

Supplement

Supplemental Table 1: Derivation cohort (n=63): Top 10 cytokines associated with left ventricular ejection fraction (LVEF). Higher relative cytokine concentrations are associated with lower LVEF values. This inverse relationship with LVEF was significant for 5 cytokines (FDR < 0.05). Estimate, the coefficient estimate from the linear regression model; r^2 , coefficient of determination (r^2) value for the model; P-value, raw p value for the model; FDR, false discovery rate calculated using Benjamini-Hochberg correction.

Cytokine	Estimate	r2	P-value	FDR
VEGFD	-15,418	0,421638	5,47E-08	2,01E-05
CLSTN2	-12,3104	0,315359	1,01E-05	0,003696
FSTL3	-14,615	0,313893	1,08E-05	0,00394
KRT19	-8,64163	0,31284	1,13E-05	0,004121
CRIM1	-20,57	0,287229	3,54E-05	0,012901
COLEC12	-14,5942	0,244778	0,000219	0,079625
CHRD1	-13,612	0,228297	0,000436	0,15771
LAIR1	-10,3162	0,222985	0,000542	0,195762
PRSS8	-12,4807	0,22271	0,000548	0,197437
LY6D	-11,7192	0,217577	0,000677	0,243021

Supplemental Table 2: Validation cohort (n=452): Similar to the derivation cohort, there is an inverse relationship between cytokine concentrations and left ventricular ejection fraction (LVEF) with high cytokine levels being associated with lower LVEF. There were 77 cytokines significantly associated with LVEF (FDR < 0.05). Estimate, the coefficient estimate from the linear regression model; r^2 , coefficient of determination (r^2) value for the model; P-value, raw p value for the model; FDR, false discovery rate calculated using Benjamini-Hochberg correction.

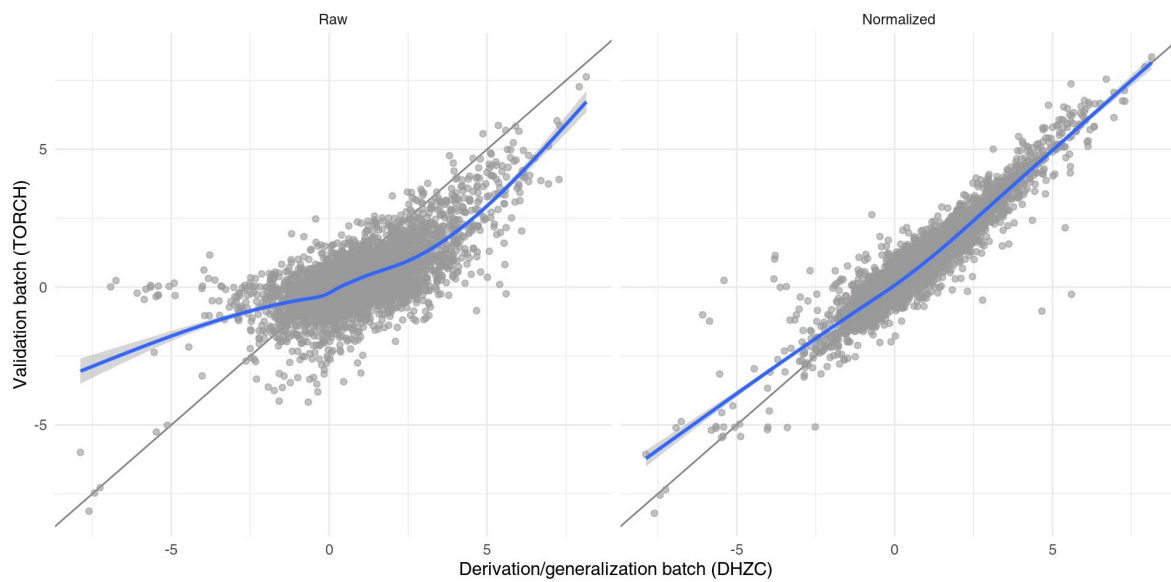
Cytokine	Estimate	r^2	P-value	FDR
COLEC12	-12,1741	0,164675	4,46E-16	1,64E-13
PLAUR	-11,1866	0,163439	6,12E-16	2,24E-13
CCL3	-7,14421	0,152285	1,04E-14	3,81E-12
LILRB4	-9,01034	0,151545	1,25E-14	4,58E-12
CXCL17	-5,54511	0,149364	2,18E-14	7,92E-12
AGRN	-10,9161	0,148426	2,75E-14	1E-11
WNT9A	-9,78385	0,141907	1,41E-13	5,11E-11
CD4	-11,4165	0,137435	4,31E-13	1,56E-10
FABP1	-4,20844	0,136129	5,96E-13	2,15E-10
LAIR1	-7,74702	0,133987	1,01E-12	3,64E-10
LGALS9	-8,96591	0,123841	1,24E-11	4,44E-09
CRIM1	-12,4333	0,122375	1,78E-11	6,35E-09
TNFSF13	-10,0253	0,121528	2,19E-11	7,79E-09
FSTL3	-7,4228	0,113642	1,5E-10	5,33E-08
CCL7	-4,43945	0,109818	3,8E-10	1,35E-07
TGFA	-7,94094	0,109175	4,44E-10	1,57E-07
CLSTN2	-6,20831	0,107495	6,67E-10	2,35E-07
HGF	-4,49271	0,104511	1,37E-09	4,82E-07
ANGPTL4	-6,68144	0,104232	1,47E-09	5,14E-07
SPON1	-7,40211	0,103125	1,92E-09	6,69E-07
IL17D	-9,61421	0,101249	3,01E-09	1,05E-06
LRRN1	7,205829	0,101132	3,1E-09	1,08E-06
LY6D	-7,43169	0,098996	5,18E-09	1,79E-06
PON3	11,39412	0,095766	1,13E-08	3,88E-06
HLA-E	-11,4467	0,095722	1,14E-08	3,91E-06
SPINK4	-4,40881	0,095501	1,2E-08	4,11E-06
LGALS4	-5,27358	0,09436	1,58E-08	5,39E-06
IL6	-2,99671	0,093813	1,8E-08	6,13E-06
NPPC	-4,98094	0,093211	2,08E-08	7,06E-06
CHRD1	-7,91593	0,092942	2,21E-08	7,51E-06
TREM2	-4,77254	0,091431	3,18E-08	1,07E-05
CXCL10	-4,17866	0,088631	6,21E-08	2,09E-05

Cytokine	Estimate	r2	P-value	FDR
EPO	-3,74666	0,087718	7,72E-08	2,59E-05
CXCL8	-4,01822	0,087691	7,77E-08	2,6E-05
MATN2	-9,39644	0,086945	9,28E-08	3,1E-05
CXCL14	-4,49222	0,08555	1,29E-07	4,31E-05
GAL	4,65288	0,082948	2,4E-07	7,98E-05
TFF2	-4,06551	0,081606	3,31E-07	0,000109
PREB	-10,3113	0,081157	3,68E-07	0,000121
SULT2A1	-4,04533	0,078762	6,5E-07	0,000214
ENPP7	-3,32201	0,077855	8,06E-07	0,000264
IL15	-6,78804	0,077687	8,39E-07	0,000274
DNER	9,589636	0,077289	9,22E-07	0,0003
CXCL9	-3,22193	0,074958	1,6E-06	0,000521
IL4R	-6,07854	0,074123	1,95E-06	0,000633
REG4	-4,97668	0,073114	2,48E-06	0,000801
BTN3A2	-6,09672	0,071531	3,61E-06	0,001162
FST	-5,18705	0,071502	3,63E-06	0,001166
EGLN1	-3,95482	0,07108	4,01E-06	0,001284
TNF	-5,94492	0,070676	4,42E-06	0,001409
IL1RN	-3,4451	0,070089	5,08E-06	0,001614
NTF3	-5,07255	0,069915	5,29E-06	0,001677
TNFRSF13B	-6,8624	0,069553	5,76E-06	0,001821
CXADR	-4,82297	0,068877	6,76E-06	0,00213
CD276	-5,47858	0,068871	6,77E-06	0,00213
TNFRSF11A	-4,2661	0,06851	7,38E-06	0,002308
SMOC2	-5,99596	0,068308	7,73E-06	0,002413
CCL25	-4,11859	0,067723	8,88E-06	0,002763
NFASC	-7,98799	0,067721	8,89E-06	0,002763
CCL28	-3,05271	0,067265	9,9E-06	0,003059
SIGLEC10	-5,64472	0,066844	1,09E-05	0,003368
PRSS8	-5,97756	0,066519	1,18E-05	0,003626
LAMA4	-6,9675	0,066442	1,2E-05	0,00368
PRELP	-8,7097	0,065305	1,57E-05	0,004801
ENPP5	5,817113	0,063325	2,51E-05	0,007643
CCL21	-4,3005	0,063229	2,57E-05	0,007793
TNFRSF4	-4,64774	0,061676	3,71E-05	0,011215
HLA-DRA	-5,76163	0,061424	3,94E-05	0,011865
CCL23	-5,004	0,061069	4,29E-05	0,012863
FASLG	4,476295	0,060662	4,72E-05	0,014115
TPP1	-5,9269	0,059997	5,53E-05	0,016466
CCL11	-4,03204	0,059247	6,6E-05	0,019599
CCL13	-2,60901	0,057756	9,39E-05	0,0278
KRT19	-3,53618	0,057209	0,000107	0,031541
LIFR	-6,6545	0,05658	0,000124	0,036485
ITM2A	-4,51045	0,056553	0,000125	0,036589
CKAP4	-5,15816	0,056407	0,000129	0,037749

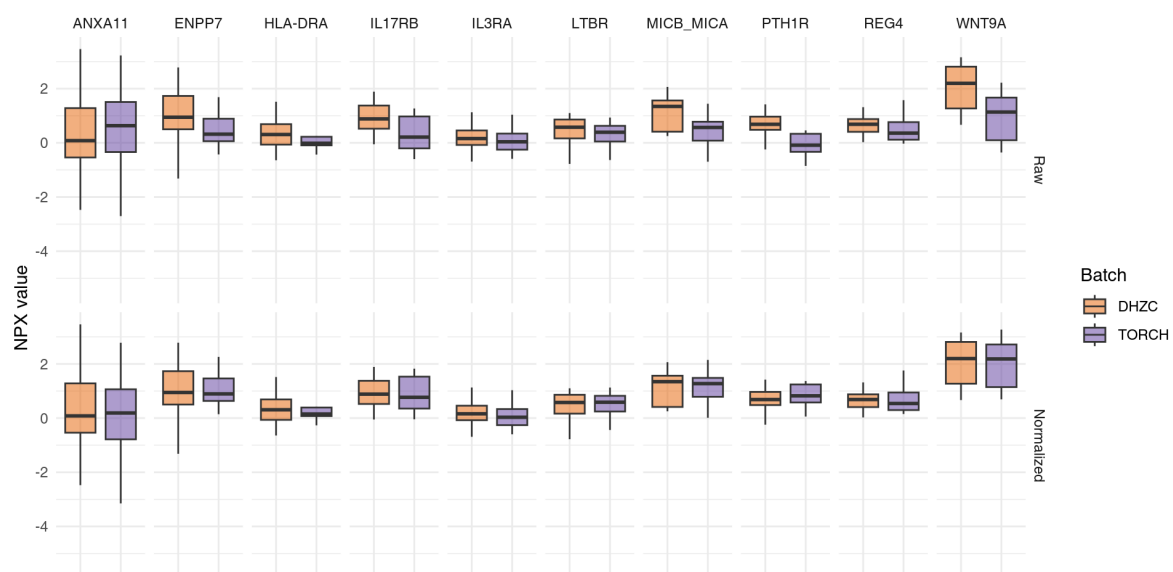
Supplemental Table 3: Replication in the validation cohort confirms that higher relative cytokine concentrations of the top 10 cytokines from the derivation cohort are associated with lower LVEF in patients with inflammatory cardiomyopathy. Estimate, the coefficient estimate from the linear regression model; r^2 , coefficient of determination (r^2) value for the model; P-value, raw p value for the model; FDR, false discovery rate calculated using Benjamini-Hochberg correction.

Cytokine	Estimate	r^2	p value	FDR
COLEC12	-12.17	0.1647	4.5e-16	1.6e-13
LAIR1	-7.747	0.134	1.0e-12	3.6e-10
CRIM1	-12.43	0.1224	1.8e-11	6.3e-09
FSTL3	-7.423	0.1136	1.5e-10	5.3e-08
CLSTN2	-6.208	0.1075	6.7e-10	2.3e-07
LY6D	-7.432	0.099	5.2e-09	1.8e-06
CHRD1	-7.916	0.09294	2.2e-08	7.5e-06
PRSS8	-5.978	0.06652	1.2e-05	0.0036
KRT19	-3.536	0.05721	0.00011	0.0315
VEGFD	-3.324	0.04488	0.00202	0.5383

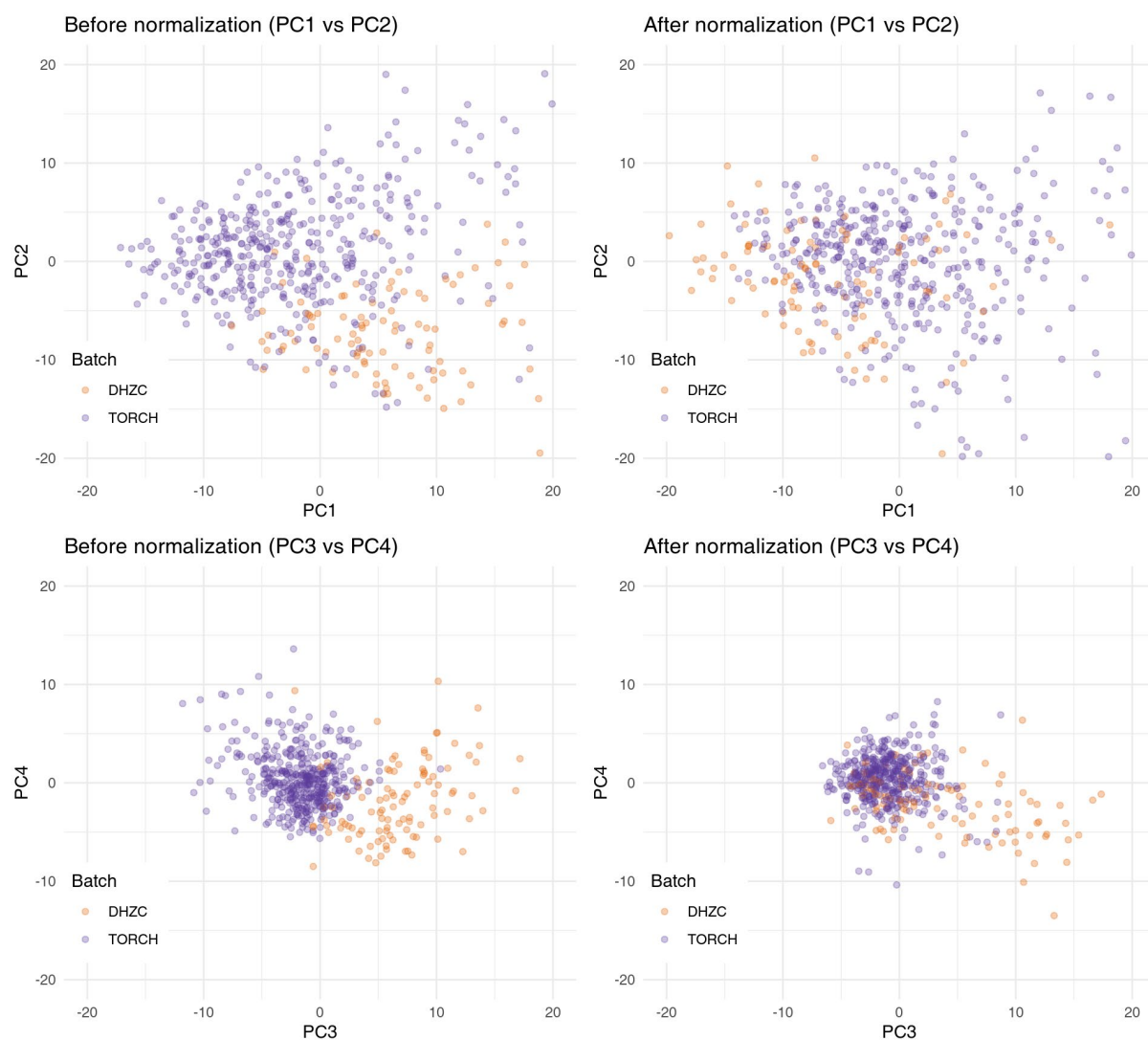
Supplemental Figure 1: NPX values of all protein assays in the first batch (X axis, derivation and generalizability cohorts) and second batch (Y axis, validation cohort) data sets for the 16 bridging samples. Each dot represents one protein assay in one sample. Left panel, raw data. Right panel, data normalized using the `olink_normalization` function from the `OlinkAnalyze` R package. In total, there were 16 samples, 368 assays and 5888 total measurements. Blue line shows a fitted LOESS model.



Supplemental Figure 2: Comparison of 10 randomly chosen protein assays across the different data sets and different normalizations for the 16 bridging samples. Top: raw data. Bottom: normalized data. In total, 16 unique samples and 640 measurements are shown.



Supplemental Figure 3: Principal component analysis of the 529 measurements before normalization (left panel) and the same measurements after normalization (right panel). Each dot represents one sample. The first two principal components are shown in the top row, and the third and fourth principal components are shown in the bottom row. The color of the dots indicates the batch of the sample.



Supplemental Figure 4: Scree plot of the principal component analysis of the 529 measurements before normalization (red) and the same measurements after normalization (blue). The x-axis shows the principal components and the y-axis shows the proportion of variance explained by each principal component.

