Supplementary Information: Predicting Causal Relationships from Biological Data: Applying Automated Causal Discovery on Mass Cytometry Data of Human Immune Cell

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Abstract
Learning the causal relationships that define a molecular system allows us to predict how the system will respond to different interventions. Distinguishing causality from mere association typically requires randomized experiments. Methods for automated causal discovery from limited experiments exist, but have so far rarely been tested in systems biology applications. In this work, we apply state-of-the art causal discovery methods on a large collection of public mass cytometry data sets, measuring intra-cellular signaling proteins of the human immune system and their response to several perturbations. We show how different experimental conditions can be used to facilitate causal discovery, and apply two fundamental methods that produce context-specific causal predictions. Causal predictions were reproducible across independent data sets from two different studies, but often disagree with the KEGG pathway databases. Within this context, we discuss the caveats we need to overcome for automated causal discovery to become a part of the routine data analysis in systems biology.

Supplementary Information This document provides supplementary information for the article *Predicting Causal Relationships from Biological Data: Applying Automated Causal Discovery on Mass Cytometry Data of Human Immune Cell*.

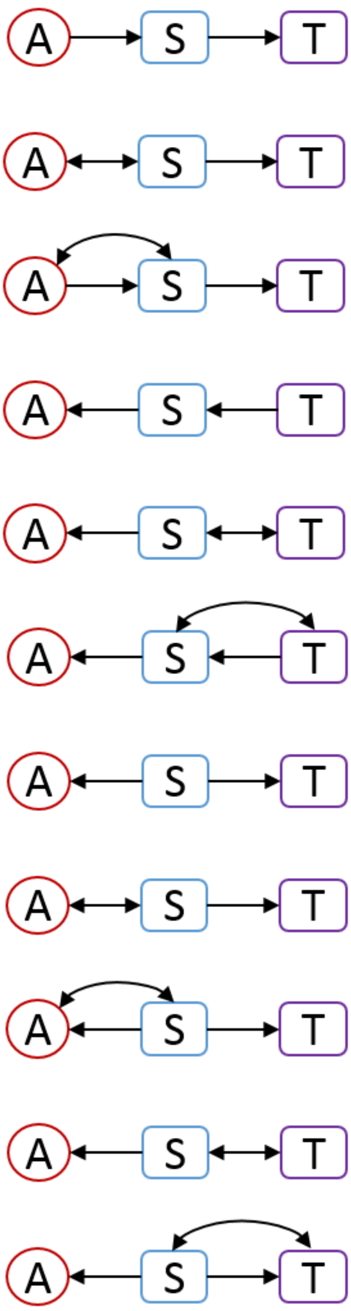

Figure 1. All possible networks for three variables A, S, T that entail A⊥ T|S allowing for confounding and no background knowledge. A bi-directed edge denotes the presence of at least one confounder that causes both endpoints.

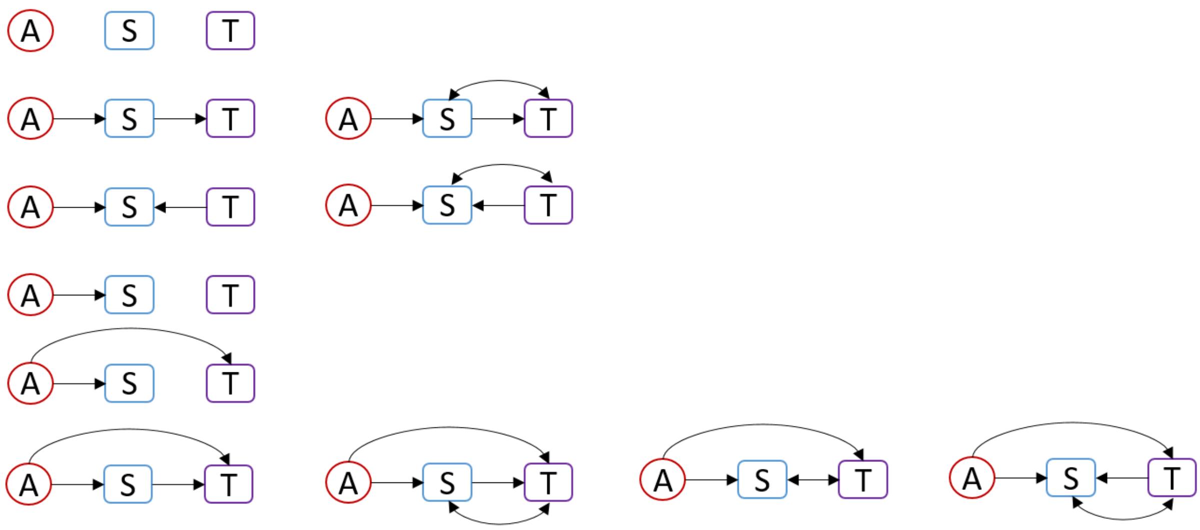

Figure 2. All possible networks for three variables A, S, T where A is known uncaused entity, in the presence of latent confounders. A bi-directed edge denotes the presence of at least one confounder that causes both endpoints.

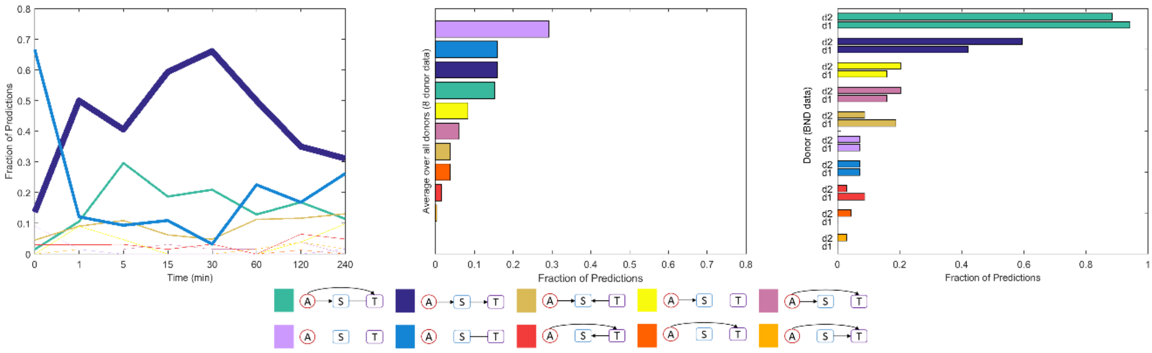

Figure 3. Distribution of highest-scoring networks for CLCD predictions in independent data sets. (left) Different time-points, (middle) different donors, (right) a matching population in bone marrow data from[1] .

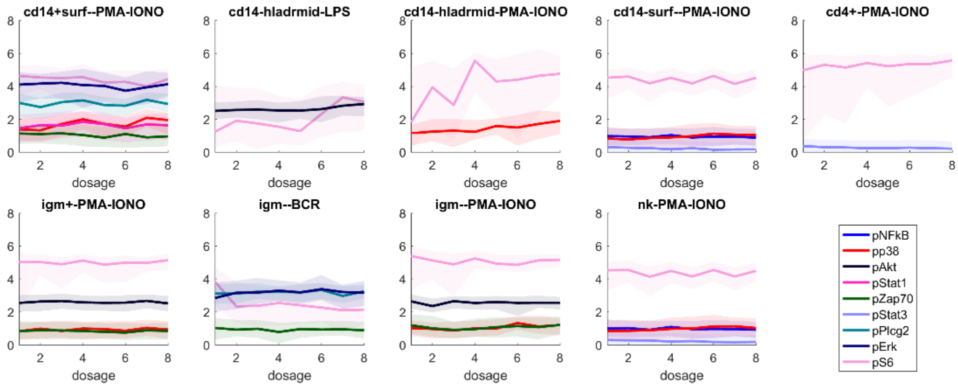

Figure 4. Response of pS6 and its CLCD predicted targets for different Rapamycin dosages

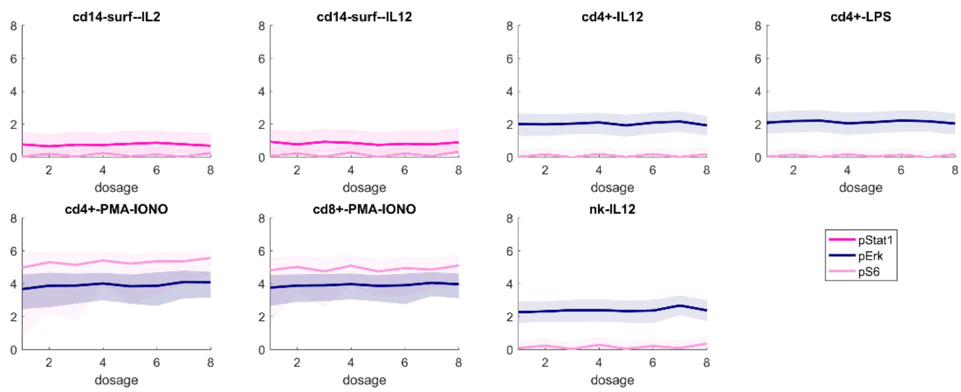

Figure 5. Response of pS6 and its BACKSHIFT predicted targets for different Rapamycin dosages

Supplementary Discussion 1: CLCD hyper-parameters sensibility analysis.

The operation of the Conservative Local Causal Discovery (CLCD) presented in the main paper depends upon three hyper-parameters: the dependence threshold α, the independence threshold β and the number N of replicated datasets where the triplet is confirmed. We perform a sensitivity analysis for these hyper-parameters, assessing whether and how their change would affect our results and conclusion.

We repeated the CLCD analysis by varying α in [0.05, 0.01, 0.005, 0.001], β in [0.1, 0.15, 0.2, 0.25] and setting N to each integer number between 5 and 15.

Supplementary Figures 6 and 7 report the average number of triplets for each value of N and for β set to 0.15 or α set to 0.001, respectively. Both figures shows the same trend: the number of triplets rapidly decreases as the number of replicated datasets increases. The vertical bars show the variations due to changes in α and in β, respectively. Notably, the number of triplets is influenced more heavily by the number N of replicated datasets than by α and β.

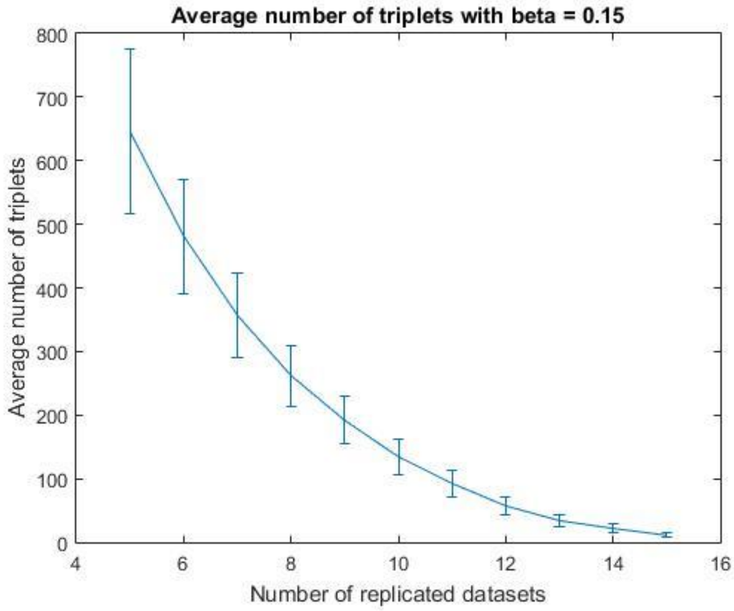

Figure 6. Number of triplets for different number of replicated datasets (x-axis) and beta hyper-parameter set to 0.15. Each point reports the average number of triplets across alpha values, while the vertical bars indicate the respective standard variation.

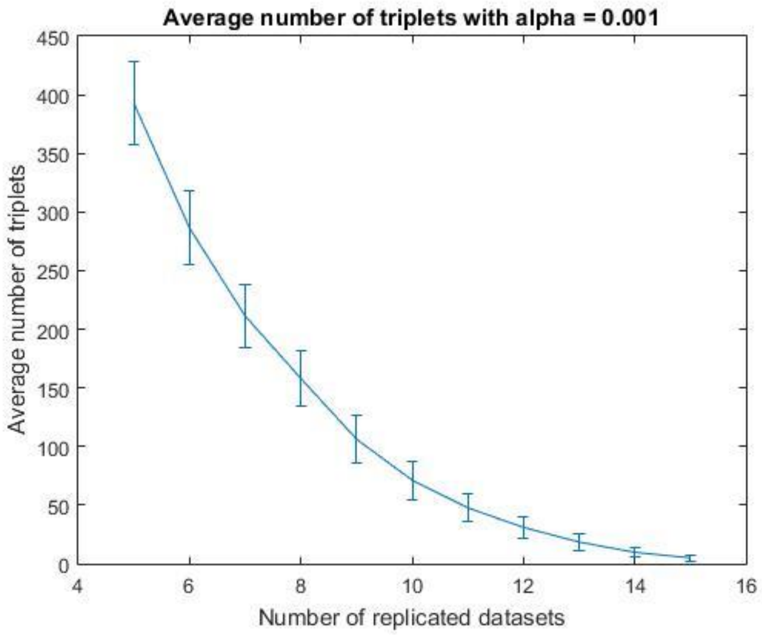

Figure 7: Number of triplets for different number of replicated datasets (x-axis) and alpha hyper-parameter set to 0.001. Each point reports the average number of triplets across beta values, while the vertical bars indicate the respective standard variation.

We then proceed to validate the triplets found for N in [5, 7, 10, 12] against the KEGG databases with the same procedure described in the main text, setting α and β to the same values used in the main paper (0.001 and 0.15, respectively). The results are reported in Supplementary Figure 8 to Figure 11:

it is possible to observe that changing the number of replicated datasets does not remarkably alter the trends in the validation results, neither the final conclusions.

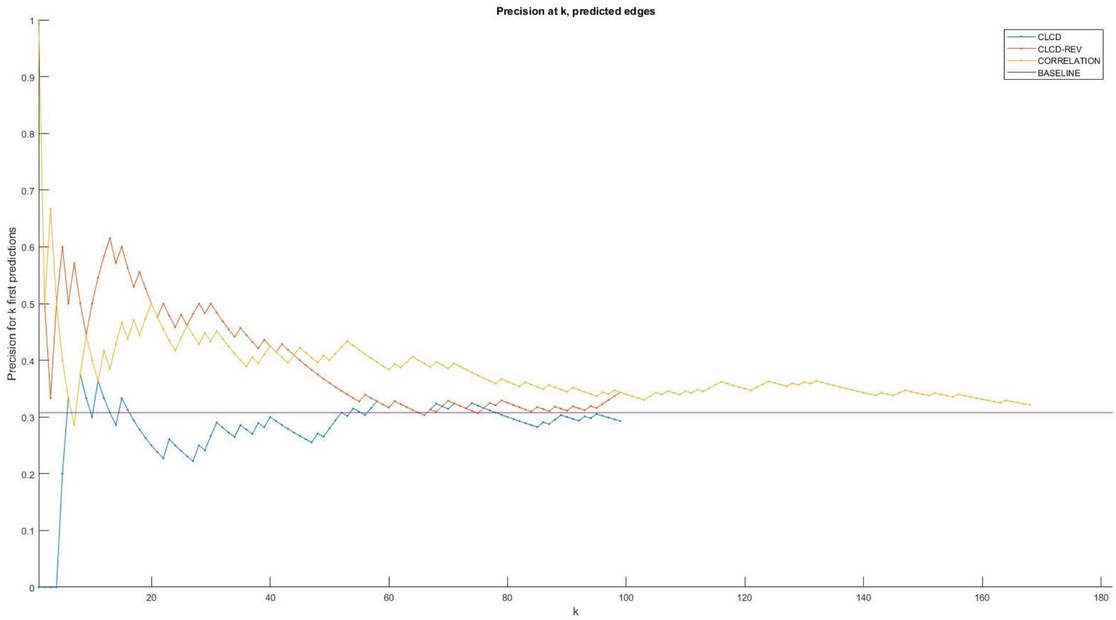

Figure 8: Precision of CLCD predictions in KEGG human pathways for number of replicated datasets set to 5. Details as in Fig.6 of the main text.

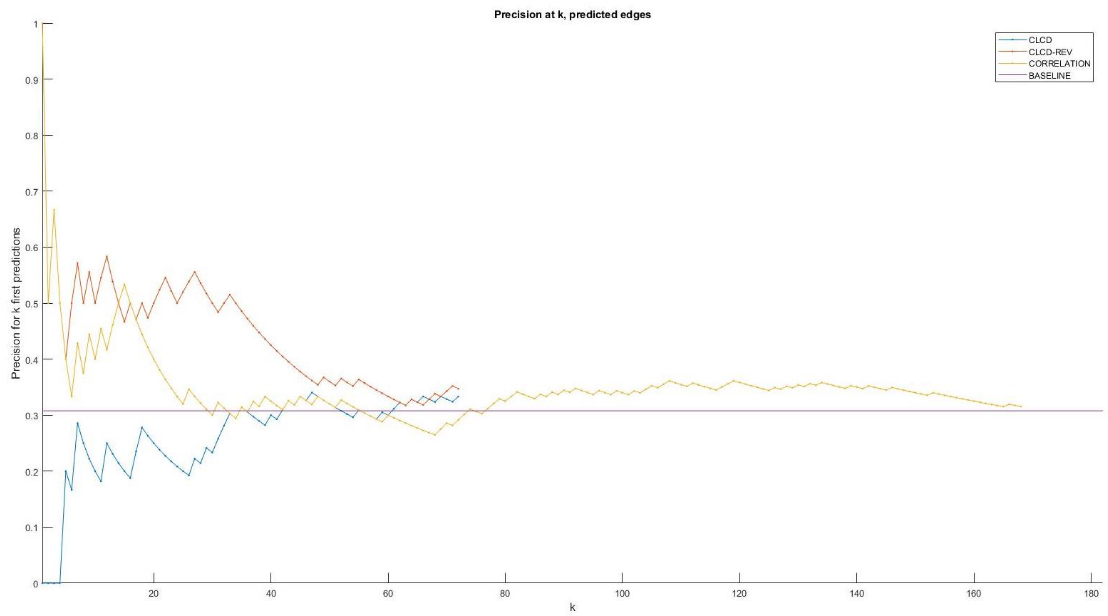

Figure 9: Precision of CLCD predictions in KEGG human pathways for number of replicated datasets set to 7. Details as in Fig.6 of the main text.

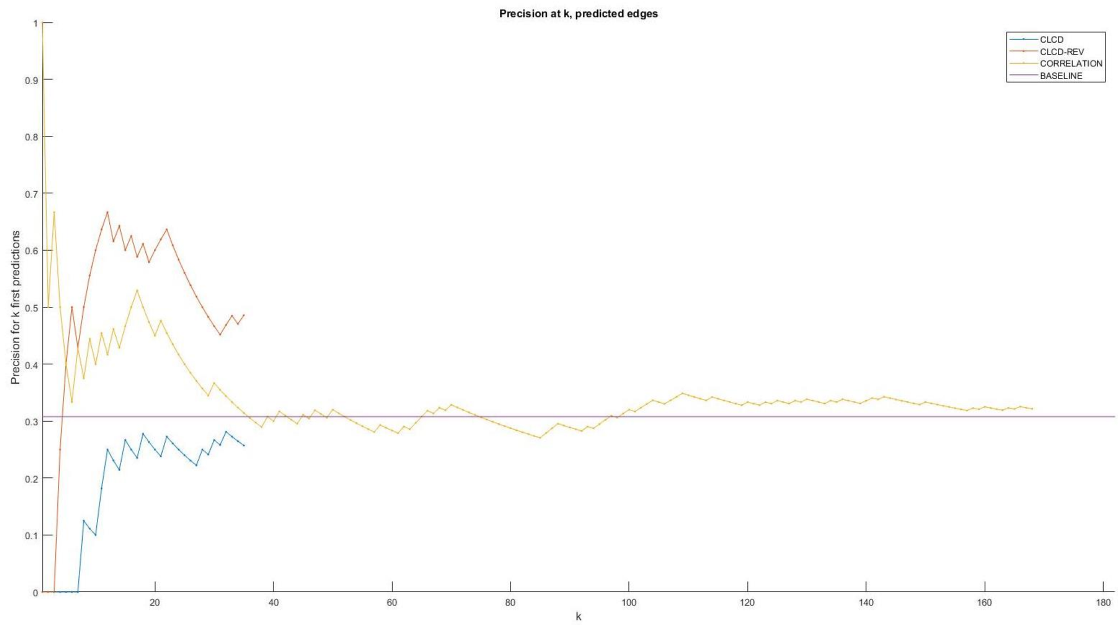

Figure 10: Precision of CLCD predictions in KEGG human pathways for number of replicated datasets set to 10 (as in the main analysis). Details as in Fig.6 of the main text.

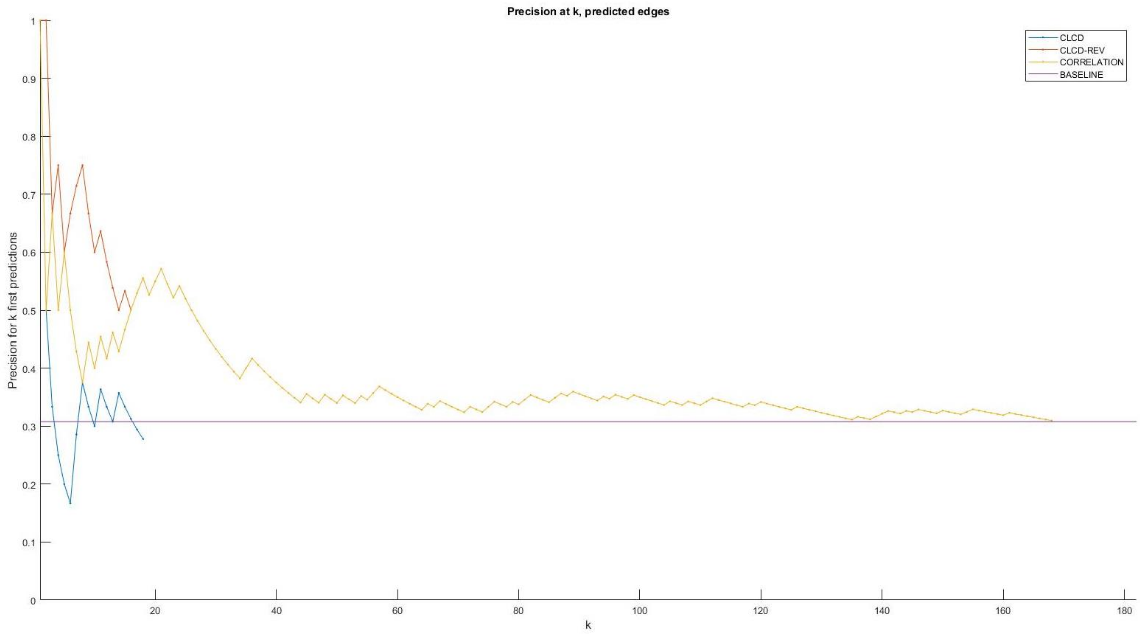

Figure 11: Precision of CLCD predictions in KEGG human pathways for number of replicated datasets set to 12. Details as in Fig.6 of the main text.

Table 1. Proteins and activators measured in[1]and[2].

Functional proteins		Activators	
Bodenmiller et al. (2012)	Bendall et al. (2011)	Bodenmiller et al. (2012)	Bendall et al. (2011)
pNkfb	pNkfb	BCR	BCR
pp38	pp38	GCSF	GCSF
pStat5	pStat5	IFNa	IFNa
pAkt		LPS	LPS
pStat1		PMA-Iono	PMA-Iono
pSHP2	pSHP2	PVO4	PVO4
pZap70/pSyk	pZap70/pSyk	IFN-g	
pSlp76/BLNK	pSlp76/BLNK	IL-2	
pBtk	pBtk	IL-3	IL-3
pPlcg2	pPlcg2	IL-12	
pStat3	pStat3	GMCSF	GMCSF
pErk	pErk		IL-7
pLat			SCF
pS6	pS6		TNFα
	Ki67		TPO
	pCrkL		Flt3L
	pMAPKAPK2		
	IkBa		
	pH3		
	pSrcFK		
	pCREB		

Table 2. Gated subpopulations in[1]and[2].

Population	**Subpopulations in Bodenmiller et al. (2012)**	**Subpopulations in Bendall et al. (2011)**
Monocytes	CD14+HLA-DR-, CD14+HLA-DR^{high} CD14+HLA-DR^{mid} CD14-HLA-DR- CD14-HLA-DR^{high} CD14-HLA-DR^{mid}	CD11b- Monocyte CD11b^{mid} Monocyte CD11b^{hi} Monocyte
T-cells	CD4+	Mature CD4+ T Naive CD4+ T
	CD8+	Naive CD8+ T Mature CD8+ T
NK	NK	NK
B-cells	Igm+ Igm-	Pre-B II Mature CD38^{lo} B Pre-B I Mature CD38^{mid} B Immature B
Dendritic cells	Dendritic	Plasmacytoid DC

Table 3. CLCD and BACKSHIFT predictions.

Algorithm	Population	Activator	Source	Target
CLCD	CD14+HLA-DR-	pVO4	pSlp76	pStat3
CLCD	CD14+HLA-DR-	pVO4	pPlcg2	pStat3
CLCD	CD14+HLA-DRmid	pVO4	pSHP2	pZap70
CLCD	CD14+HLA-DRmid	pVO4	pSlp76	pZap70
CLCD	CD14+HLA-DRmid	LPS	pp38	pBtk
CLCD	CD14+surf	pVO4	pStat5	pStat3
CLCD	CD14+surf	pVO4	pStat5	pBtk
CLCD	CD14+surf	pVO4	pSHP2	pStat3
CLCD	CD14+surf	pVO4	pSlp76	pp38
CLCD	CD14+surf	pVO4	pSlp76	pStat3
CLCD	CD14+surf	pVO4	pSlp76	pBtk
CLCD	CD14+surf	pVO4	pPlcg2	pZap70
CLCD	CD14+surf	pVO4	pPlcg2	pStat3
CLCD	CD14+surf	pVO4	pPlcg2	pBtk
CLCD	CD14+surf	PMA-IONO	pp38	pPlcg2
CLCD	CD14+surf	PMA-IONO	pErk	pZap70
CLCD	CD14+surf	PMA-IONO	pS6	pp38
CLCD	CD14+surf	PMA-IONO	pS6	pStat1
CLCD	CD14+surf	PMA-IONO	pS6	pZap70
CLCD	CD14+surf	PMA-IONO	pS6	pPlcg2
CLCD	CD14+surf	PMA-IONO	pS6	pErk
CLCD	CD14-HLA-DR-	pVO4	pPlcg2	pZap70
CLCD	CD14-HLA-DR-	pVO4	pPlcg2	pStat3
CLCD	CD14-HLA-DRmid	pVO4	pSlp76	pSHP2
CLCD	CD14-HLA-DRmid	pVO4	pSlp76	pZap70
CLCD	CD14-HLA-DRmid	pVO4	pPlcg2	pZap70
CLCD	CD14-HLA-DRmid	LPS	pp38	pAkt
CLCD	CD14-HLA-DRmid	LPS	pErk	pAkt
CLCD	CD14-HLA-DRmid	LPS	pS6	pAkt
CLCD	CD14-HLA-DRmid	PMA-IONO	pS6	pp38
CLCD	CD14-surf-	pVO4	pSHP2	pStat3
CLCD	CD14-surf-	pVO4	pSlp76	pStat3
CLCD	CD14-surf-	pVO4	pPlcg2	pStat3
CLCD	CD14-surf-	LPS	pErk	pPlcg2
CLCD	CD14-surf-	PMA-IONO	pp38	pStat3
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CLCD	CD14-surf-	PMA-IONO	pErk	pStat3
CLCD	CD14-surf-	PMA-IONO	pS6	pNFkB
CLCD	CD14-surf-	PMA-IONO	pS6	pp38
CLCD	CD14-surf-	PMA-IONO	pS6	pStat3
CLCD	CD4+	IL12	pSlp76	pp38
CLCD	CD4+	IL12	pSlp76	pZap70
CLCD	CD4+	GMCSF	pSlp76	pStat3
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CLCD	CD8+	pVO4	pStat5	pStat3
CLCD	CD8+	pVO4	pSHP2	pStat3

CLCD	CD8+	pVO4	pSlp76	pZap70
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CLCD	CD8+	PMA-IONO	pErk	pStat3
CLCD	Igm+	pVO4	pZap70	pp38
CLCD	Igm+	pVO4	pPlcg2	pSHP2
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CLCD	Igm+	PMA-IONO	pS6	pZap70
CLCD	Igm-	pVO4	pZap70	pBtk
CLCD	Igm-	pVO4	pSlp76	pSHP2
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CLCD	Igm-	PMA-IONO	pS6	pZap70
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CLCD	NK	pVO4	pSHP2	pStat3
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BACKSHIFT	CD8+	PMA-IONO	pPlcg2	pS6
BACKSHIFT	CD8+	PMA-IONO	pErk	pS6
BACKSHIFT	CD8+	PMA-IONO	pErk	pS6
BACKSHIFT	CD8+	PMA-IONO	pErk	pS6
BACKSHIFT	CD8+	PMA-IONO	pErk	pS6
BACKSHIFT	CD8+	PMA-IONO	pErk	pS6
BACKSHIFT	CD8+	PMA-IONO	pErk	pS6
BACKSHIFT	CD8+	PMA-IONO	pLat	pS6
BACKSHIFT	NK	BCR	pStat3	pNFkB

BACKSHIFT	NK	GMCSF	pStat3	pNFkB
BACKSHIFT	NK	IL2	pStat3	pNFkB
BACKSHIFT	NK	IFNg	pStat5	pp38
BACKSHIFT	NK	IFNg	pp38	pStat5
BACKSHIFT	NK	IFNg	pp38	pStat3
BACKSHIFT	NK	IL3	pBtk	pSlp76
BACKSHIFT	NK	IFNg	pPlcg2	pSlp76
BACKSHIFT	NK	IFNg	pp38	pBtk
BACKSHIFT	NK	BCR	pAkt	pPlcg2
BACKSHIFT	NK	GMCSF	pAkt	pPlcg2
BACKSHIFT	NK	IFNg	pAkt	pPlcg2
BACKSHIFT	NK	IL3	pAkt	pPlcg2
BACKSHIFT	NK	LPS	pAkt	pPlcg2
BACKSHIFT	NK	Ref	pAkt	pPlcg2
BACKSHIFT	NK	GMCSF	pZap70	pPlcg2
BACKSHIFT	NK	IL12	pZap70	pPlcg2
BACKSHIFT	NK	GMCSF	pSlp76	pPlcg2
BACKSHIFT	NK	GMCSF	pSlp76	pPlcg2
BACKSHIFT	NK	pVO4	pSlp76	pPlcg2
BACKSHIFT	NK	pVO4	pSlp76	pPlcg2
BACKSHIFT	NK	GMCSF	pErk	pPlcg2
BACKSHIFT	NK	IL3	pErk	pPlcg2
BACKSHIFT	NK	Ref	pAkt	pErk
BACKSHIFT	NK	IFNa	pPlcg2	pErk
BACKSHIFT	NK	IL3	pPlcg2	pErk
BACKSHIFT	NK	IL12	pS6	pErk
BACKSHIFT	NK	PMA-IONO	pp38	pS6
BACKSHIFT	NK	PMA-IONO	pPlcg2	pS6

References

1. Bendall, S. C. et al. Single-Cell Mass Cytometry of Differential Immune and Drug Responses Across a Human Hematopoietic Continuum. Science 332, 687–696 (2011).

2. Bodenmiller, B. et al. Multiplexed mass cytometry profiling of cellular states perturbed by small-molecule regulators. Nature biotechnology 30, 858–867 (2012).