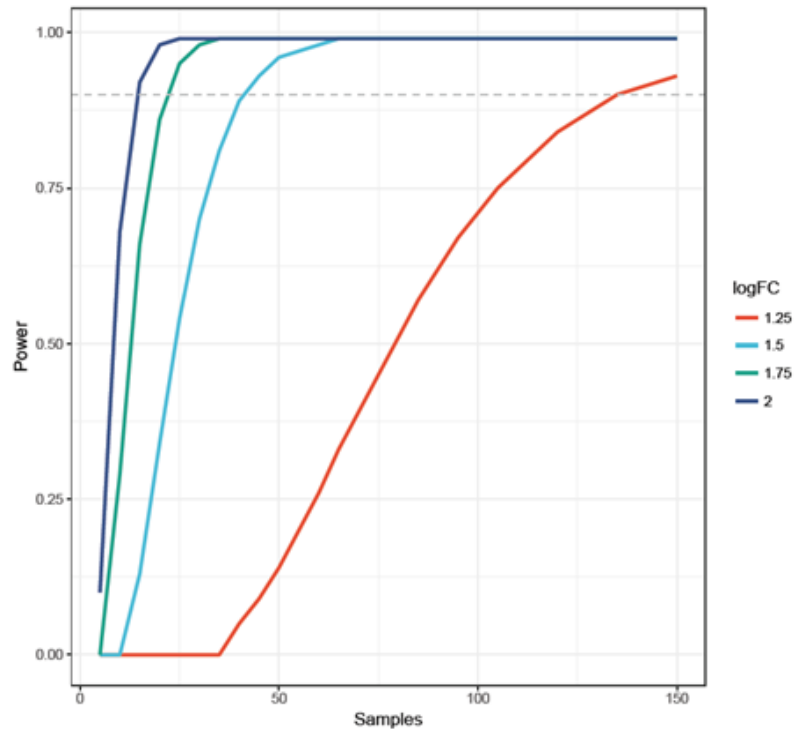
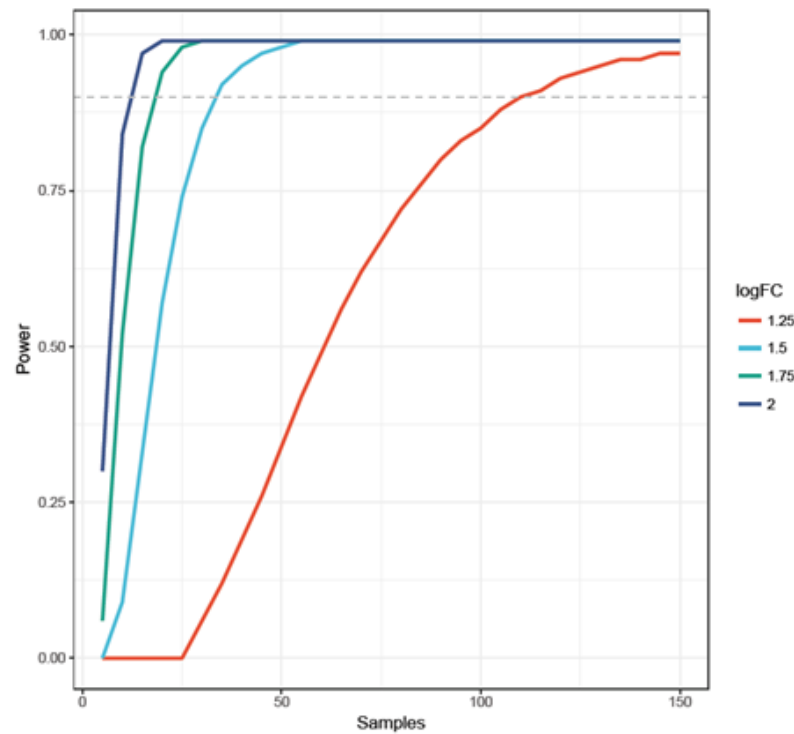
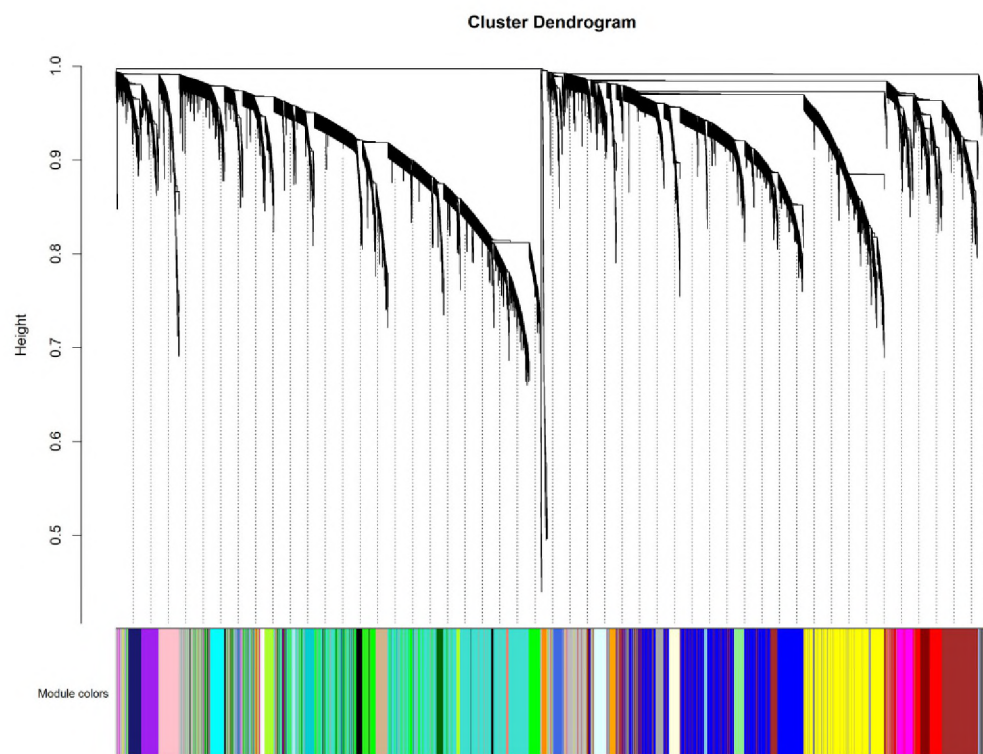
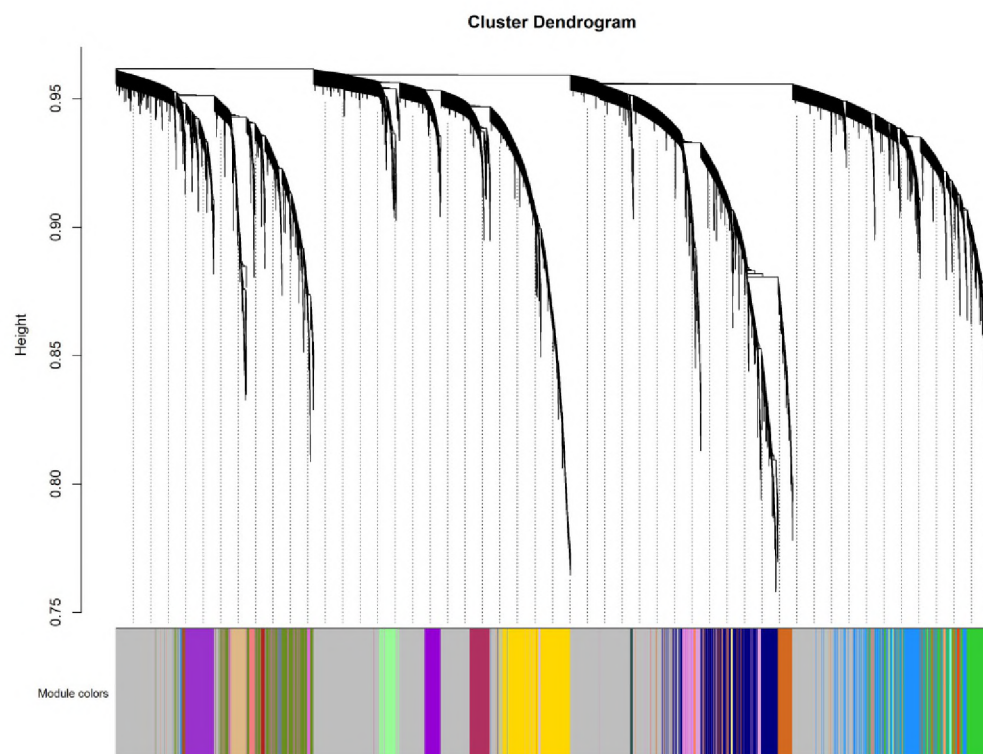


a**b****Supplementary Figure 1. Statistical power calculations for differential expression analysis.**

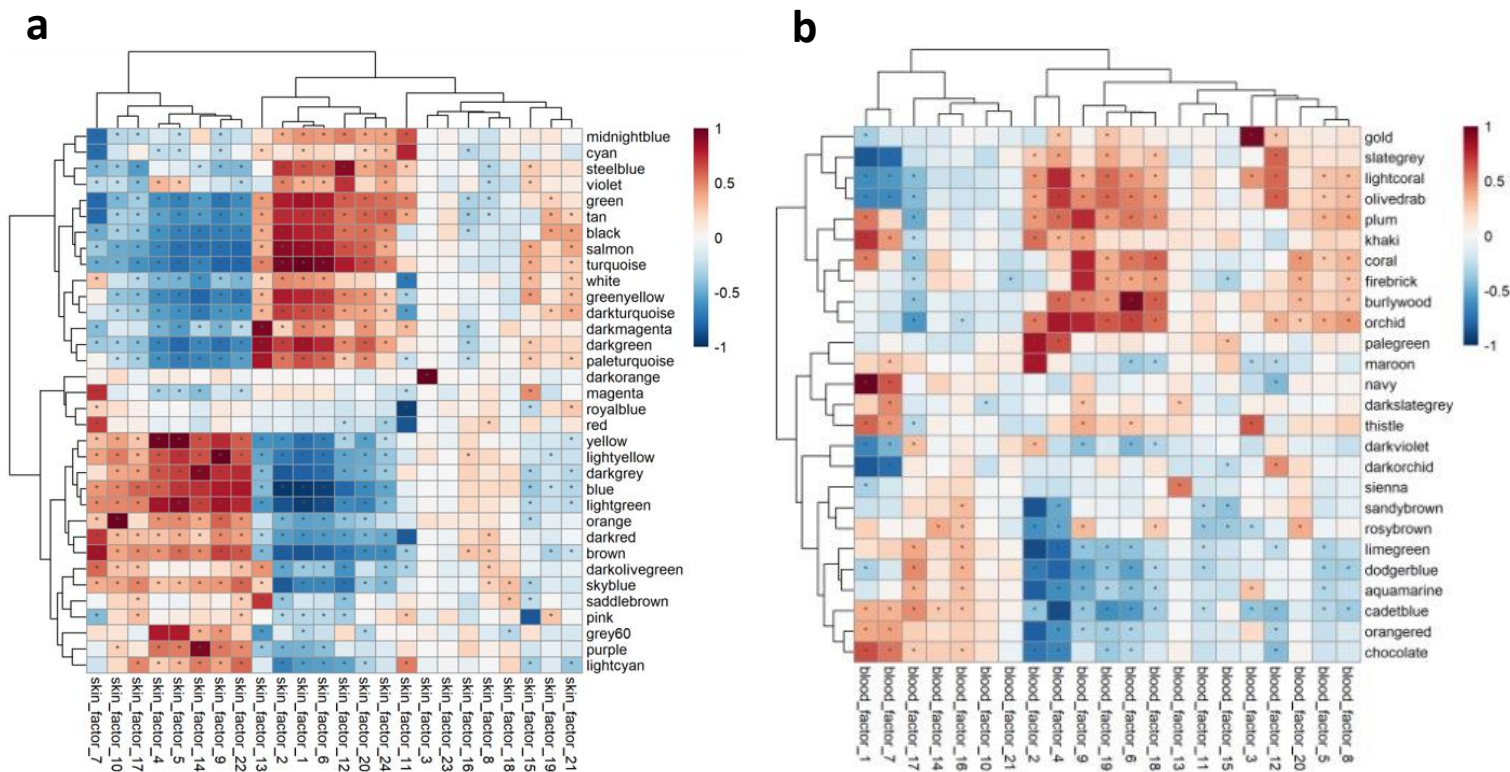
Power curves projected across an expected range of fold changes based on the assumption that **(a)** 1% or **(b)** 5% of genes are likely to prove prognostic. Power calculations were performed using the method of Guo et al (2014) and parameters derived from our pilot study (Foulkes et al 2018); we calculated the requisite sample size to achieve 90% power (grey dotted line on plot) to detect differential expression associated with response.

b**b**

Supplementary Figure 2. Grouping of genes in skin and blood into co-expressed gene modules using WGCNA.

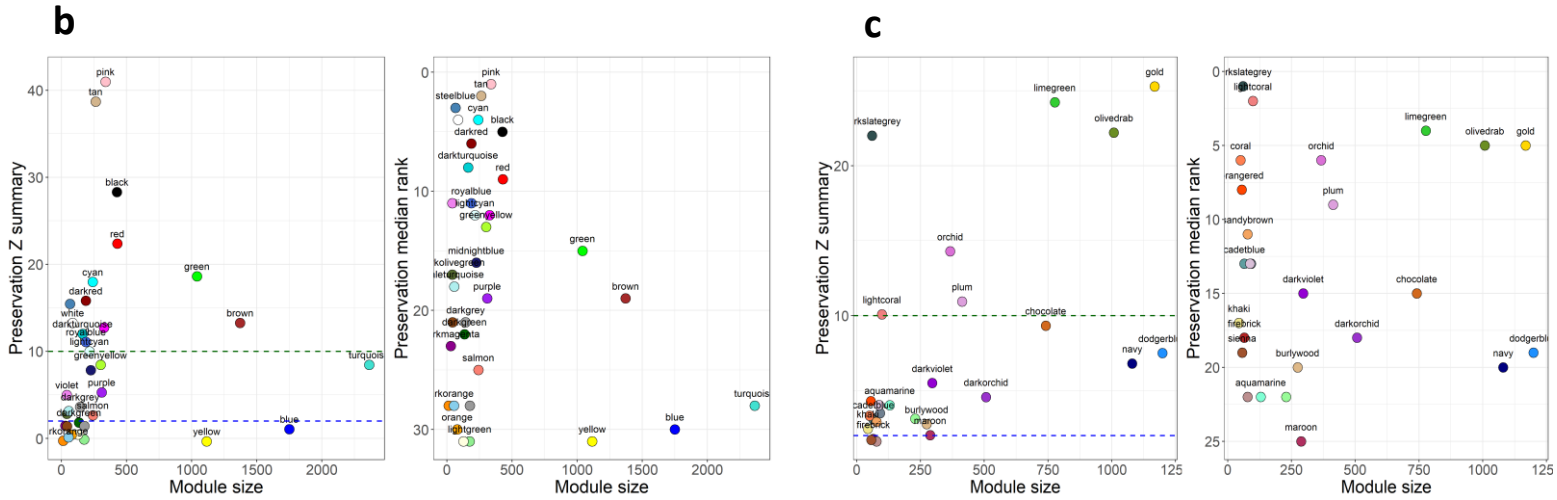
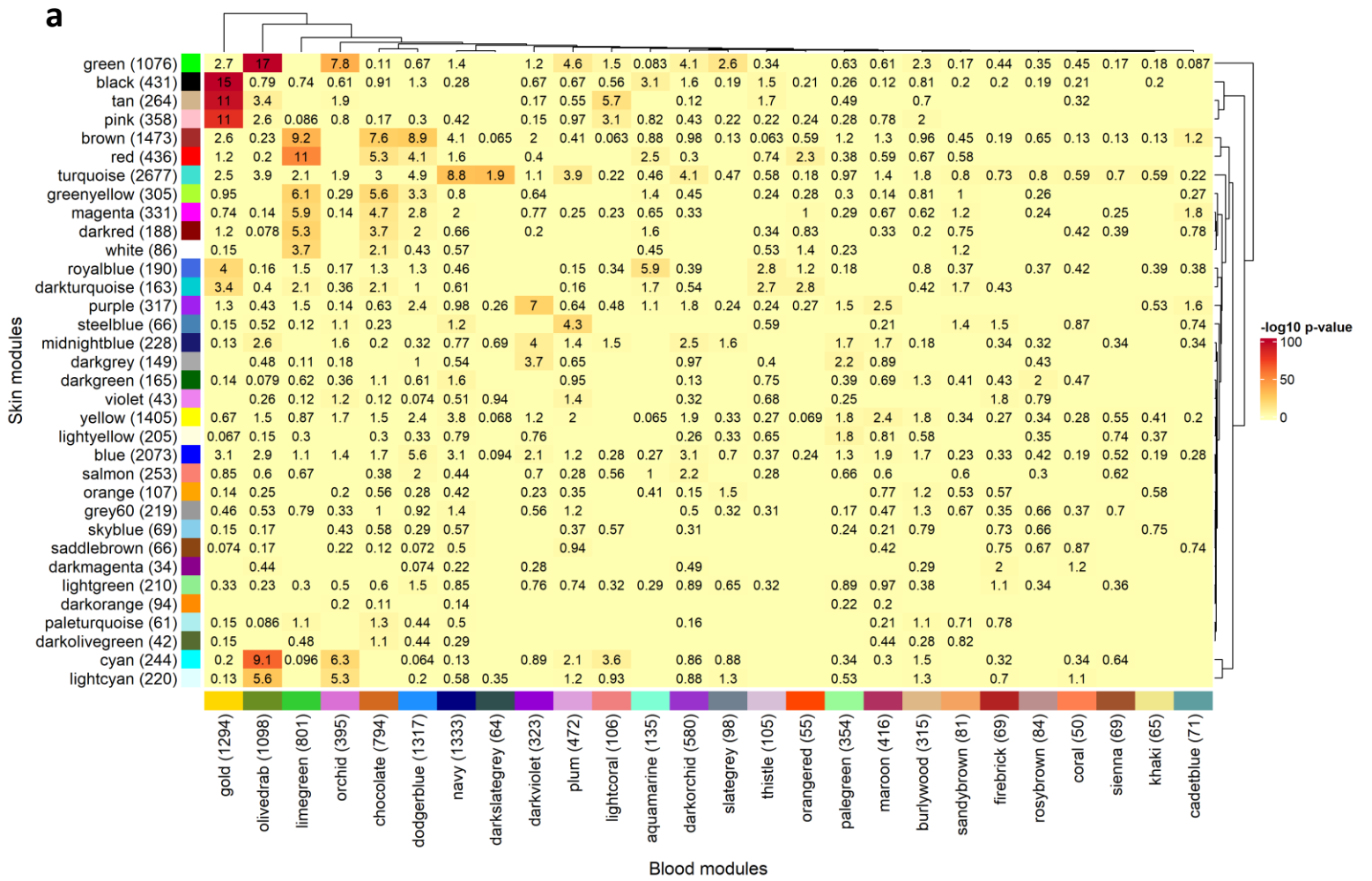
WGCNA, a dimensionality reduction method for omics data, was used to group the skin and blood RNA-Seq data into co-expressed gene modules. Briefly, WGCNA works by calculating the correlation between each pair of genes in an expression matrix; the resulting correlation matrix, after some transformations, is then clustered, allowing genes with similar expression profiles to be grouped into modules. Further details are available in the supplementary methods. **(a)** shows hierarchical clustering of genes in the skin data, annotated by colour-coded module assignment and **(b)** shows the same for blood. WGCNA identified 34 modules in skin and 26 modules in blood.

Abbreviations: WGCNA, weighted gene correlation network analysis.



Supplementary figure 3. WGCNA and ICA identify similar gene expression signatures.

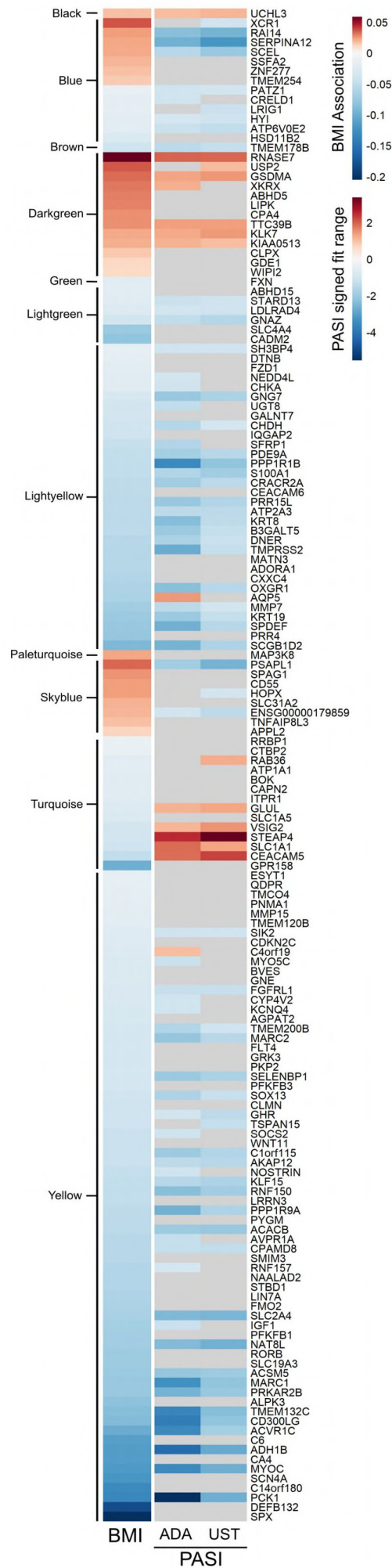
Correlations between module eigengenes (y-axis) and latent factor values (x-axis) in **(a)** skin and **(b)** blood. The high degree of positive correlation shown in these heatmaps demonstrates that WGCNA and ICA converged on similar gene expression profiles, providing cross-validation of these dimensionality reduction methods.



Supplementary Figure 4. Module preservation analysis identifies modules with similar patterns of co-expression in skin and blood, and vice versa.

WGCNA was used to derive co-expressed gene modules separately in skin and blood; we then sought to identify which modules in skin showed similar patterns of co-expression in blood, and vice versa. We first looked for pairs of modules between skin and blood with significant overlap in gene contents. **(a)** shows gene overlap between the skin and blood modules. The heatmap is coloured by $-\log_{10}$ p-values from right tailed fisher's exact test and the numbers in each cell correspond to the percentage of the union of genes in each module pair that overlap. We also used tested module preservation between the skin and blood modules using functionality available in the WGCNA R package. We derived two composite module preservation scores, preservation Z summary and median rank. **(b)** shows composite scores from testing preservation of the skin modules in blood and **(c)** shows the scores derived from testing preservation of the blood modules in skin. In each plot the left panel shows preservation Z summary and the right panel shows median rank. Each score is plotted against module size. The blue horizontal line indicates moderate evidence for preservation and the green horizontal line indicates strong evidence for preservation. The black, pink, and tan modules in skin exhibited strong evidence for preservation in blood and were found to have the most significant gene overlap with the gold module in blood. The green skin module was also strongly preserved in blood and exhibited significant gene overlap with the olivedrab module in blood.

Abbreviations: WGCNA, weighted gene correlation network analysis.

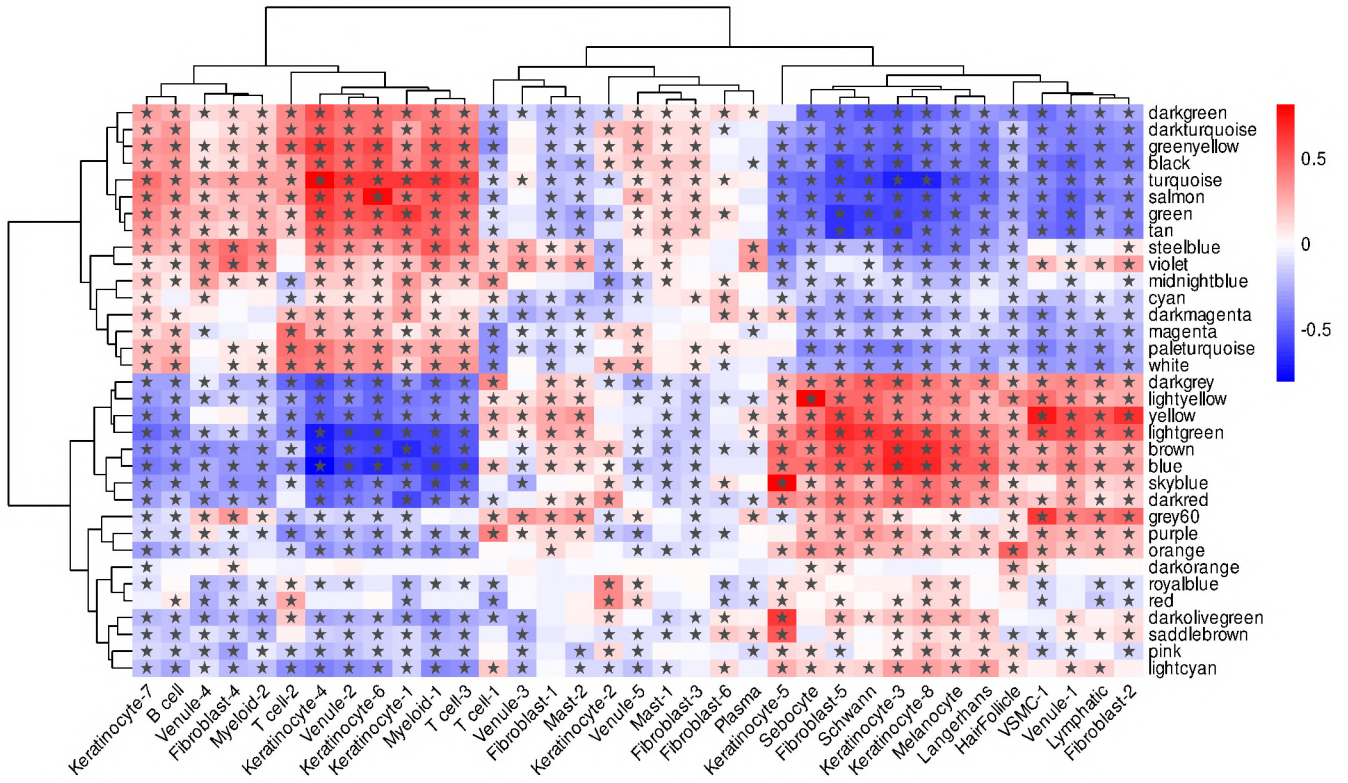


Supplementary figure 5. A transcriptome signature associated with BMI in non-lesional skin (NLS) is associated with disease severity in lesional skin.

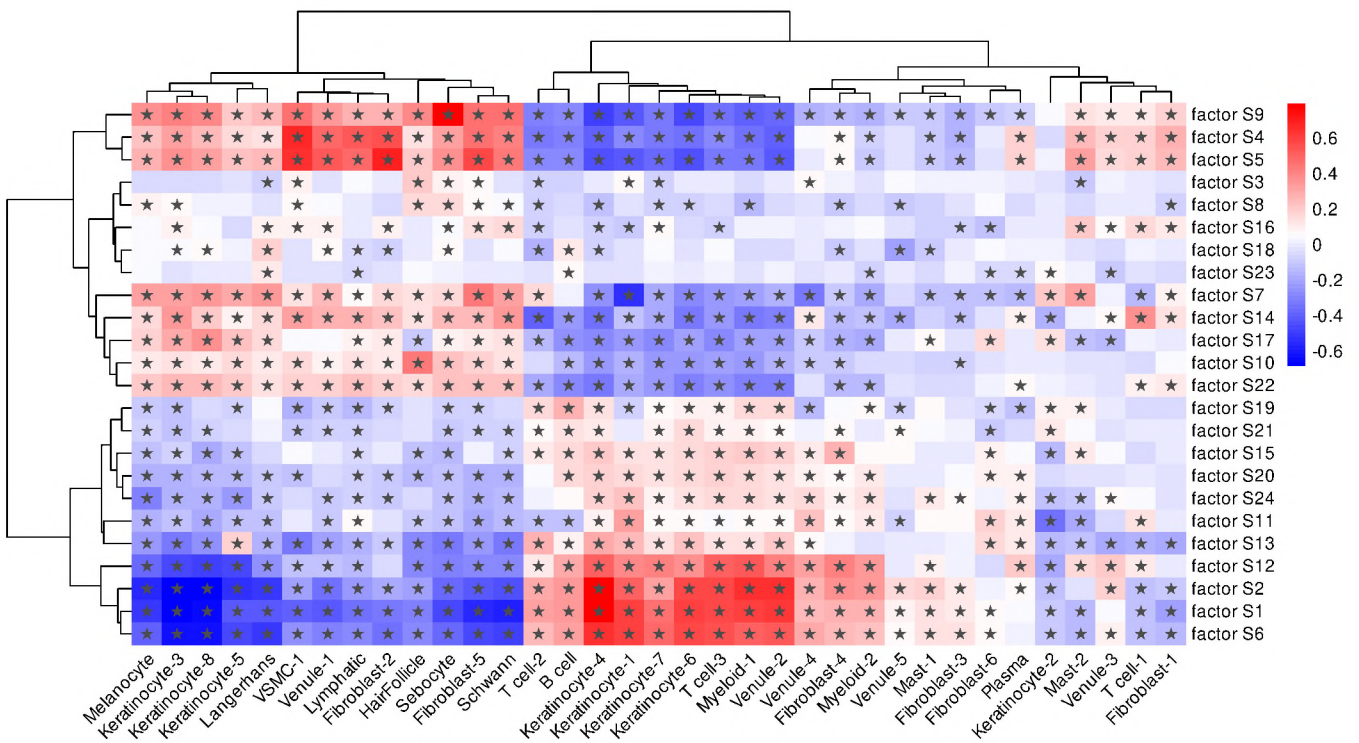
This heatmap shows genes that were assigned to modules by WGCNA and exhibited a significant association with BMI in NLS based on differential expression analysis; their associations with BMI in NLS and PASI in LS in each drug cohort are shown. Red indicates a positive association, blue indicates a negative association, and grey indicates a non-significant association. Of note, genes in the lightyellow module were negatively associated with BMI in NLS and negatively associated with PASI in LS in both drug cohorts.

Abbreviations: BMI, body mass index; WGCNA, weighted gene correlation network analysis; NLS, non-lesional skin; PASI, psoriasis area and severity index; LS, lesional skin.

a

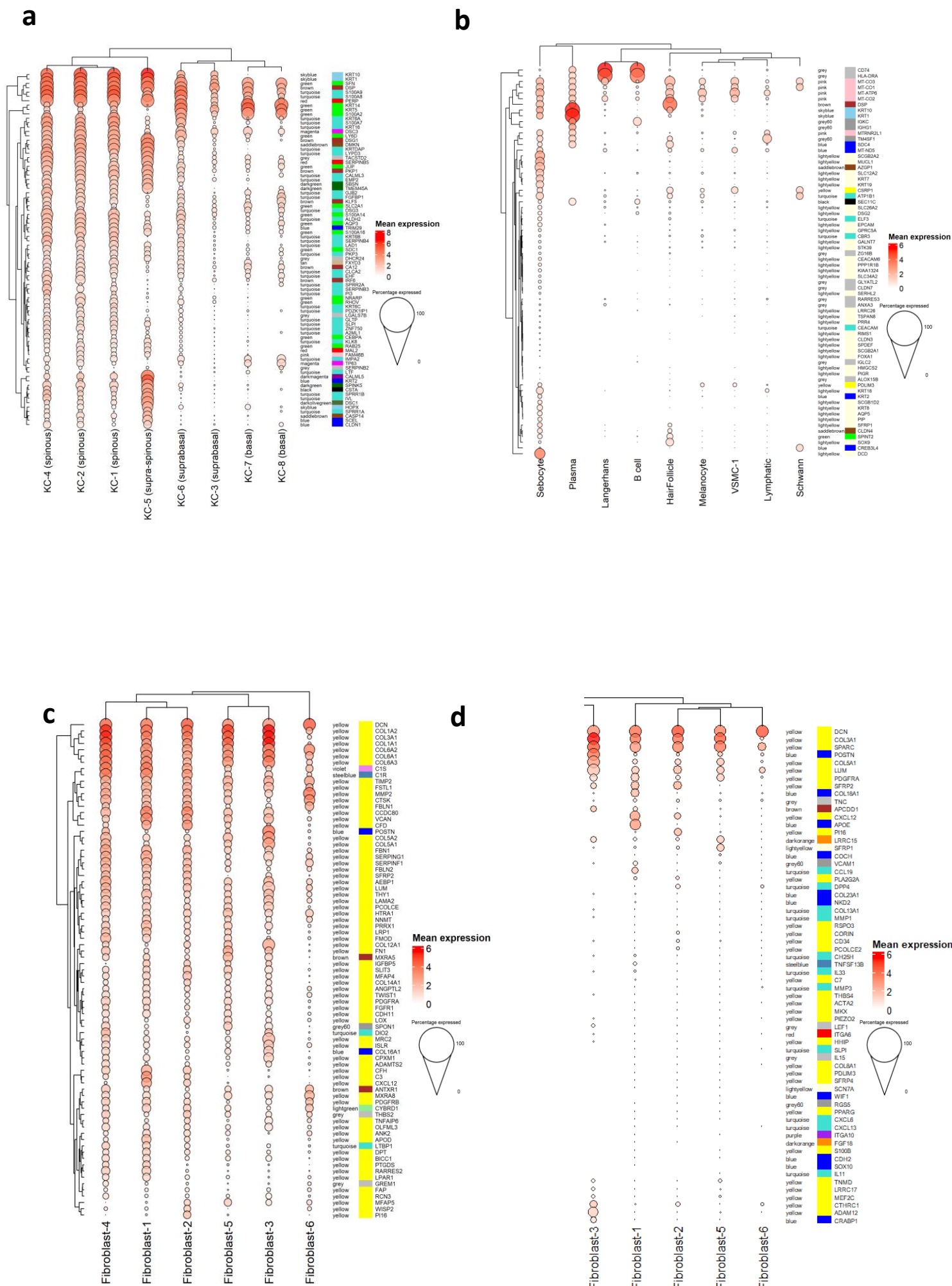


b

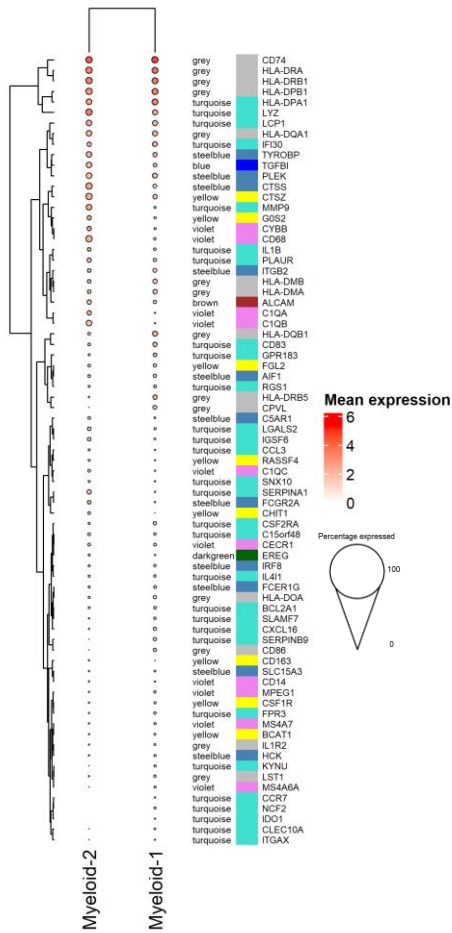


Supplementary Figure 6. Cell type deconvolution of the gene modules and latent factors in skin.

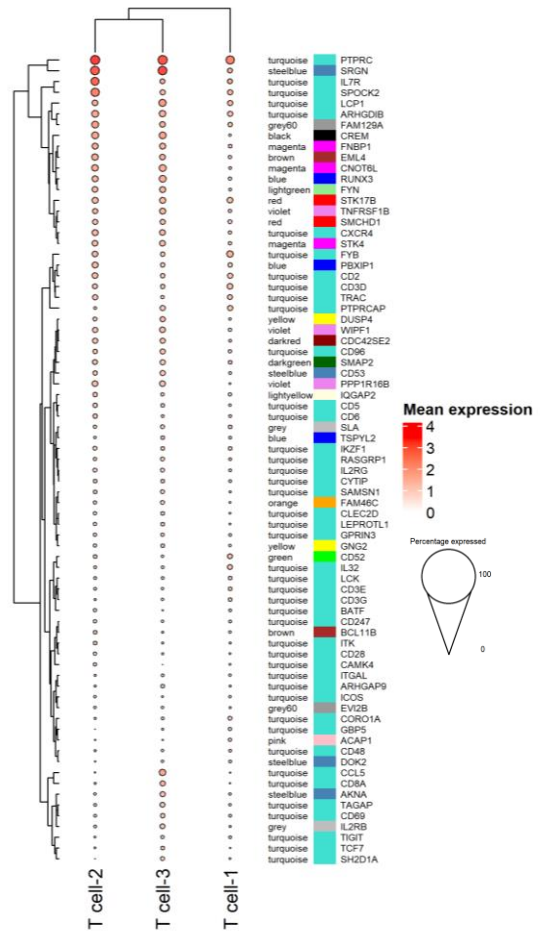
We derived predicted cell-type fractions for the skin RNA-Seq data (discovery and replication cohorts combined) using CibersortX and a skin single cell transcriptome atlas published by Hughes et al (2020), publicly available on the Single Cell Portal (https://singlecell.broadinstitute.org/single_cell). We then correlated the predicted cell-type fractions with **(a)** module eigengenes, derived by WGCNA, and **(b)** latent factor values, derived by ICA. Asterisks (*) indicate statistical significance (adjusted p-value<0.05). *Abbreviations:* WGCNA, weighted gene correlation network analysis; ICA, independent component analysis.



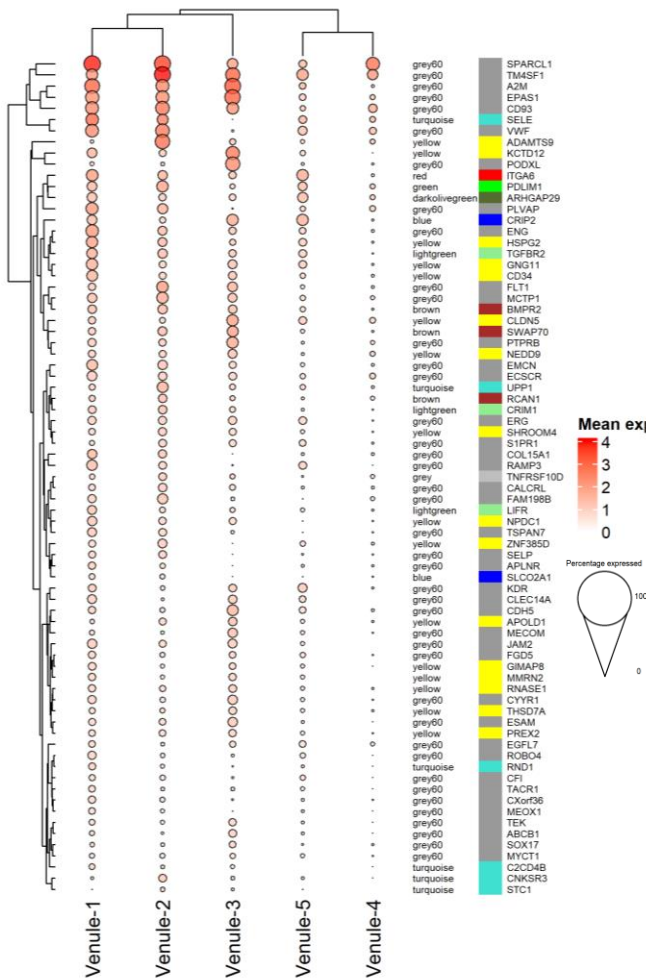
e



f

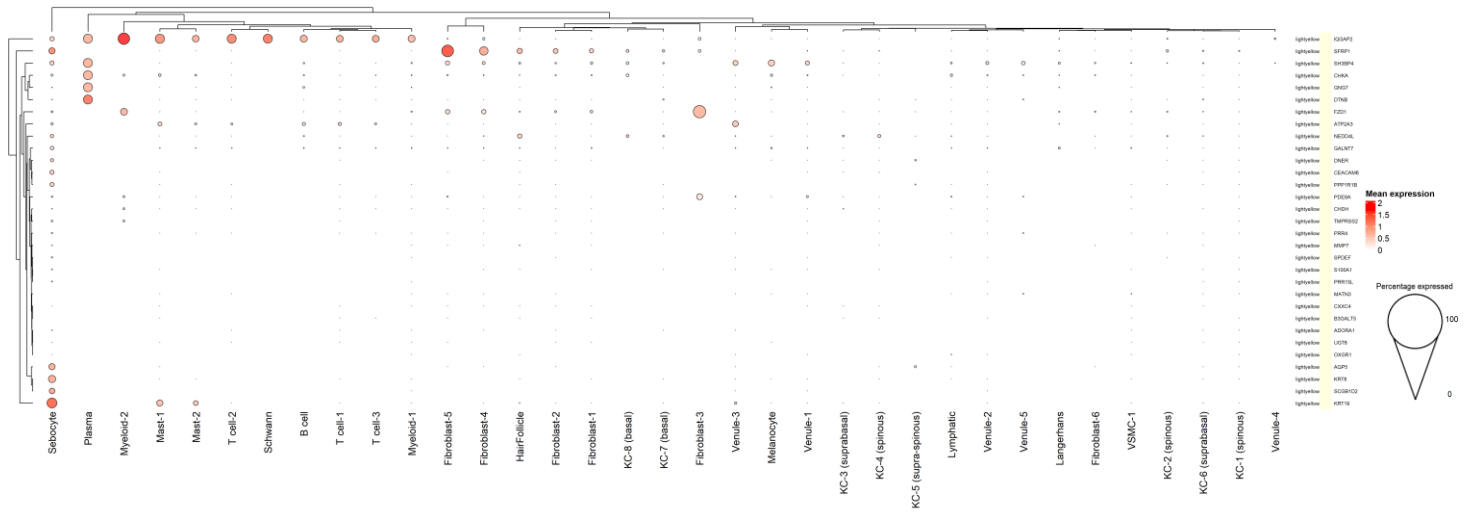


g



Supplementary Figure 7. Expression of cell cluster marker genes in a skin single cell transcriptome atlas.

Heatmaps showing the mean expression within specified cell clusters (columns) of the top 80 marker genes (ranked by average log fold change; rows) in **(a)** keratinocytes, **(b)** sebocytes, **(c)** fibroblasts, **(e)** myeloid cells, **(f)** T-cells, and **(g)** venules. This data was derived from a skin single cell transcriptome atlas published by Hughes et al (2020), publicly available on the Single Cell Portal (https://singlecell.broadinstitute.org/single_cell). The row annotation indicates the modules to which these genes were assigned in our dataset. **(d)** Shows the expression in this single cell atlas data of marker genes, identified by Steele et al (2024), which differentiate between different sub-types of fibroblasts.



Supplementary Figure 8. Expression of BMI-associated genes in a skin single cell transcriptome atlas. Heatmaps showing the mean expression within skin cell clusters (columns) of BMI-associated DEGs that overlap with the lightyellow module. This data was derived from the skin single cell transcriptome atlas published by Hughes et al (2020), publicly available on the Single Cell Portal (https://singlecell.broadinstitute.org/single_cell).
Abbreviations: BMI, body mass index.

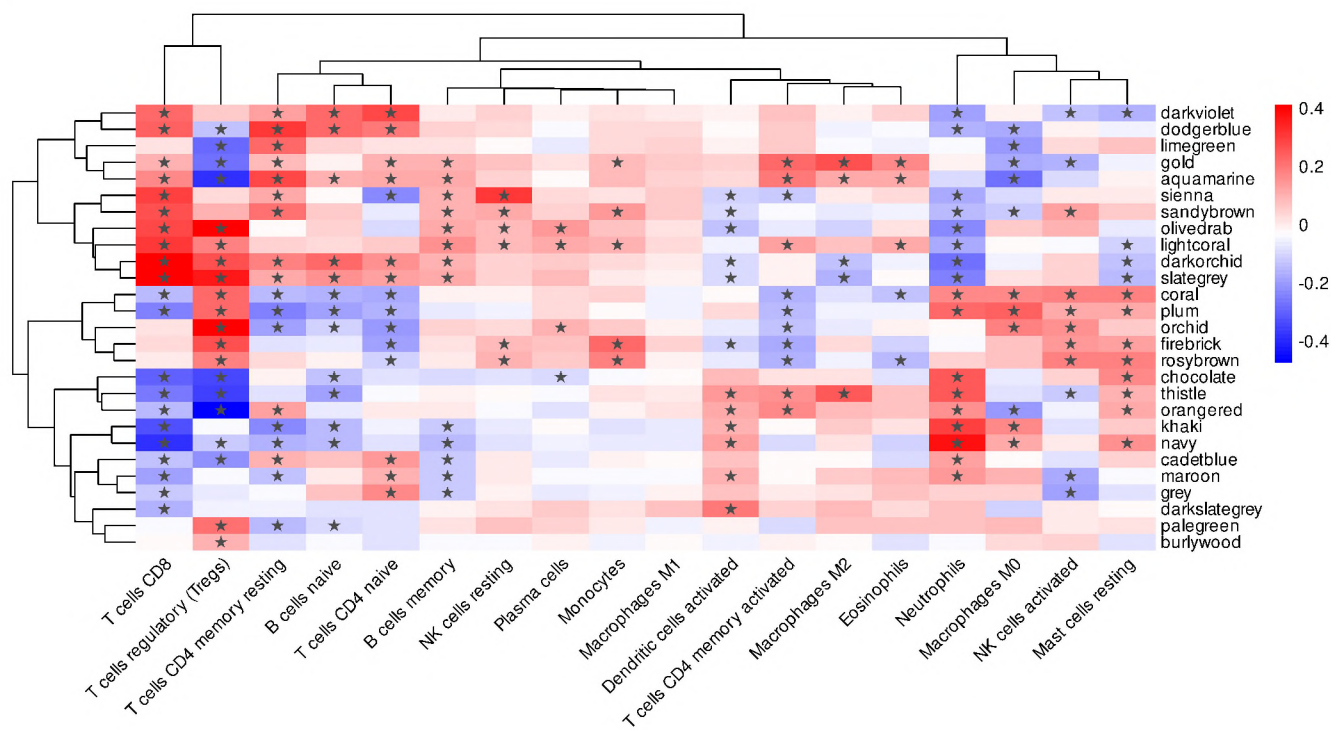


Supplementary Figure 9. Further exemplar module and latent factor-trait correlation plots.

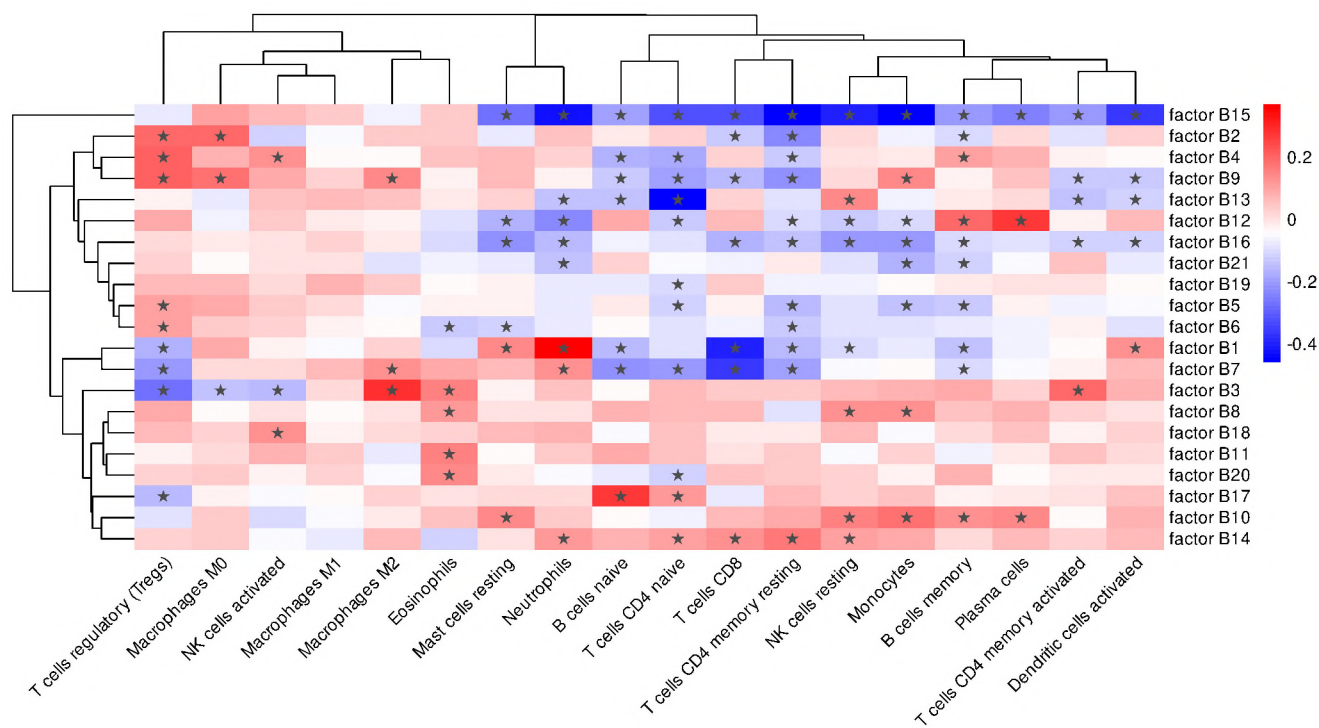
Scatter plots of further exemplar WGCNA module and ICA factor trait associations with disease severity (PASI). Each point represents a single sample, is marked with a symbol according to drug cohort and colour-coded according to timepoint (blue = 0w, green = 1w, red = 4w, orange = 12w). The grey shading indicates 95% confidence intervals. The title banner provides information on the tissue and drug cohort. Module membership is denoted opposite the y axis. Curves represent natural-spline fits (3 d.f.) with 95 % confidence bands.

Abbreviations: PASI, Psoriasis Area and Severity Index; WGCNA, Weighted gene correlation network analysis; ICA independent component analysis; w, weeks

a



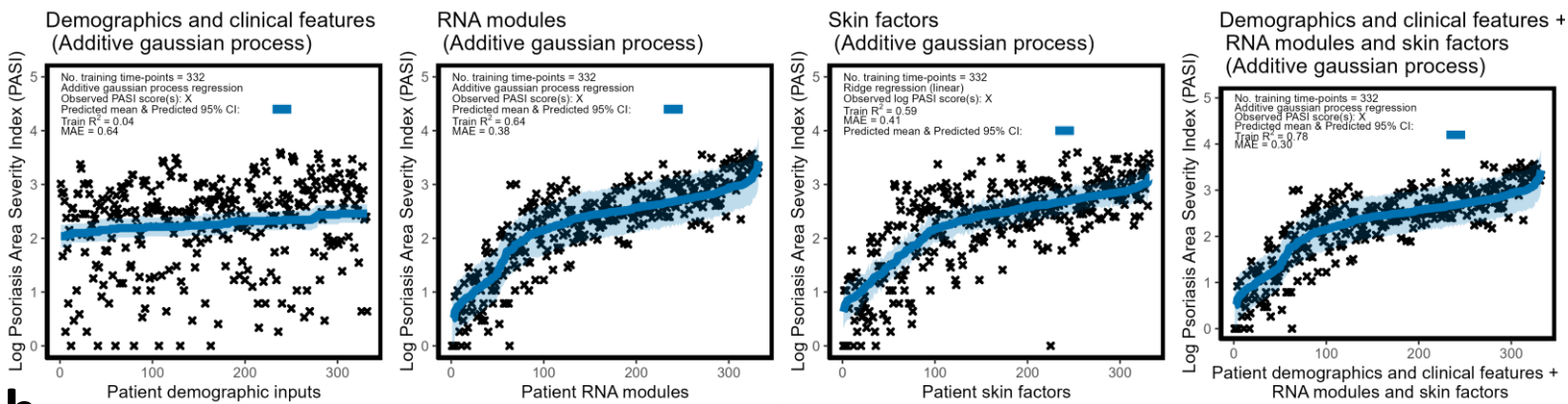
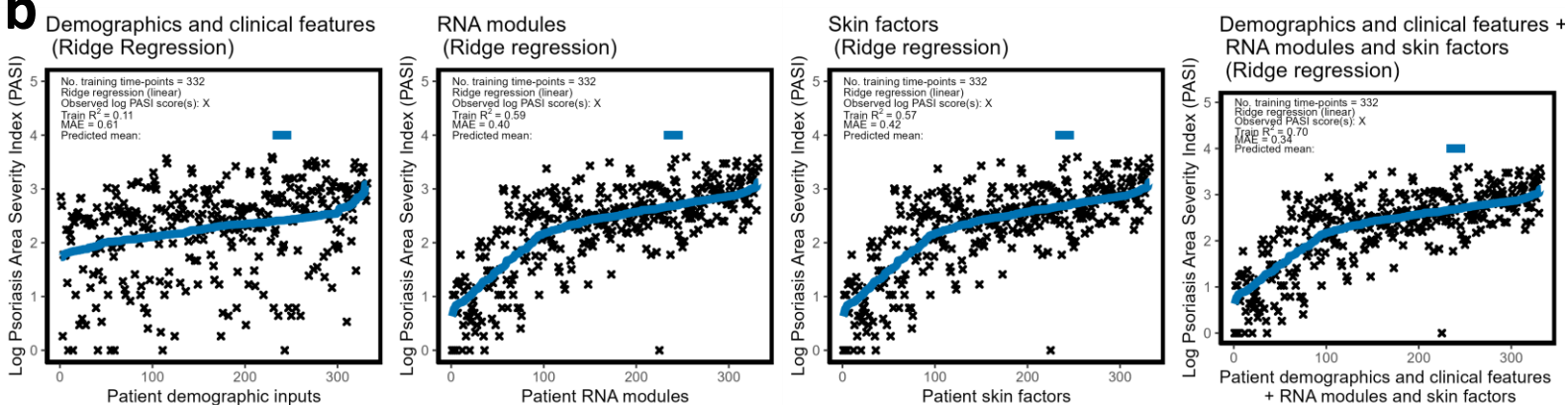
b



Supplementary Figure 10. Cell type deconvolution of the gene modules and latent factors in blood.

We derived predicted cell-type fractions for the blood RNA-Seq data using CibersortX and the LM22 reference dataset. We then correlated the predicted cell-type fractions with **(a)** module eigengenes, derived by WGCNA, and **(b)** latent factor values, derived by ICA. Asterisks (*) indicate statistical significance (adjusted p-value<0.05).

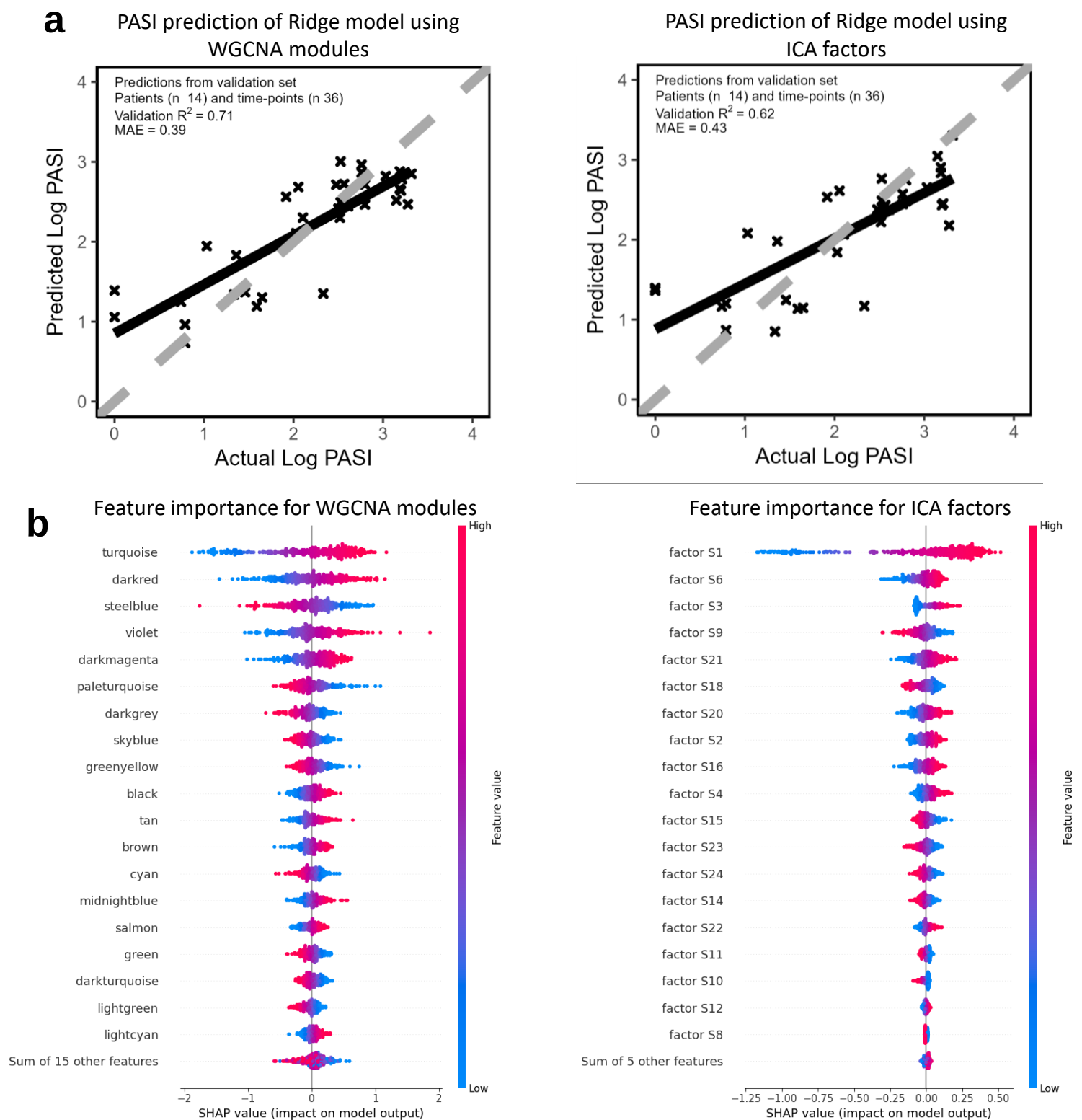
Abbreviations: WGCNA, weighted gene correlation network analysis; ICA, independent component analysis.

a**b**

Supplementary Figure 11. Prediction of PASI based on module eigengenes and latent factors in lesional skin and demographic and clinical features using additive gaussian process regression and linear ridge regression.

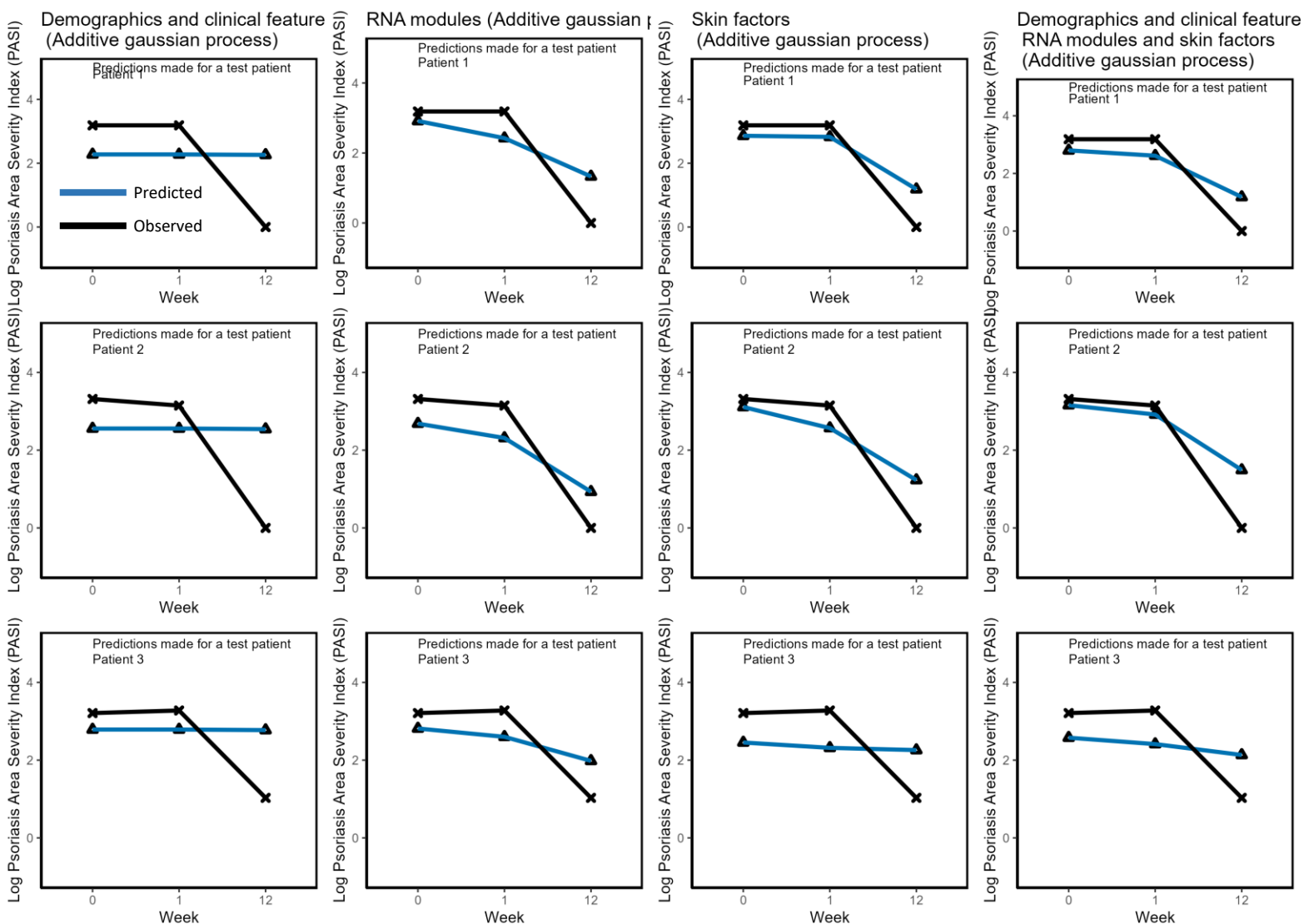
(a) Additive gaussian process regression models depicting the relationship between module eigengenes and latent factor values in lesional skin and demographic and clinical features (discovery and replication cohorts combined) and log scaled PASI. Top row: the first regression model was trained on patient demographic and clinical information. The next two regression models were trained on module eigengenes or latent factors. The third regression model was trained on all features. **(b)** Ridge regression (baseline) models depicting the relationship between patient inputs and PASI. The observed log PASI scores from the training dataset ($n=332$ time-points) are depicted by the cross symbols. The shaded regions represent the additive gaussian process models predicted 95% confidence intervals.

Abbreviations: PASI, psoriasis area and severity index.



Supplementary Figure 12. Prediction of PASI based on module eigengenes and latent factors in lesional skin and demographic and clinical features using linear ridge regression.

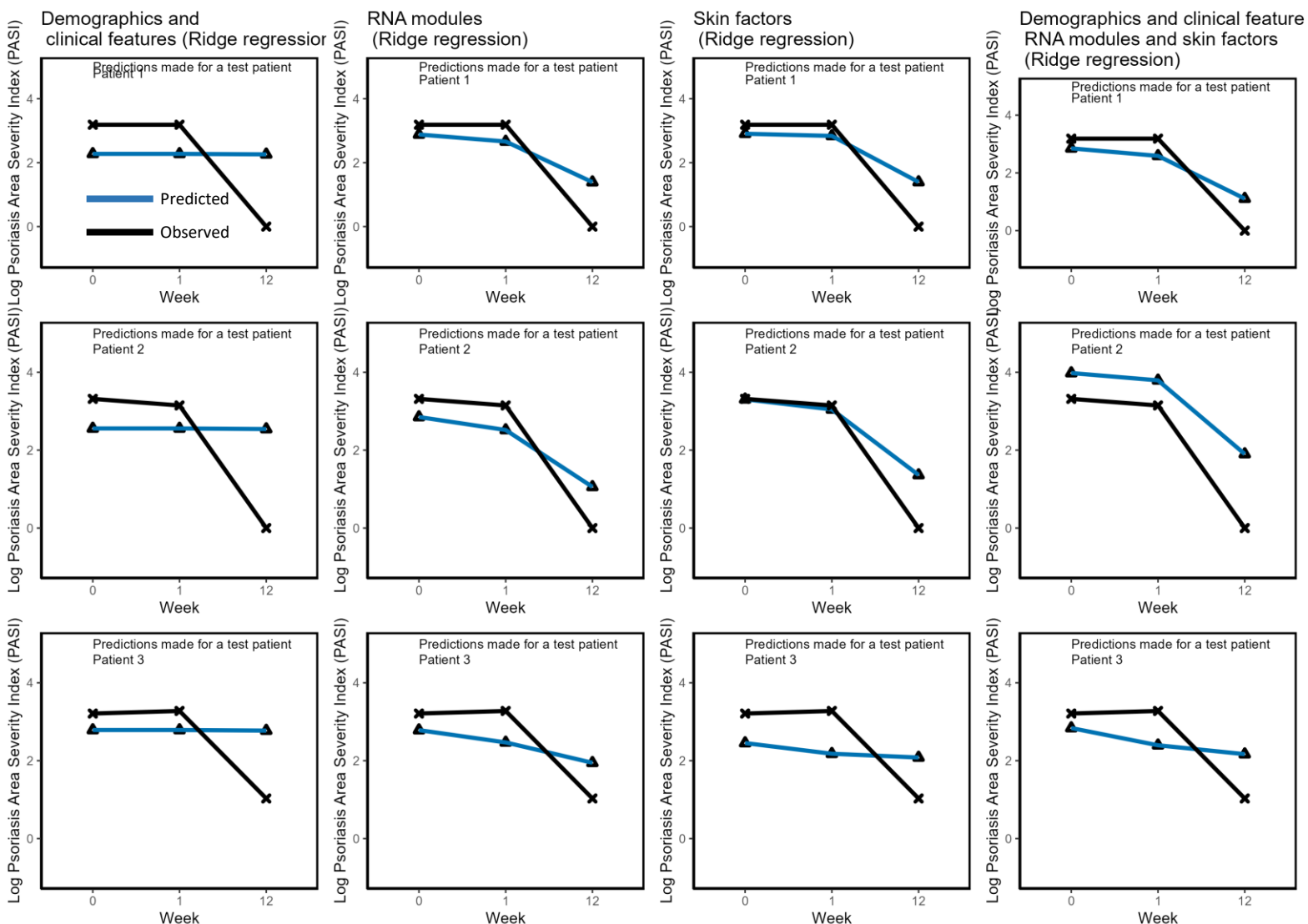
(a) Linear (ridge) regression models depicting the relationship between module eigengenes and latent factor values in lesional skin and demographic and clinical features (discovery and replication cohorts combined) and log scaled PASI. The performance comparison between the predicted and actual log PASI scores were optimized on the validation dataset. Among all features, modules eigengenes and latent factors gave the best performance. Demographic and clinical features made no difference to performance (Supplementary Fig. 12). The observed log PASI scores from the training dataset ($n=332$ time-points) are depicted by the cross symbols. **(b)** Scatter plots show the relative feature importance determined using the SHAP (SHapley Additive exPlanations) method. SHAP values were calculated using a model-agnostic approach, where model features are independently altered and the resulting change in the predicted output is recorded while keeping other features unchanged. SHAP values on the right side of the x-axis indicate features decreasing PASI, whilst those shifting right indicate the opposite. *Abbreviations:* PASI, psoriasis area and severity index; SHAP, SHapley Additive exPlanations.



Supplementary Figure 13. Predicted PASI trajectories across time based on gaussian process regression.

Patient trajectories predicted by the additive gaussian process regression models from a randomly shuffled 10-fold held-out testing dataset. The first regression model was trained on patient demographic and clinical information. The next two regression models were trained on module eigengenes or latent factors. The final regression model was trained on all features.

Abbreviations: PASI, psoriasis area and severity index.

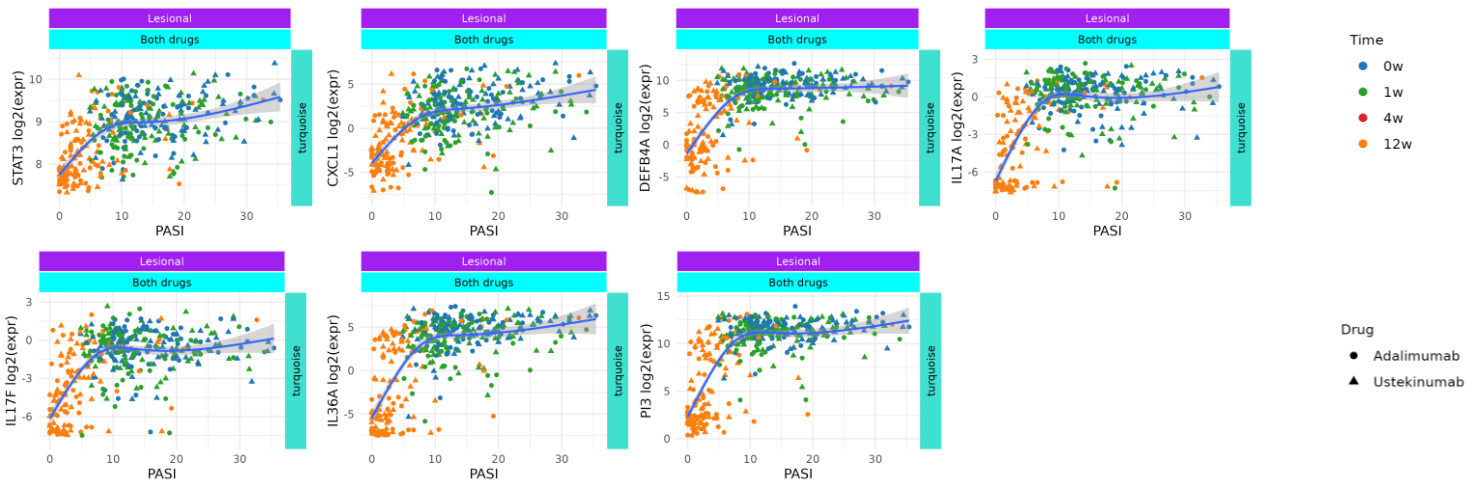


Supplementary Figure 14. Predicted PASI trajectories across time based on linear ridge regression.

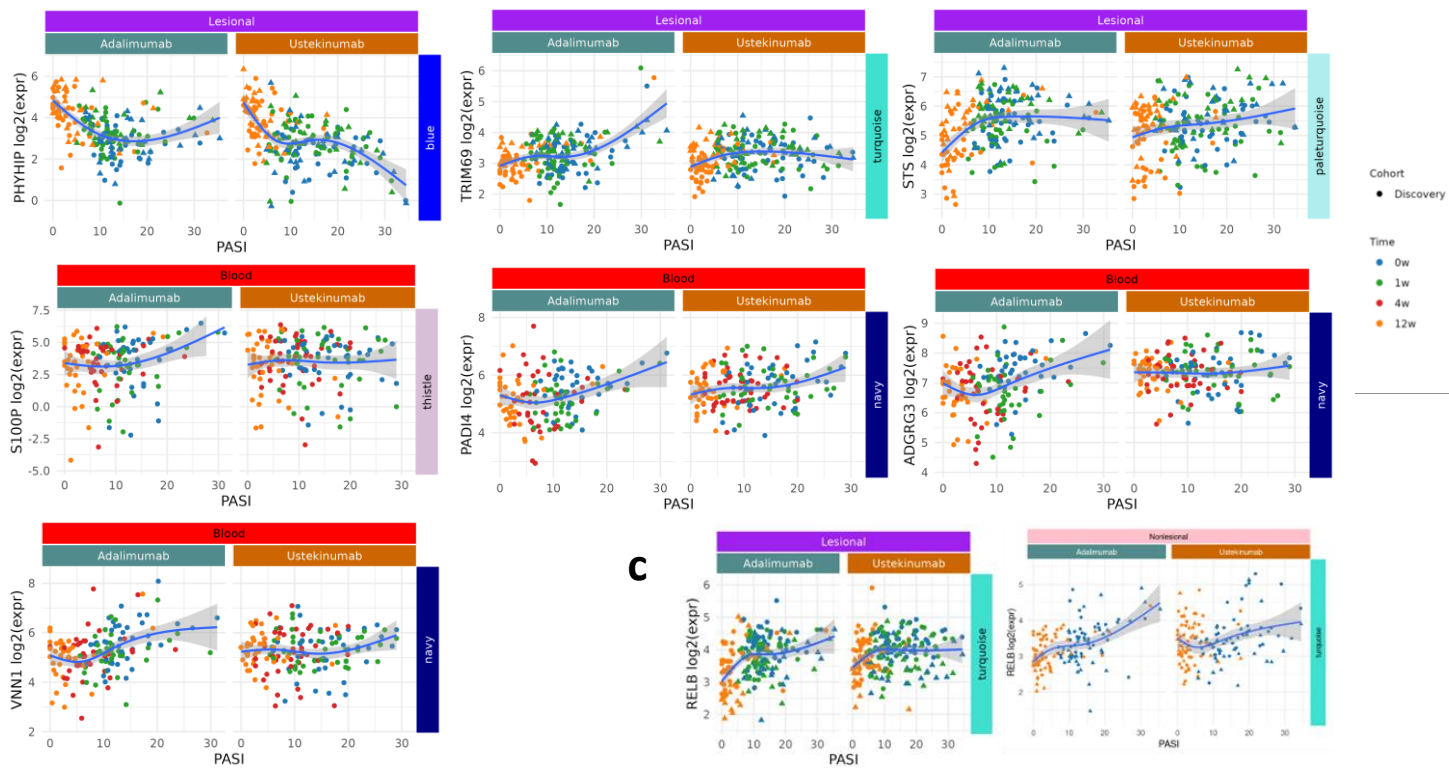
Patient trajectories predicted by the linear ridge regression models from a randomly shuffled 10-fold held-out testing dataset. The first regression model was trained on patient demographic and clinical information. The next two regression models were trained on module eigengenes or latent factors. The final regression model was trained on all features.

Abbreviations: PASI, psoriasis area and severity index.

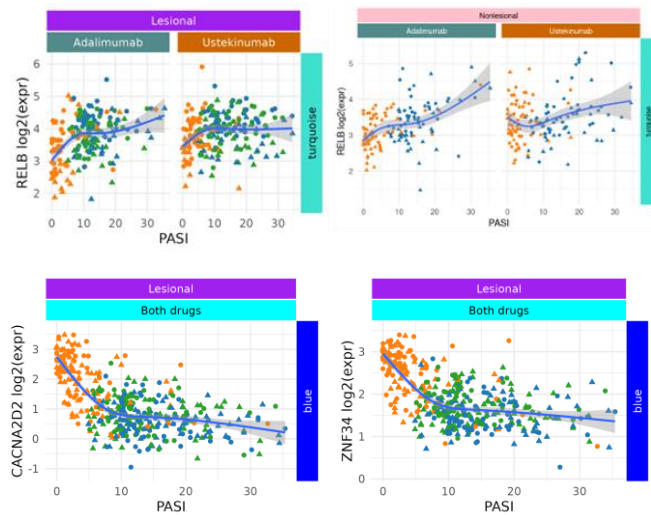
a



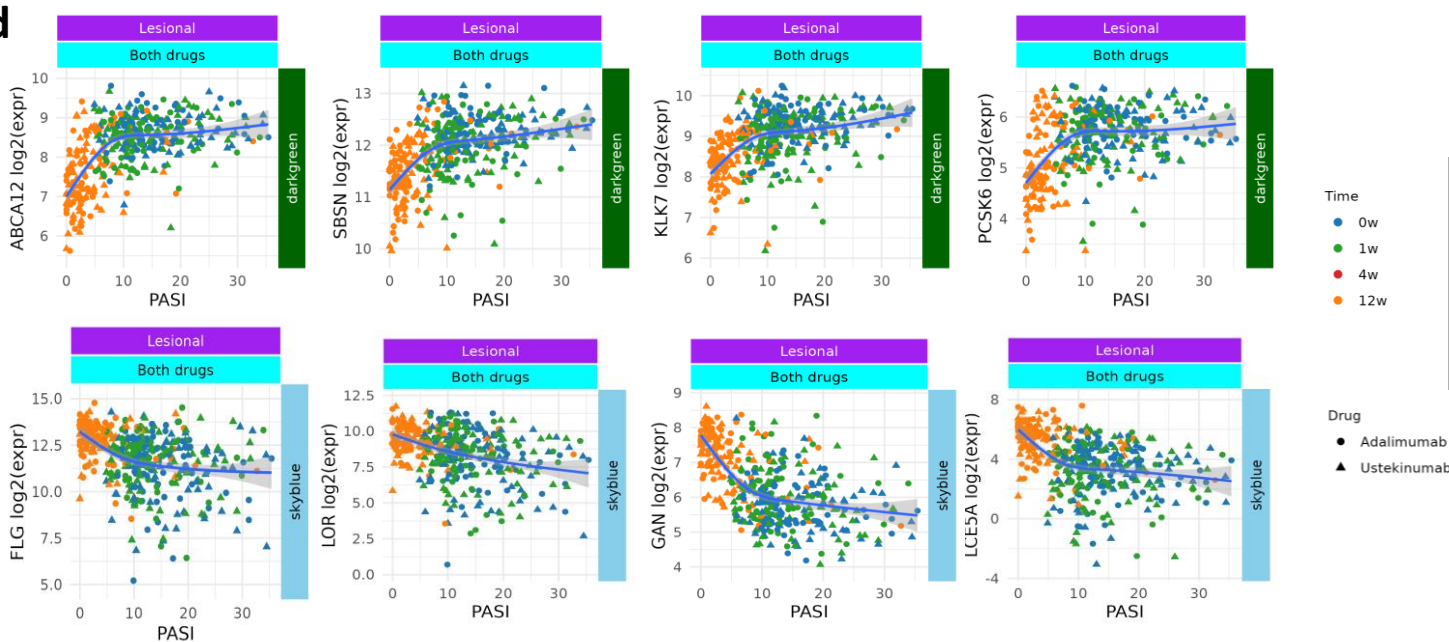
b



C



•

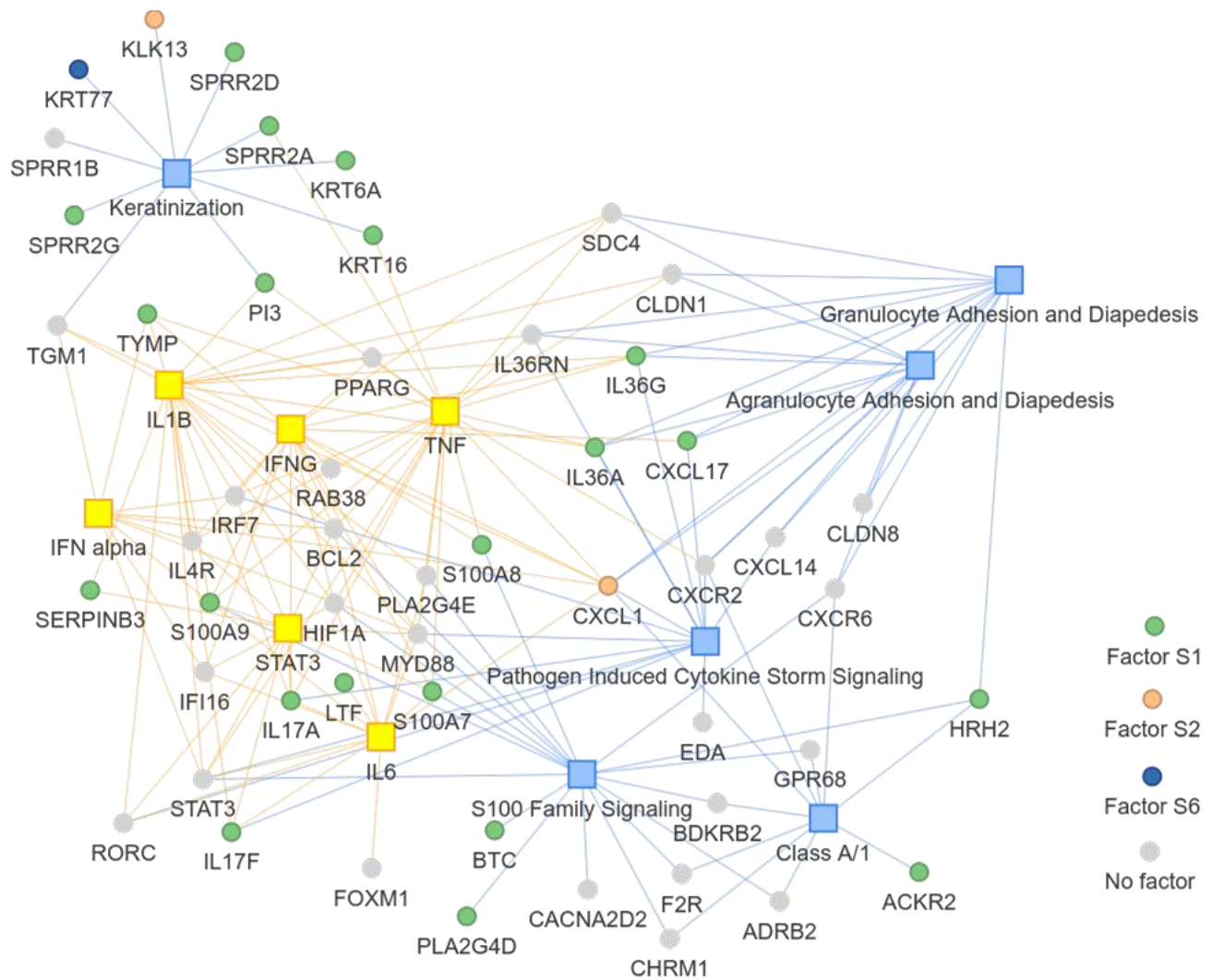


Supplementary Figure 15. Further examples of gene-level associations with disease severity in skin and blood.

Scatter plots of the log₂-CPM expression against PASI of further example disease severity-associated genes. Each point represents a single sample, is marked with a symbol according to drug cohort and colour-coded according to timepoint (blue = 0w, green = 1w, red = 4w, orange = 12w). The grey shading indicates 95% confidence intervals. The title banner provides information on the tissue and drug cohort. Module membership is denoted opposite the y axis. **(a)** Exemplars; **(b)** drug-specific examples; **(c)** PASI-associated signature genes, identified through SHAP analysis of blue and turquoise modules (Fig. 4D); **(d)** skin barrier genes that were also members of the darkgreen or skyblue modules in skin.

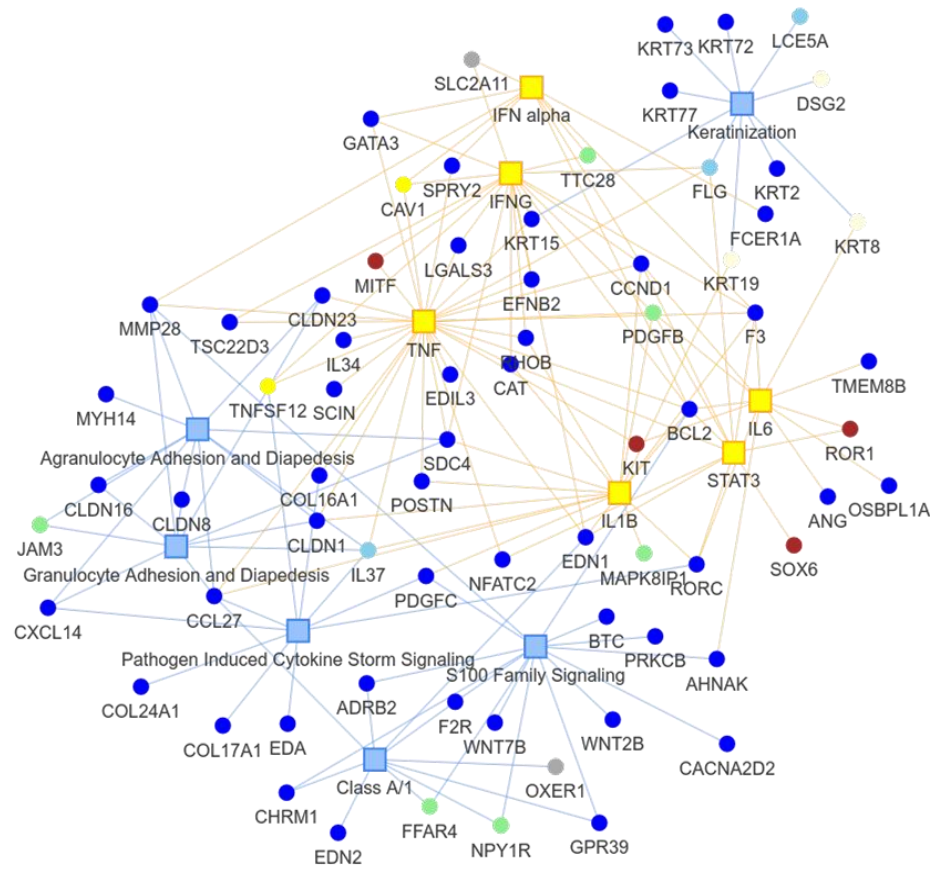
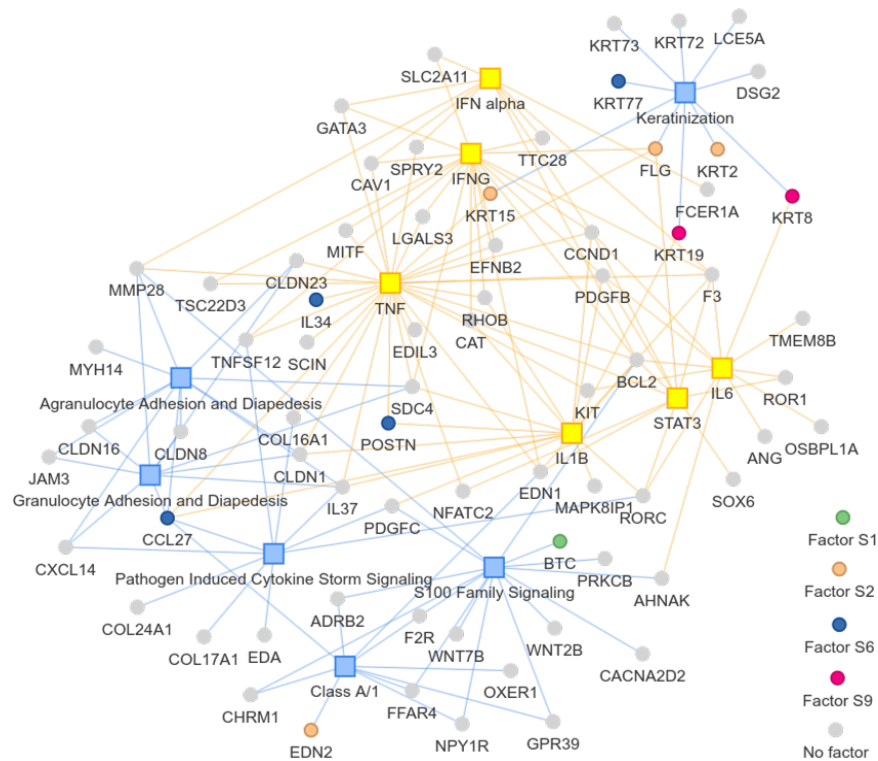
Curves represent natural-spline fits (3 d.f.) with 95 % confidence bands.

Abbreviations: CPM, counts per million; PASI, psoriasis area and severity index; w, week; SHAP, SHapley Additive exPlanations.



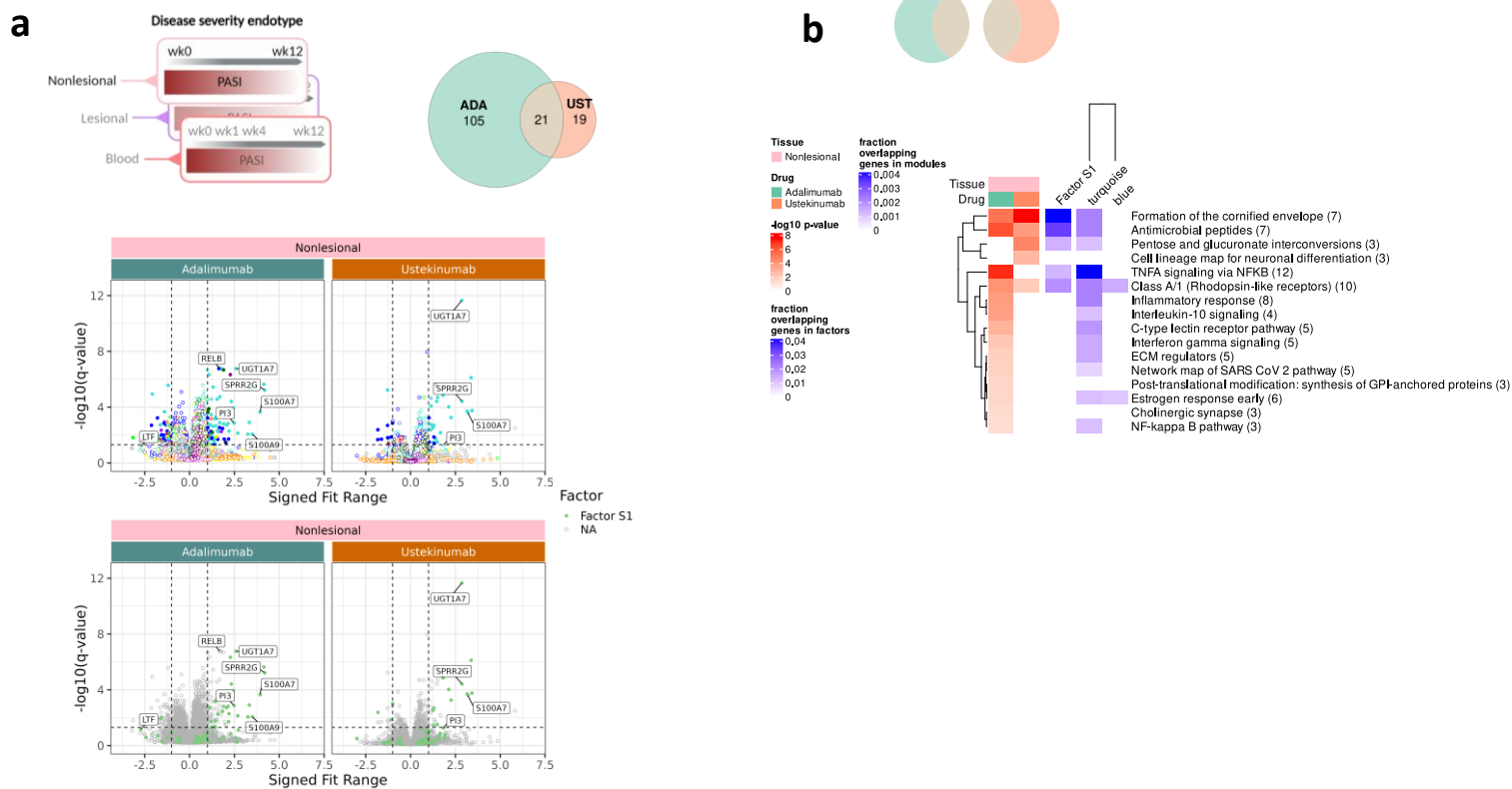
Supplementary Figure 16. Network analysis of the top disease severity-associated genes in lesional skin for the combined drug cohort.

Genes (circles) are coloured according to associated skin factors, upstream regulators (yellow squares) and canonical pathways (blue squares) were identified by IPA from all strongly disease severity-associated genes.

a**b**

Supplementary Figure 17. Network analysis of top negative disease severity-associated genes in lesional skin for the combined drug cohort.

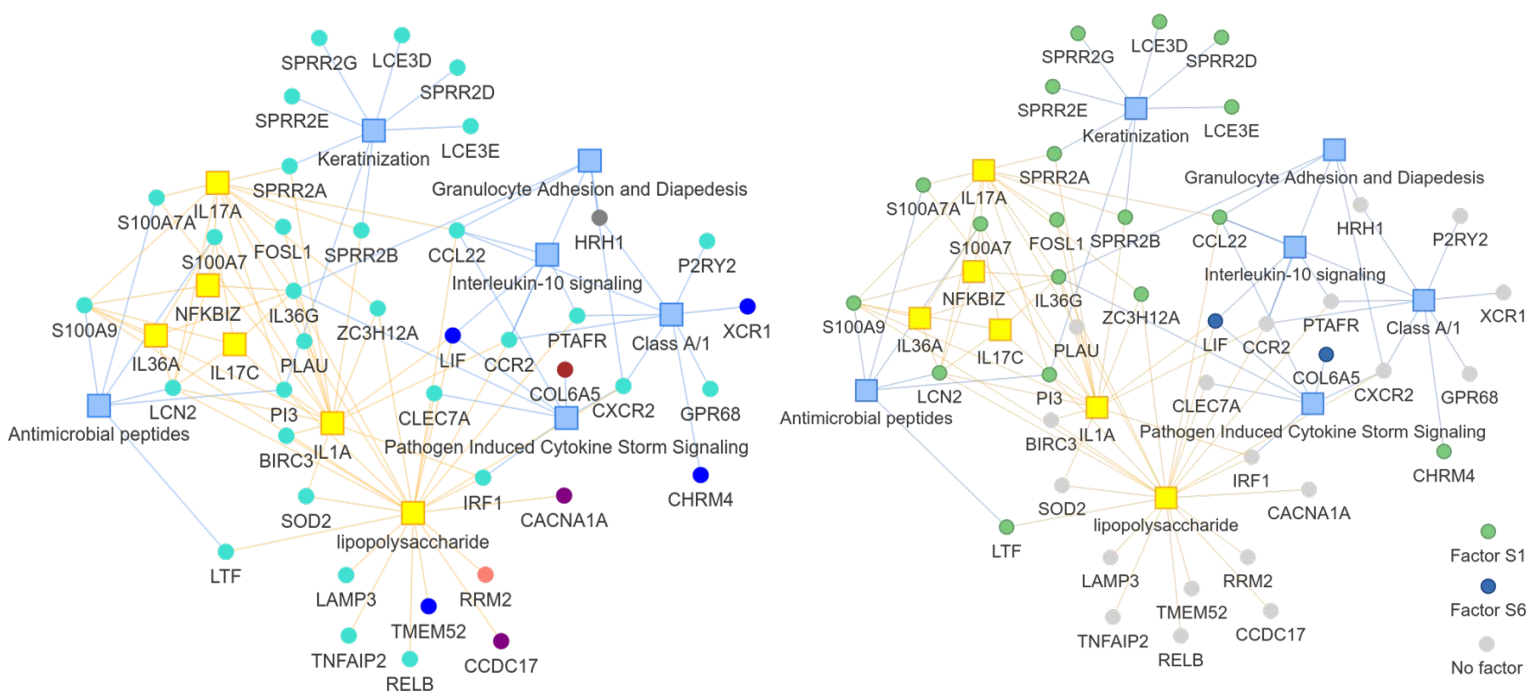
Networks are colour coded **(a)** according to their WGCNA module, and **(b)** according to associated skin factors. Genes (circles) are coloured according to associated skin factors, upstream regulators (yellow squares) and canonical pathways (blue squares) were identified by IPA from all strongly disease severity-associated genes.



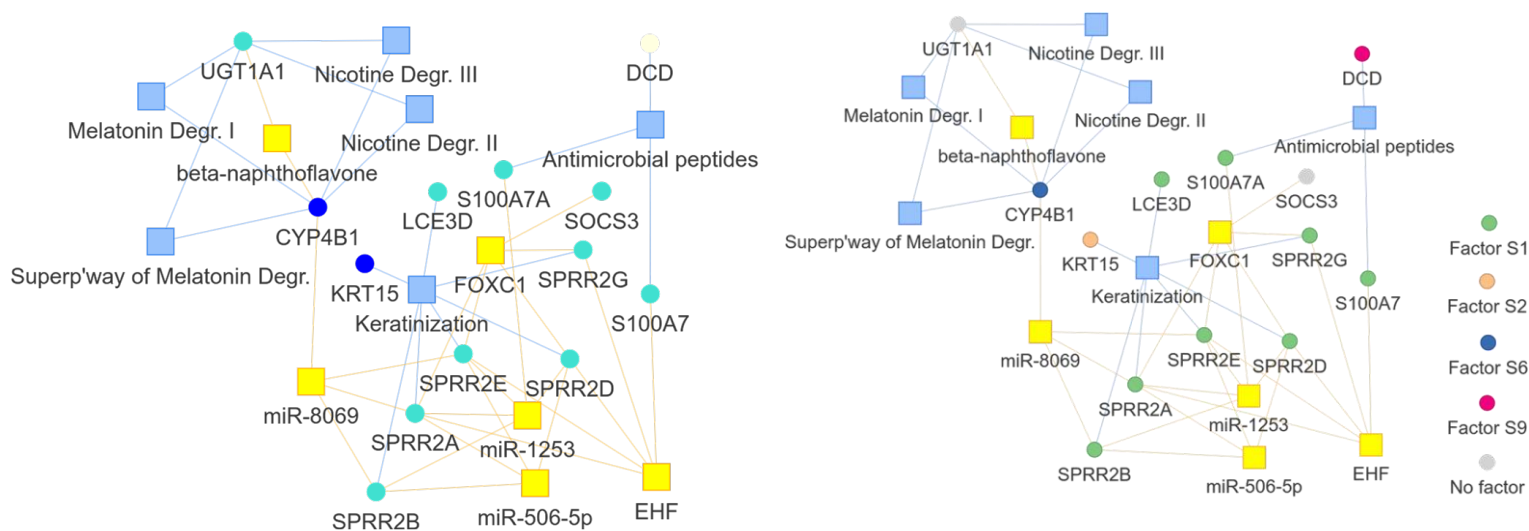
Supplementary figure 18. Disease severity endotypes in non-lesional skin (NLS).

(a) (Upper left) Schematic. (Upper right) Venn Diagram showing overlap of genes in NLS with significant ($q\text{-value} < 0.05$) non-linear association (natural spline with 3 degrees of freedom) of expression with disease severity (DS), measured by PASI, in the adalimumab and ustekinumab cohorts. (Lower) Volcano plots of gene expression within the discovery and replication cohorts, faceted by drug cohort and plotted against signed fit range (overall direction and magnitude of DS association); points are coloured according to the WGCNA modules and ICA latent factors; example genes are labelled. **(b)** Metascape pathways from all co-expressed strongly DS-associated genes in each drug cohort, broken down by WGCNA module. The red heatmap shows the $-\log_{10} p\text{-value}$, the blue shows the fraction of overlapping genes. The blue heatmap is normalised by the number of genes in the union of WGCNA module and Metascape pathway. *Abbreviations:* ADA, adalimumab; UST, ustekinumab; NLS, non-lesional skin; DS, disease severity; WGCNA, weighted gene correlation network analysis; ICA, independent component analysis.

a



b

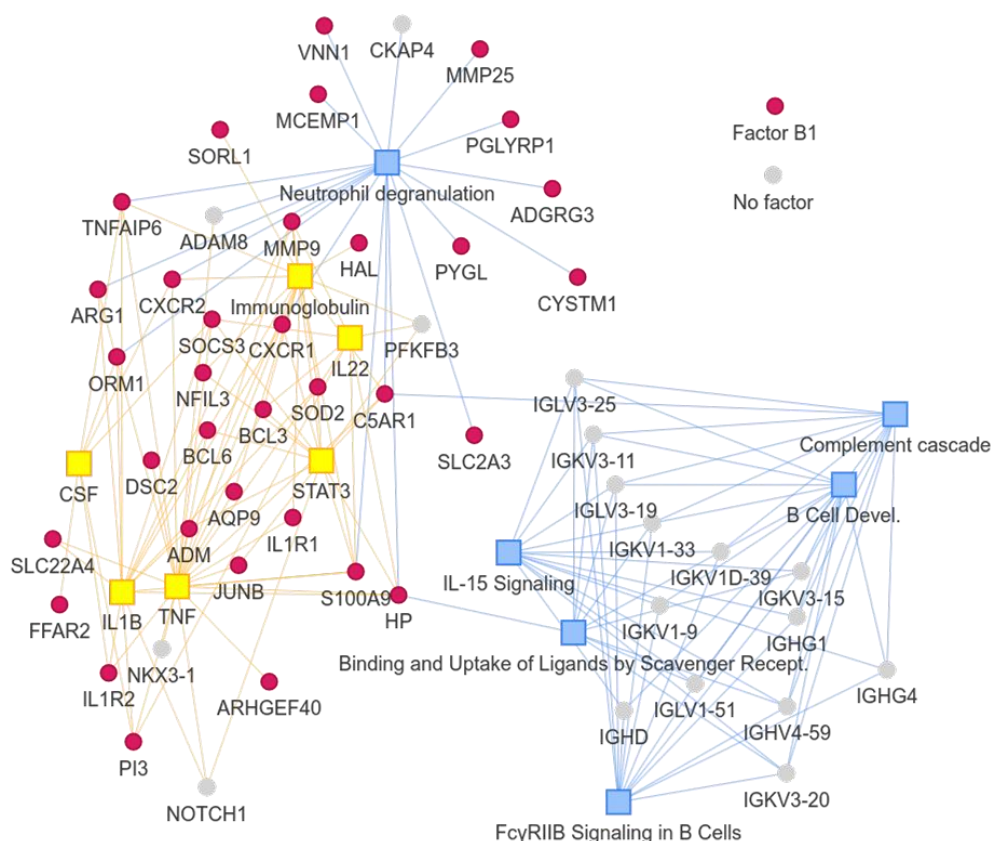


Supplementary Figure 19. Network analysis of top negative disease severity-associated genes in non-lesional skin (NLS).

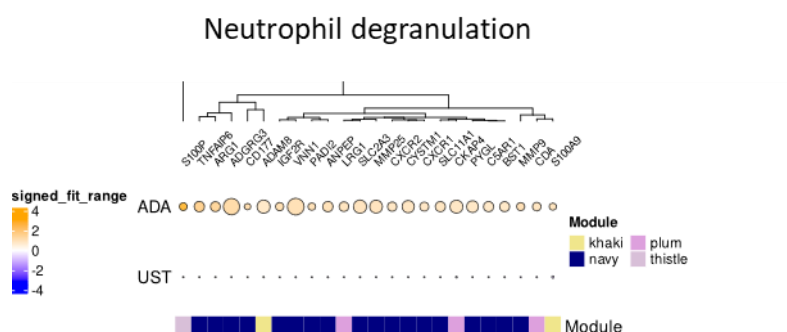
Networks are shown for **(a)** the adalimumab cohort, colour coded according to their WGCNA module (left), and according to associated latent factors (right), and **(b)** the ustekinumab cohort, colour coded according to their WGCNA module (left), and according to associated skin factors (right). Significant genes (circles), upstream regulators (yellow squares) and canonical pathways (blue squares) were identified by IPA.

Abbreviations: WGCNA, weighted gene correlation network analysis; IPA, Ingenuity Pathway Analysis.

a



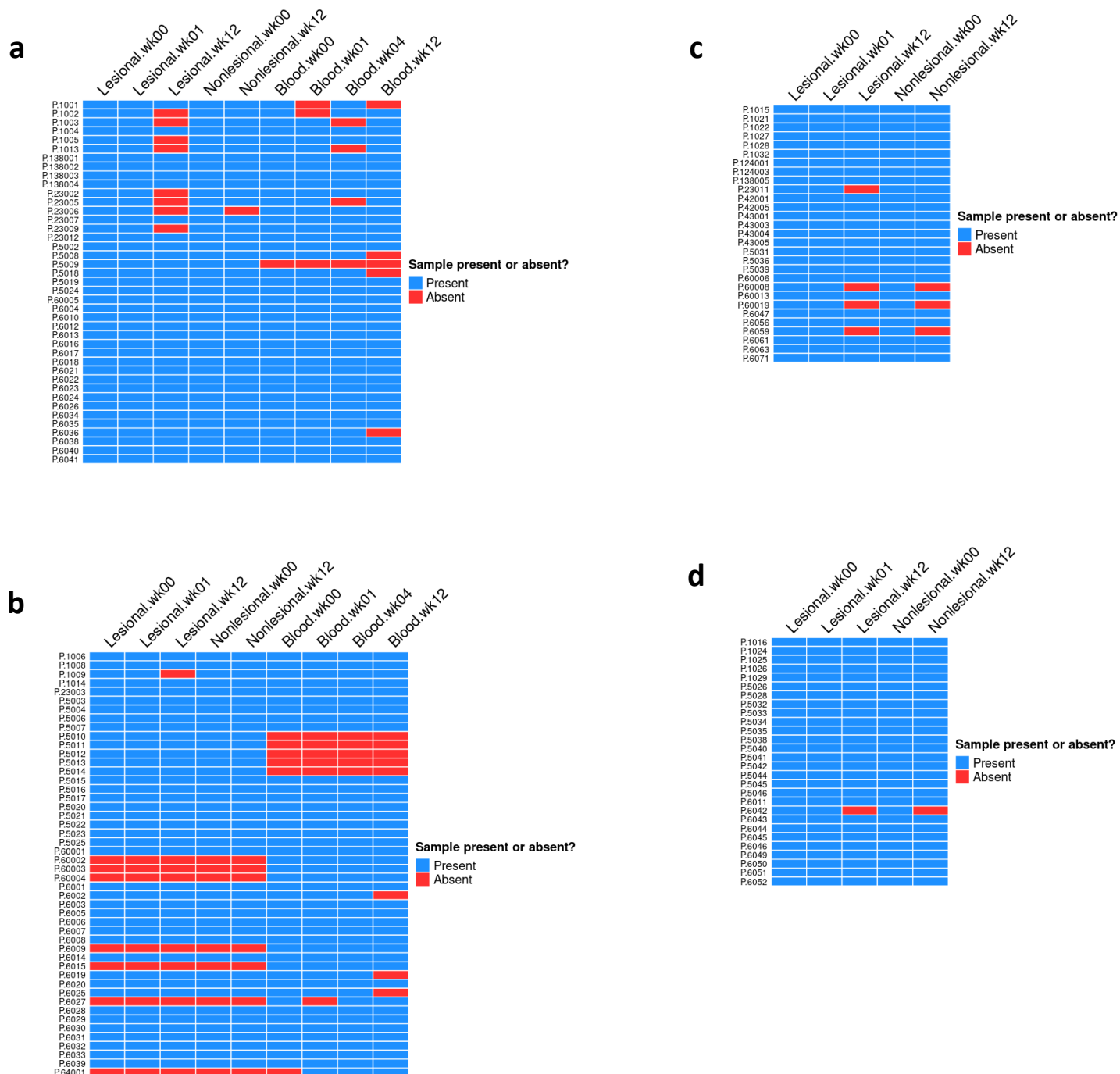
b



Supplementary Figure 20. Functional analysis of the top disease severity-associated genes in blood for the adalimumab cohort.

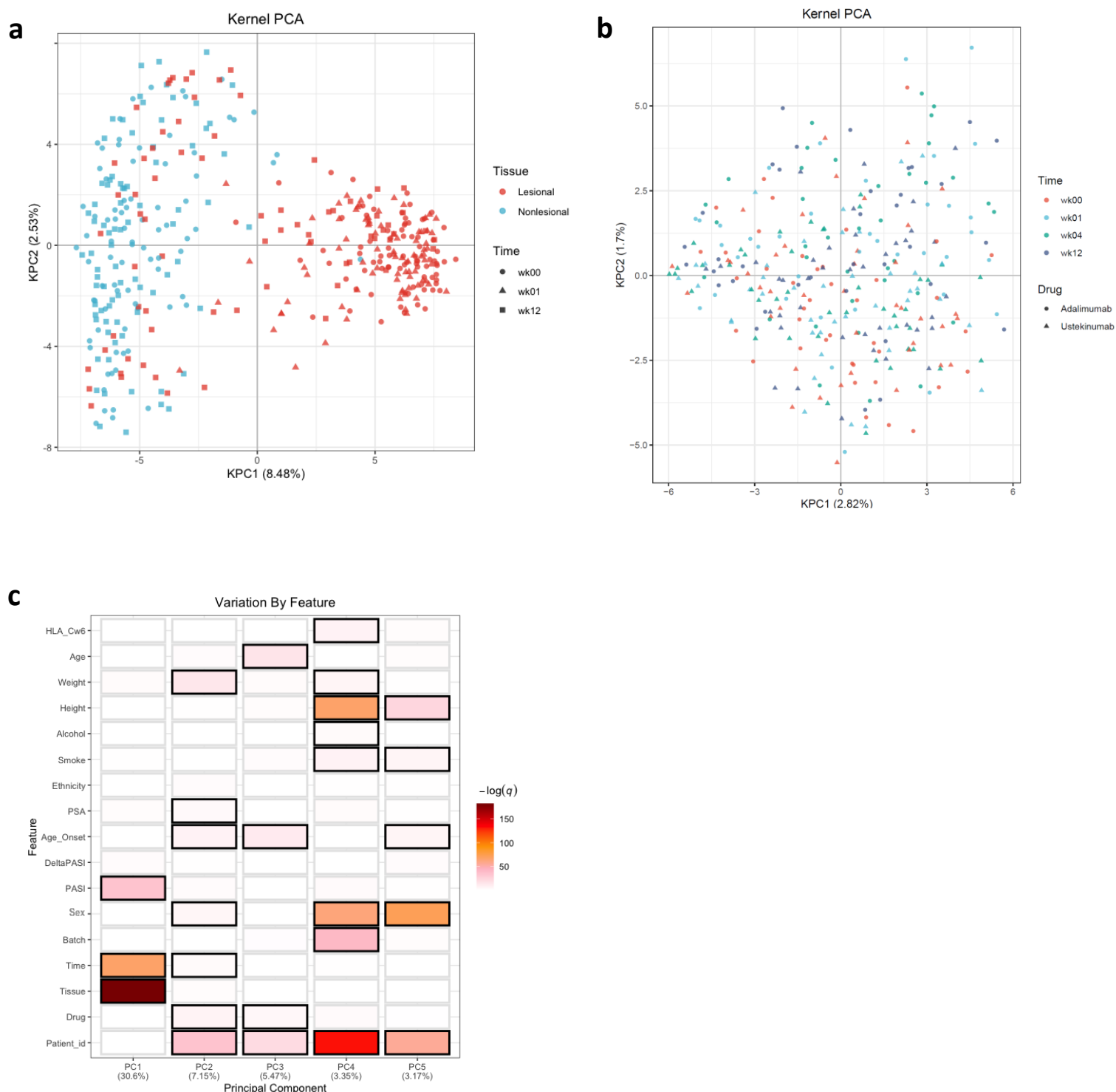
(a) Network analysis of the top disease severity-associated genes in blood for the adalimumab cohort. Genes (circles) are coloured according to associated latent factors, upstream regulators (yellow squares) and canonical pathways (blue squares) were identified by IPA from all strongly disease severity-associated genes. **(b)** Dot plots of the disease severity-associated genes within the Metascape neutrophil degranulation pathway. Gene expression is separated by drug cohort and clustered by signed fit range. The radius of the dot represents significance $-\log_{10}$ q-value and colour represents signed fit range. Module membership is recorded below each gene.

Abbreviations: IPA, Ingenuity Pathway Analysis.



Supplementary figure 21. Graphical representations of RNA-Seq sample completeness.

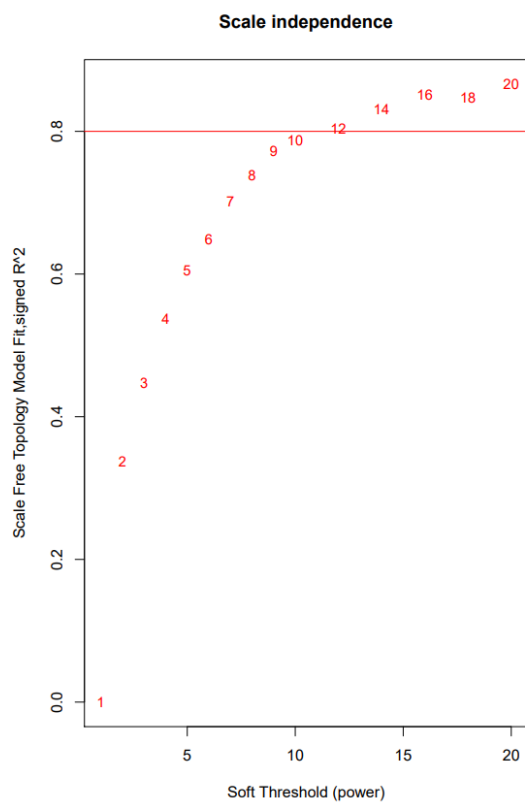
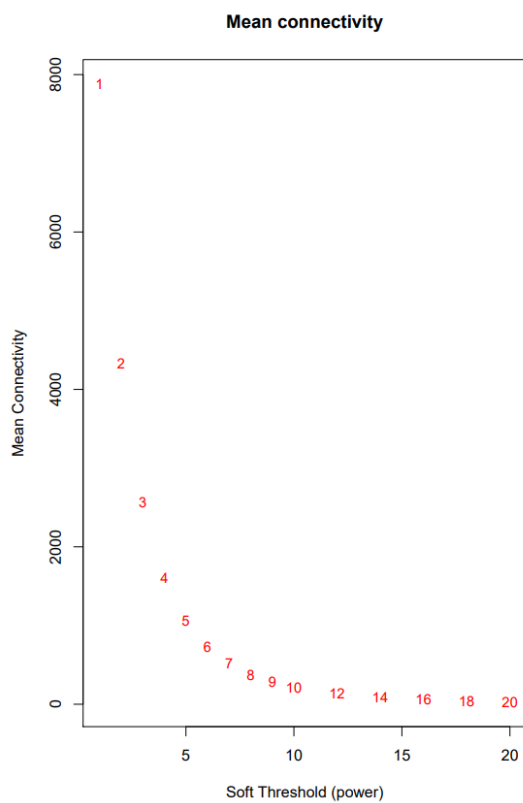
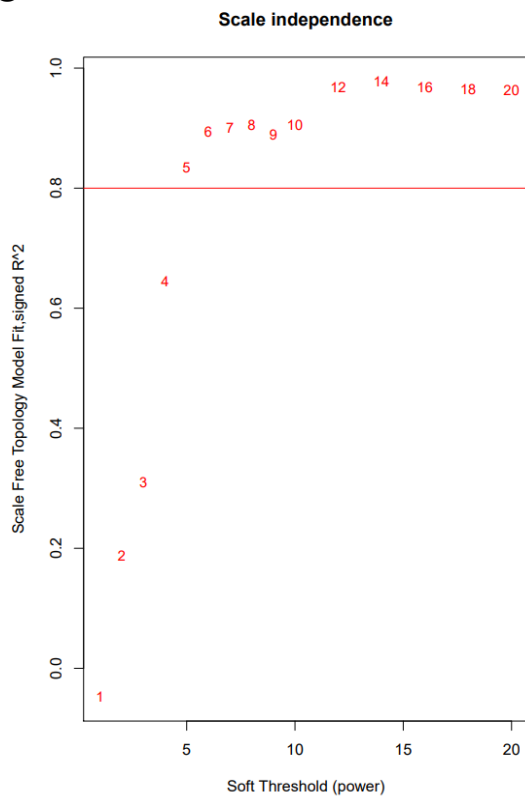
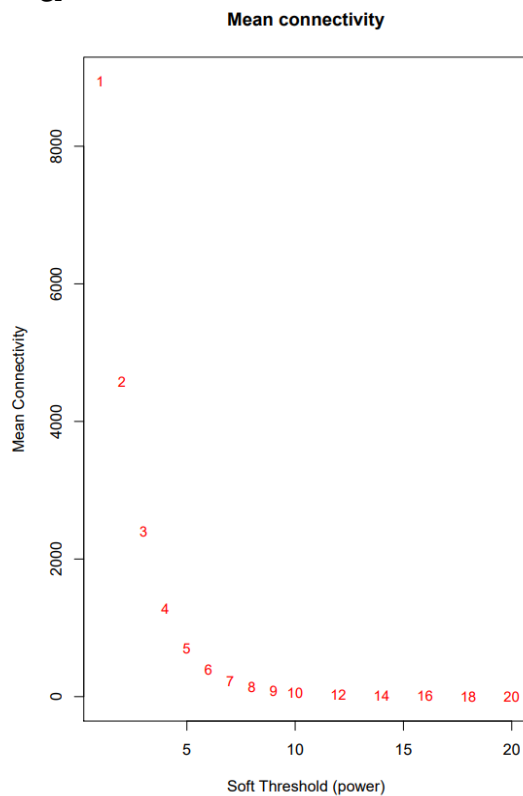
Graphs are shown for the **(a)** adalimumab group and **(b)** ustekinumab group in the discovery cohort, and the **(c)** adalimumab group and **(d)** ustekinumab group in the replication cohort. In each graph, patients are displayed on the x-axis and tissue-times are displayed on the y-axis. Blue indicates that a sample was collected, sequenced and used for analysis at the corresponding tissue-time for the corresponding patient; red indicates a missing sample for the corresponding tissue-time and patient.



Supplementary Figure 22. Drivers of transcriptomic variation in skin and blood.

As an exploratory analysis, prior to conducting gene-level differential expression analysis or dimensionality reduction with WGCNA or ICA, we used Kernel PCA to explore the effect of tissue type, time point and drug on transcriptomic variation in the discovery cohort skin and blood RNA-Seq data. PCA plots of the first two principal components in **(a)** skin and **(b)** blood are shown. We used statistical analysis to investigate associations between the first five principal components in skin and an extended set of clinical and demographic traits; this is visualised in **(c)**.

Abbreviations: WGCNA, weighted gene correlation network analysis; ICA, independent component analysis; PCA, principal component analysis.

a**b****c****d**

Supplementary Figure 23. Identifying appropriate soft-thresholding powers for WGCNA in skin and blood.

WGCNA involves creation of a gene-gene correlation matrix; prior to hierarchical clustering of this matrix, the correlation estimates are raised to a power in order to amplify the differences between high and low correlations; this power is chosen based on scale independence and mean connectivity. The scale independence (**a, c**) and mean connectivity (**b, d**) of the candidate soft-thresholding powers in skin (**a, b**) and blood (**c, d**). The smallest power that passed an R² threshold of 0.8 was selected for the downstream module identification steps. In skin this was 12 and in blood this was 5. Further details are available in the supplementary methods.

Supplementary Table 1a. Demographic information of study recruits for PSORT-D

		Overall n=89	Adalimumab n=41	Ustekinumab n=48
Biologic Naive, n (%)	No	27 (30.3)	10 (24.4)	17 (35.4)
	Yes	62 (69.7)	31 (75.6)	31 (64.6)
Ethnicity, n (%)	Asian or Asian British	6 (6.7)	3 (7.3)	3 (6.2)
	Black or Black British	2 (2.2)	1 (2.4)	1 (2.1)
	White	80 (89.9)	37 (90.2)	43 (89.6)
	Other	1 (1.1)		1 (2.1)
Sex, n (%)	F	33 (37.1)	15 (36.6)	18 (37.5)
	M	56 (62.9)	26 (63.4)	30 (62.5)
PsA, n (%)	Negative	62 (69.7)	27 (65.9)	35 (72.9)
	Positive	27 (30.3)	14 (34.1)	13 (27.1)
Flexural, n (%)	No	53 (59.6)	23 (56.1)	30 (62.5)
	Not Done	4 (4.5)	2 (4.9)	2 (4.2)
	Yes	32 (36.0)	16 (39.0)	16 (33.3)
Scalp, n (%)	No	17 (19.1)	9 (22.0)	8 (16.7)
	Not Done	4 (4.5)	2 (4.9)	2 (4.2)
	Yes	68 (76.4)	30 (73.2)	38 (79.2)
Palms, n (%)	No	66 (74.2)	33 (80.5)	33 (68.8)
	Not Done	4 (4.5)	2 (4.9)	2 (4.2)
	Yes	19 (21.3)	6 (14.6)	13 (27.1)
Soles, n (%)	No	67 (75.3)	32 (78.0)	35 (72.9)
	Not Done	4 (4.5)	2 (4.9)	2 (4.2)
	Yes	18 (20.2)	7 (17.1)	11 (22.9)
Nails, n (%)	No	25 (28.1)	13 (31.7)	12 (25.0)
	Not Done	4 (4.5)	2 (4.9)	2 (4.2)
	Yes	60 (67.4)	26 (63.4)	34 (70.8)
Age, mean (SD)		44.4 (12.3)	41.4 (10.3)	46.9 (13.4)
Age of onset, mean (SD)		22.6 (13.2)	21.2 (10.8)	23.9 (15.1)
wk00 PASI, mean (SD)		15.3 (5.9)	14.5 (5.2)	15.9 (6.4)
wk01 PASI, mean (SD)		13.7 (6.0)	12.4 (5.0)	14.8 (6.6)
wk04 PASI, mean (SD)		9.1 (5.7)	8.3 (5.2)	9.8 (6.0)
wk12 PASI, mean (SD)		3.9 (4.9)	4.1 (6.1)	3.8 (3.8)
wk00 DLQI, mean (SD)		17.5 (7.0)	16.9 (6.9)	17.9 (7.1)
wk01 DLQI, mean (SD)		15.3 (7.2)	14.3 (6.5)	16.2 (7.7)
wk04 DLQI, mean (SD)		9.7 (6.7)	7.9 (5.6)	11.2 (7.2)
wk12 DLQI, mean (SD)		4.2 (5.2)	3.6 (4.5)	4.6 (5.7)
Cw6, n (%)	Negative	46 (56.1)	23 (56.1)	23 (56.1)
	Positive	36 (43.9)	18 (43.9)	18 (43.9)
DeltaPASI, mean (SD)		0.7 (0.2)	0.8 (0.2)	0.7 (0.2)
Smoking, n (%)	No	27 (30.3)	12 (29.3)	15 (31.2)
	Yes	62 (69.7)	29 (70.7)	33 (68.8)
Drink Alcohol, n (%)	No	24 (27.0)	4 (9.8)	20 (41.7)
	Yes	65 (73.0)	37 (90.2)	28 (58.3)
Alcohol (units/week), mean (SD)		8.3 (16.7)	8.5 (10.2)	8.1 (20.8)
BMI, mean (SD)		30.8 (6.4)	31.6 (7.0)	30.1 (5.7)
BMI status, n (%)	Healthy weight (>=18.5 <30)	17 (19.3)	8 (19.5)	9 (19.1)
	Obese (>=30)	44 (50.0)	23 (56.1)	21 (44.7)
	Overweight (>=25 <30)	27 (30.7)	10 (24.4)	17 (36.2)

Supplementary Table 1b. Demographic information of study recruits for PSORT-R

		Overall n=57	Adalimumab n=29	Ustekinumab n=28
Biologic Naive, n (%)	No	8 (14.0)	1 (3.4)	7 (25.0)
	Yes	49 (86.0)	28 (96.6)	21 (75.0)
Ethnicity, n (%)	Asian or Asian British	2 (3.5)	1 (3.4)	1 (3.6)
	Other	2 (3.5)	2 (6.9)	
	White	52 (91.2)	26 (89.7)	26 (92.9)
	Black or Black British	1 (1.8)		1 (3.6)
Sex, n (%)	F	28 (49.1)	13 (44.8)	15 (53.6)
	M	29 (50.9)	16 (55.2)	13 (46.4)
PsA, n (%)	Negative	39 (68.4)	16 (55.2)	23 (82.1)
	Positive	18 (31.6)	13 (44.8)	5 (17.9)
Flexural, n (%)	No	24 (42.1)	14 (48.3)	10 (35.7)
	Yes	33 (57.9)	15 (51.7)	18 (64.3)
Scalp, n (%)	No	7 (12.3)	5 (17.2)	2 (7.1)
	Yes	50 (87.7)	24 (82.8)	26 (92.9)
Palms, n (%)	No	42 (73.7)	20 (69.0)	22 (78.6)
	Yes	15 (26.3)	9 (31.0)	6 (21.4)
Soles, n (%)	No	43 (75.4)	20 (69.0)	23 (82.1)
	Not Done	1 (1.8)	1 (3.4)	
	Yes	13 (22.8)	8 (27.6)	5 (17.9)
Nails, n (%)	No	24 (42.1)	11 (37.9)	13 (46.4)
	Yes	33 (57.9)	18 (62.1)	15 (53.6)
Age, mean (SD)		46.2 (12.5)	44.3 (11.6)	48.2 (13.4)
Age of onset, mean (SD)		24.1 (15.4)	22.0 (13.5)	26.1 (17.1)
wk00 PASI, mean (SD)		16.2 (7.6)	16.2 (7.2)	16.3 (8.2)
wk01 PASI, mean (SD)		14.4 (6.9)	14.0 (6.8)	14.7 (7.1)
wk04 PASI, mean (SD)		9.1 (5.1)	8.6 (4.7)	9.6 (5.5)
wk12 PASI, mean (SD)		3.9 (4.4)	4.2 (4.8)	3.7 (4.0)
wk00 DLQI, mean (SD)		17.0 (6.1)	17.9 (5.4)	16.1 (6.8)
wk01 DLQI, mean (SD)		14.3 (6.7)	14.1 (6.4)	14.5 (7.1)
wk04 DLQI, mean (SD)		8.8 (6.7)	8.0 (5.4)	9.6 (7.8)
wk12 DLQI, mean (SD)		3.4 (4.2)	4.6 (5.2)	2.1 (2.1)
Cw6, n (%)	Negative	27 (48.2)	12 (41.4)	15 (55.6)
	Positive	29 (51.8)	17 (58.6)	12 (44.4)
DeltaPASI, mean (SD)		0.7 (0.3)	0.7 (0.3)	0.7 (0.3)
Smoking, n (%)	No	21 (36.8)	12 (41.4)	9 (32.1)
	Yes	36 (63.2)	17 (58.6)	19 (67.9)
Drink Alcohol, n (%)	No	21 (36.8)	16 (55.2)	5 (17.9)
	Yes	36 (63.2)	13 (44.8)	23 (82.1)
Alcohol (units/week), mean (SD)		7.1 (10.6)	4.3 (7.9)	10.1 (12.2)
BMI, mean (SD)		32.2 (8.5)	33.7 (8.7)	30.7 (8.2)
BMI status, n (%)	Healthy weight ($\geq 18.5 < 30$)	13 (22.8)	4 (13.8)	9 (32.1)
	Obese (≥ 30)	29 (50.9)	17 (58.6)	12 (42.9)
	Overweight ($\geq 25 < 30$)	15 (26.3)	8 (27.6)	7 (25.0)

Supplementary Table 2: PASI prediction performance of Ridge models. Shown are means $\pm$ SD for 20 randomly shuffled 10-fold testing datasets.

Inputs	Test MAE	Test R^2
Demographics/clinical features WGCNA modules ICA factors	0.47 $\pm$ 0.10	0.50 $\pm$ 0.10
All WGCNA modules	0.45 $\pm$ 0.06	0.54 $\pm$ 0.09
All ICA factors	0.46 $\pm$ 0.10	0.50 $\pm$ 0.11

Supplementary Table 3: Performance metrics for modules at the gene-level using additive Gaussian process models. Mean performance metrics $\pm$ SD for testing datasets.

Model inputs	Test MAE	Test R^2
Top 10 Factor S1 genes	0.47 ± 0.06	0.40 ± 0.10
Top 10 Factor S2 genes	0.48 ± 0.06	0.37 ± 0.15
Top 10 Factor S9 genes	0.54 ± 0.08	0.21 ± 0.16
Top 10 Factor S6 genes	0.51 ± 0.08	0.26 ± 0.14
Top 10 Factor S8 genes	0.62 ± 0.09	0.04 ± 0.09
Top 10 Factor S21 genes	0.64 ± 0.08	-0.02 ± 0.05

Supplementary Table 4: Performance metrics for modules at the gene-level using additive Gaussian process models. Mean performance metrics $\pm$ SD for testing datasets.

Model inputs	Test MAE	Test R^2
Top 10 Turquoise genes	0.43 ± 0.06	0.47 ± 0.13
Top 10 Violet genes	0.52 ± 0.07	0.29 ± 0.13
Top 10 Steelblue genes	0.57 ± 0.07	0.16 ± 0.14
Top 10 Blue genes	0.47 ± 0.07	0.44 ± 0.12
Top 10 Tan genes	0.50 ± 0.06	0.33 ± 0.09

Supplementary Table 5: Pearson correlations between factors and baseline PASI

Factor	Correlation	P-value	Adjusted p-value
S18	-0.278	0.00092	0.01286
S2	0.275	0.00107	0.01286
S1	0.245	0.00366	0.02925
S17	0.228	0.00685	0.04110
S10	-0.170	0.04587	0.22020
S23	-0.149	0.07913	0.31585
S16	0.143	0.09212	0.31585
S21	0.125	0.14280	0.42841
S12	0.109	0.20286	0.51030
S13	0.097	0.25614	0.51030
S9	-0.096	0.26254	0.51030
S24	-0.093	0.27603	0.51030
S4	-0.090	0.29293	0.51030
S14	-0.089	0.29768	0.51030
S3	-0.071	0.40563	0.63005
S8	-0.069	0.42003	0.63005
S15	0.060	0.48076	0.67871
S20	-0.056	0.51191	0.68255
S19	0.045	0.59873	0.74658
S5	0.042	0.62215	0.74658
S11	-0.031	0.71812	0.82071
S6	0.021	0.80188	0.87478
S7	0.011	0.90199	0.94121
S22	0.004	0.96012	0.96012

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