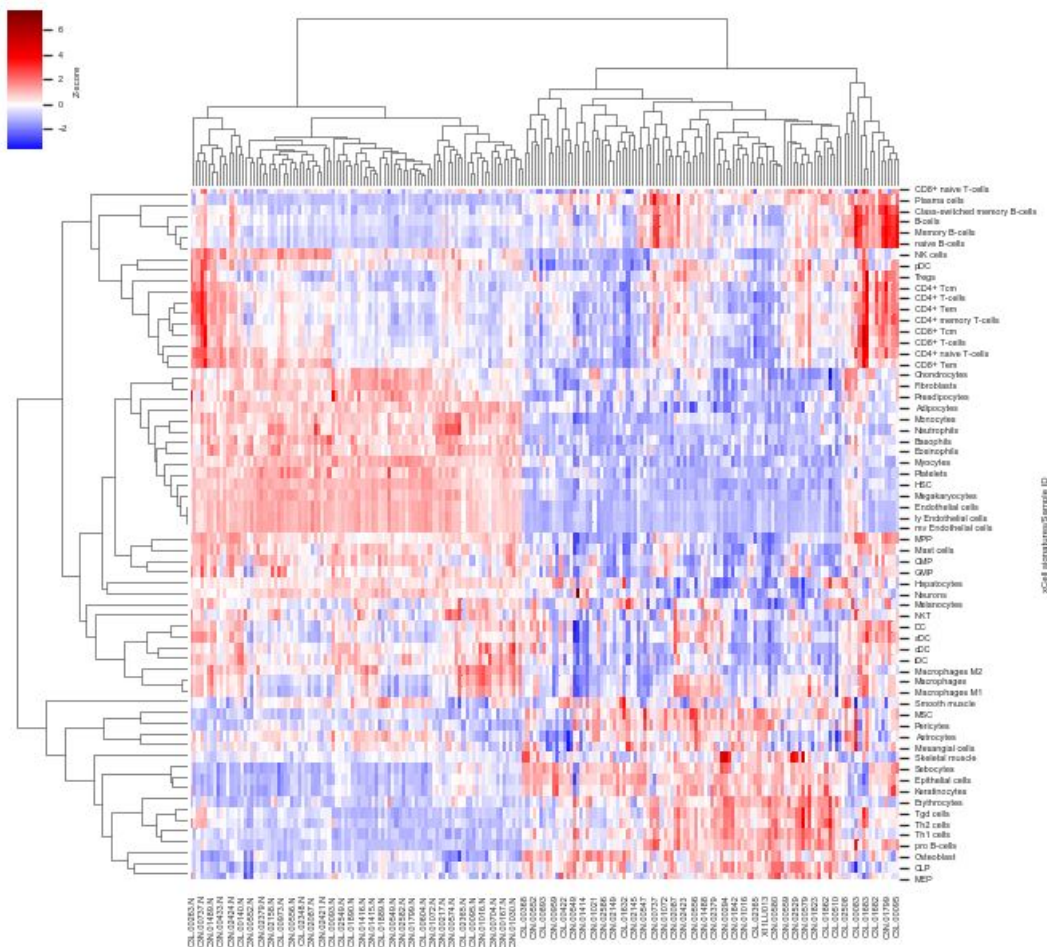
# Phosphopeptide vs. Sample Heatmap

- 5256 peptides
- 211 samples

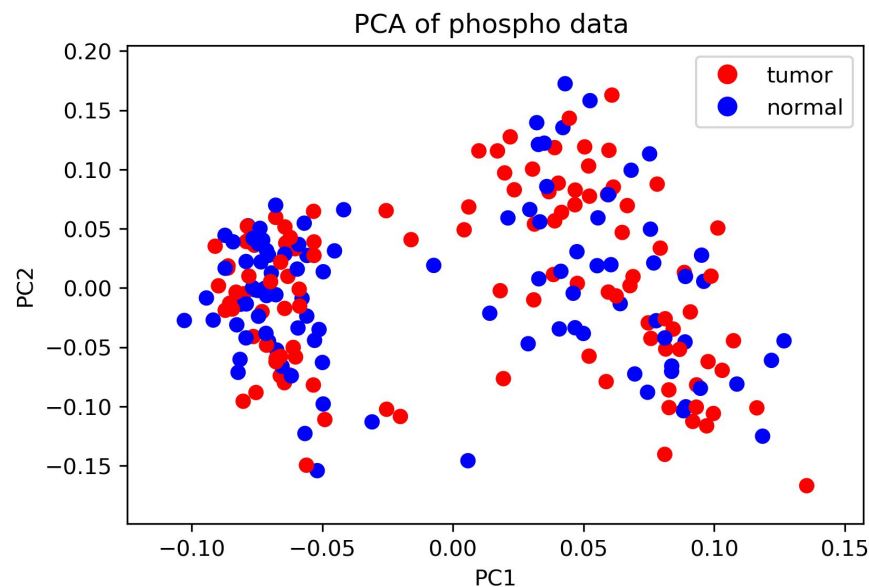
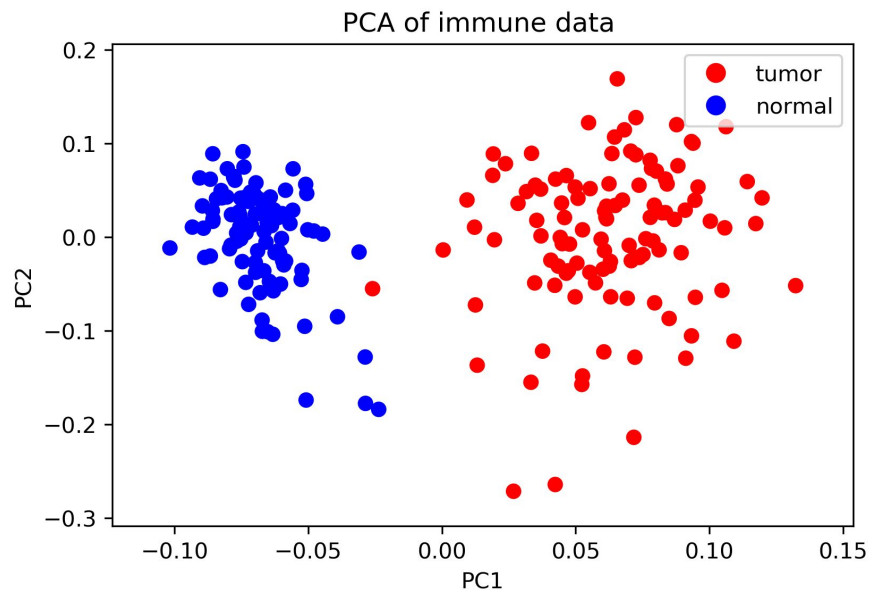


# Immune Cell vs. Sample Heatmap

- 64 immune cells
- 211 samples



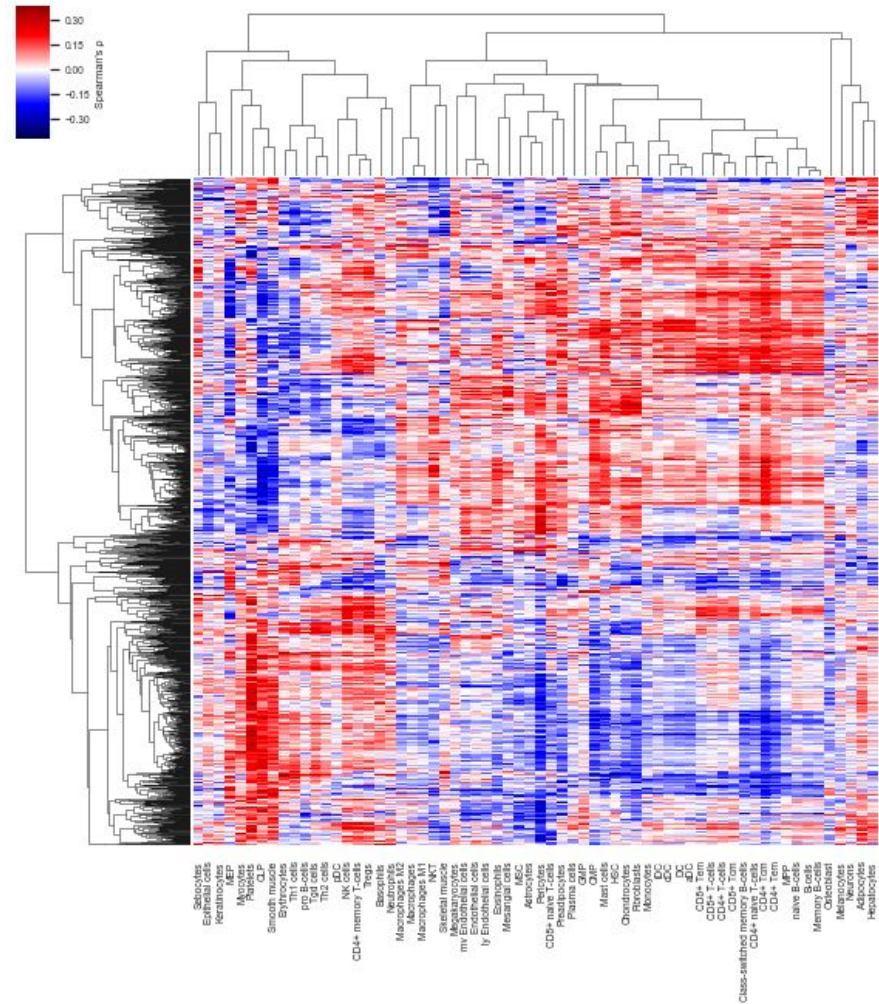
# Principal Component Analysis (PCA)





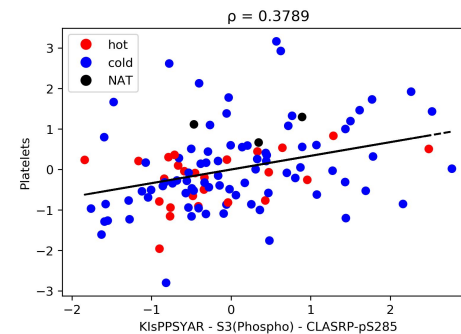
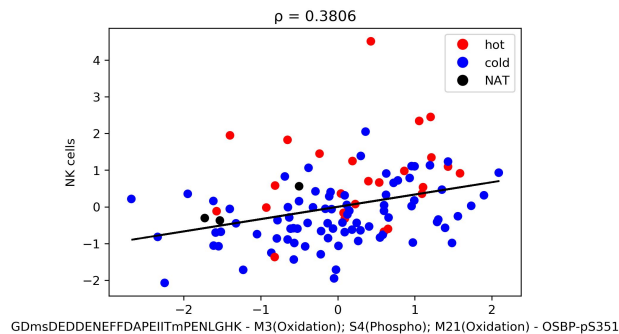
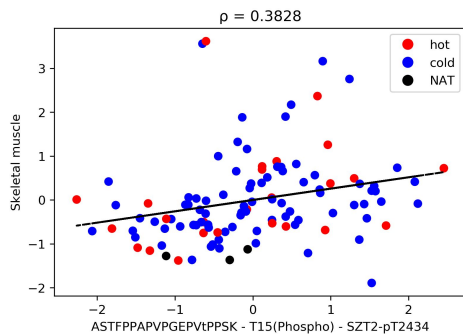
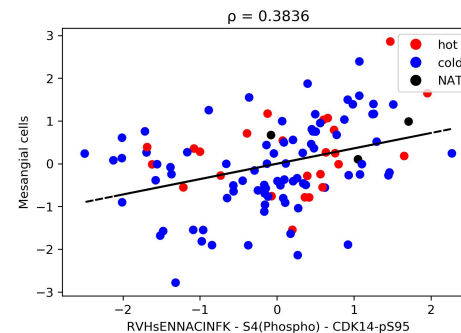
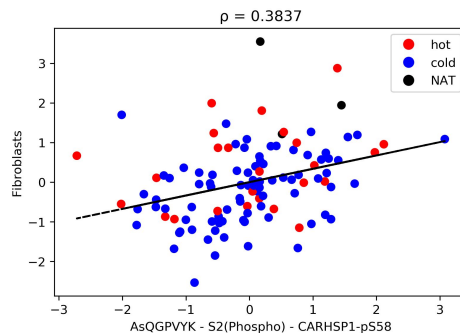
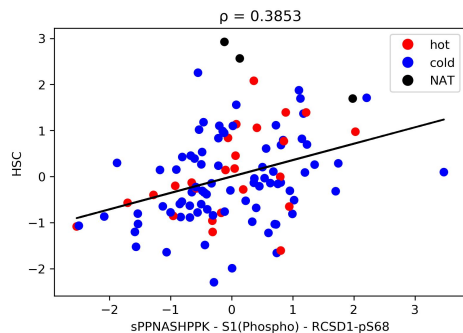
# Phosphopeptide vs. Immune Cell Heatmap

- 1584 peptides
- 64 immune cells

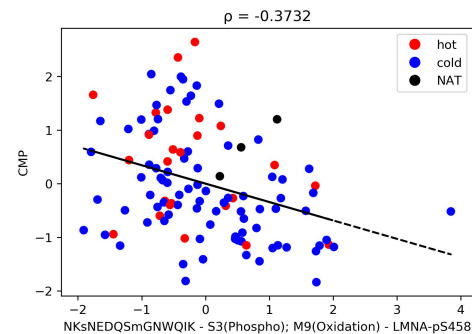
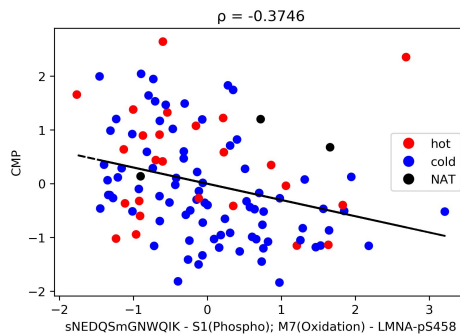
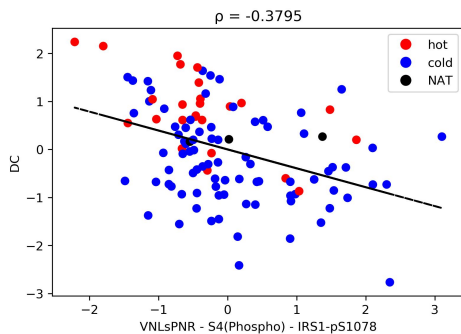
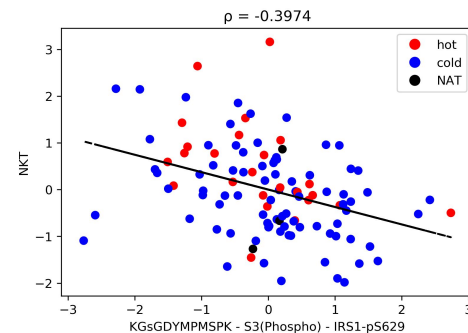
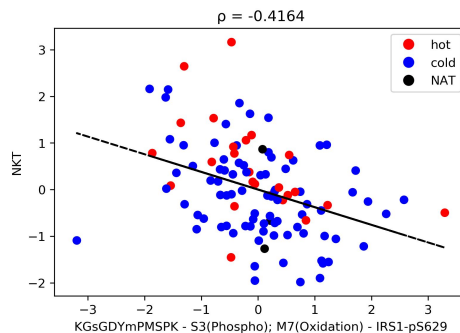
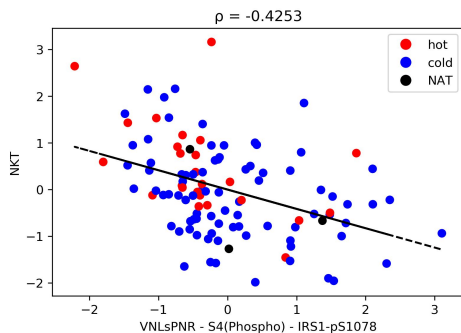




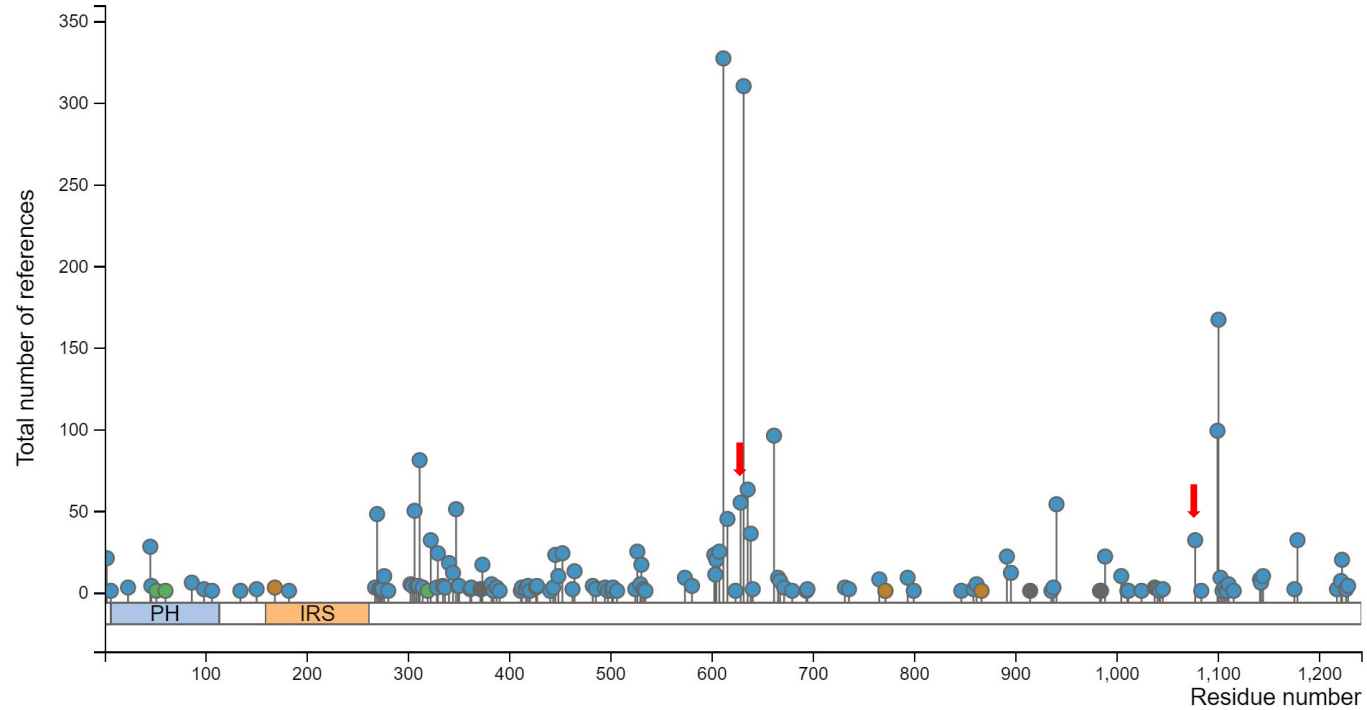
# Most Correlated Peptides and Immune Cells



# 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

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A193 ALDOC

|    | A       | B               | C                      | D             | E             | F                 | G                  | H                     | I           | J            | K             | L          | M                 | N       | O       |
|----|---------|-----------------|------------------------|---------------|---------------|-------------------|--------------------|-----------------------|-------------|--------------|---------------|------------|-------------------|---------|---------|
| 1  | gene    | Uniprot Protein | Aliases                | localization  | cells         |                   | 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    | intracellular | LTI           |                   | Th2                | NCR+ ILC3             | NCR-ILC3    | Th17         |               |            |                   |         |         |
| 3  | ALDH1L1 | O75891          | Cytosolic 1 ALDH1L1    | FTHFD         | astrocyte     |                   |                    |                       |             |              |               |            |                   |         |         |
| 4  | ARG1    | P05089          | Arginase-1 ARG1        |               | intracellular | m2c micro         | macroph            | ILC2                  |             |              |               |            |                   |         |         |
| 5  | AXL     | P30530          | Tyrosine-p AXL UFO     |               | extracellular | tissue associated | Mac                |                       |             |              |               |            |                   |         |         |
| 6  | BACH2   | O9BYV9          | Transcript BACH2       |               | intracellular | germinal center   | B                  |                       |             |              |               |            |                   |         |         |
| 7  | BATF    | Q16520          | Basic leuc BATF        |               | intracellular | Tfh               | Th2                | Th2                   | Th17        |              |               |            |                   |         |         |
| 8  | BATF3   | O9NR55          | Basic leuc BATF3       | SN1           | intracellular | classical D       | Th17               |                       |             |              |               |            |                   |         |         |
| 9  | BTLA    | Q27649          | B- and T-ly BTLA       |               | extracellular | follicular Th     |                    |                       |             |              |               |            |                   |         |         |
| 10 | CCL1    | P22362          | C-C motif (CCL1) SCYA  | secreted      | M2a           | M2b               |                    |                       |             |              |               |            |                   |         |         |
| 11 | CCL11   | P51671          | Eotaxin (C-CCL11) SCY  | secreted      | M1            | m1 microglia      |                    |                       |             |              |               |            |                   |         |         |
| 12 | CCL14   | Q16627          | C-C motif (CCL14) NCC  | secreted      | M2a           |                   |                    |                       |             |              |               |            |                   |         |         |
| 13 | CCL15   | Q16663          | C-C motif (CCL15) MIF  | secreted      | M1            | m1 microglia      |                    |                       |             |              |               |            |                   |         |         |
| 14 | CCL16   | O15467          | C-C motif (CCL16) IL18 | secreted      | M2c           | m2c microglia     |                    |                       |             |              |               |            |                   |         |         |
| 15 | CCL17   | O92583          | C-C motif (CCL17) SCY  | secreted      | M2a           |                   |                    |                       |             |              |               |            |                   |         |         |
| 16 | CCL18   | P55774          | C-C motif (CCL18) AM   | secreted      | M2a           | m2c micro         | M2c                |                       |             |              |               |            |                   |         |         |
| 17 | CCL19   | O99731          | C-C motif (CCL19) ELC  | secreted      | M1            | m1 microglia      |                    |                       |             |              |               |            |                   |         |         |
| 18 | CCL2    | P13500          | C-C motif (CCL2) MCP   | secreted      | M1            | M2a               | m1 microglia       |                       |             |              |               |            |                   |         |         |
| 19 | CCL20   | P78556          | C-C motif (CCL20) LAR  | secreted      | M1            | M2b               | m1 microglia       |                       |             |              |               |            |                   |         |         |
| 20 | CCL22   | O00626          | C-C motif (CCL22) MD   | secreted      | M2a           |                   |                    |                       |             |              |               |            |                   |         |         |
| 21 | CCL23   | P55773          | C-C motif (CCL23) MIF  | secreted      | M2a           |                   |                    |                       |             |              |               |            |                   |         |         |
| 22 | CCL24   | O00175          | C-C motif (CCL24) MP   | secreted      | M2a           |                   |                    |                       |             |              |               |            |                   |         |         |
| 23 | CCL26   | O9Y258          | C-C motif (CCL26) SCY  | secreted      | M2a           |                   |                    |                       |             |              |               |            |                   |         |         |
| 24 | CCL3    | P10147          | C-C motif (CCL3) GOS1  | secreted      | M1            | m1 micro          | effector CI        | basophil              | ILC1        |              |               |            |                   |         |         |
| 25 | CCL4    | P13236          | C-C motif (CCL4) LAG3  | secreted      | M1            | m1 micro          | effector CD8       | T                     |             |              |               |            |                   |         |         |
| 26 | CCL5    | P13501          | C-C motif (CCL5) D175  | secreted      | M1            | m1 micro          | M2d                | effector CD8          | T           |              |               |            |                   |         |         |
| 27 | CCL8    | P80075          | C-C motif (CCL8) MCP   | secreted      | M1            | m1 microglia      |                    |                       |             |              |               |            |                   |         |         |
| 28 | CCR1    | P32246          | C-C chem CCR1          | CMK           | extracellular | Th1               |                    |                       |             |              |               |            |                   |         |         |
| 29 | CCR10   | P46092          | C-C chem CCR10         | GPI           | extracellular | Th22              |                    |                       |             |              |               |            |                   |         |         |
| 30 | CCR2    | P41597          | C-C chem CCR2          | CMK           | extracellular | M2c               | classical monocyte |                       |             |              |               |            |                   |         |         |
| 31 | CCR3    | P51677          | C-C chem CCR3          | CMK           | extracellular | basophil          | eosinophil         | Th2                   |             |              |               |            |                   |         |         |
| 32 | CCR4    | P51679          | C-C chem CCR4          | CMK           | extracellular | Th2               | Th17               | Th22                  |             |              |               |            |                   |         |         |
| 33 | CCR5    | P51681          | C-C chem CCR5          | CMK           | extracellular | Th1               | macrophage         | intermediate monocyte |             |              |               |            |                   |         |         |
| 34 | CCR6    | P51684          | C-C chem CCR6          | CKR1          | extracellular | Th17              | Th22               | LTI                   | NCR-ILC3    |              |               |            |                   |         |         |
| 35 | CCR7    | P32248          | C-C chem CCR7          | CMK           | extracellular | classical D       | LTI                | naive CD8             | T           |              |               |            |                   |         |         |
| 36 | CCR8    | P51685          | C-C chem CCR8          | CKR1          | extracellular | Th2               |                    |                       |             |              |               |            |                   |         |         |
| 37 | CCR9    | P51686          | C-C chem CCR9          | GPR           | extracellular | ILC2              |                    |                       |             |              |               |            |                   |         |         |
| 38 | CD101   | O93033          | Immunogl CD101         | EW            | extracellular | Treg              |                    |                       |             |              |               |            |                   |         |         |
| 39 | CD14    | P08571          | Monocyte CD14          |               | extracellular | monocytic         | intermedi          | classical m           | classical D | inflamm      | macroph       | neutrophil | tissue associated | Mac     |         |
| 40 | CD151   | P48509          | CD151 ant CD151        | TSF           | extracellular | platelet          |                    |                       |             |              |               |            |                   |         |         |
| 41 | CD160   | O95971          | CD160 ant CD160        | BY1           | extracellular | NKT               |                    |                       |             |              |               |            |                   |         |         |
| 42 | CD163   | Q86V87          | Scavenger CD163        | M1            | extracellular | m2a micro         | macroph            | M2a                   | M2c         | classical m  | m2c microglia |            |                   |         |         |
| 43 | CD164   | Q04900          | Slalomuc CD164         |               | extracellular | stem cells        |                    |                       |             |              |               |            |                   |         |         |
| 44 | CD177   | Q8N6Q3          | CD177 ant CD177        | NB            | extracellular | neutrophil        |                    |                       |             |              |               |            |                   |         |         |
| 45 | CD180   | O99467          | CD180 ant CD180        | LYE           | extracellular | Marginal Zone     | B                  |                       |             |              |               |            |                   |         |         |
| 46 | CD19    | P15391          | B-lymphoc CD19         |               | extracellular | B                 | Marginal           | 2                     | memory B    | regulatory B |               |            |                   |         |         |

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