

## Supplemental information

### A time-resolved proteomic and prognostic map of COVID-19

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Patient state	Descriptor	Score
Uninfected	No clinical or virological evidence of infection	0
Ambulatory	No limitation of activities	1
	Limitation of activities	2
Hospitalised - mild disease	No oxygen therapy	3
	Oxygen by mask or nasal prongs	4
Hospitalised - severe disease	Non-invasive ventilation or high-flow oxygen	5
	Intubation and mechanical ventilation	6
	Ventilation + additional organ support (vasopressors, RRT, ECMO)	7
Dead	Death	8

Supplementary Table 1. **WHO ordinal scale for clinical improvement in COVID-19 as used in the study** (World Health Organisation 2020).

	All patients		No invasive mechanical ventilation						Invasive mechanical ventilation				Deceased**	
	All patients		Max WHO 3 No supplemental oxygen		Max WHO 4 Supplemental low flow oxygen		Max WHO 5 Supplemental high flow oxygen		Max WHO 6 Invasive mechanical ventilation		Max WHO 7 additional organ replacement therapy			
<b>Number of patients</b>	139	100%	23	17%	33	24%	14	10%	6	4%	63	45%	17	12%
<b>Sex</b>														
Female	44	32%	13	57%	8	24%	3	21%	1	17%	19	30%	3	18%
Male	95	68%	10	43%	25	76%	11	79%	5	83%	44	70%	14	82%
<b>Age, years (Median, IQR)</b>	61	50 - 71	49	35 - 70	63	48 - 71	62	49 - 85	64	59 - 71	62	53 - 72	69	55 - 77
≥65	57	41%	6	26%	16	48%	6	43%	3	50%	26	41%	11	65%
<b>BMI (kg/m<sup>2</sup>, Median, IQR)</b>	27.8	24.7 - 31.9	25.4	23.0 - 30.6	27.2	23.3 - 30.3	27.1	23.3 - 34.9	26.6	24.6 - 28.1	29.4	25.7 - 34.1	29.0	24.8 - 31.0
< 25 kg/m <sup>2</sup>	40	29%	10	43%	13	39%	3	21%	2	33%	12	20%	4	24%
≥ 25 kg/m <sup>2</sup>	97	71%	13	57%	20	61%	11	79%	4	66%	49	80%	13	76%
<b>Pre-existing conditions</b>														
CCI (Median, IQR)	3	1 - 4	1	0 - 3	4	1 - 5	3	1 - 6	2.5	2 - 5	3	1 - 4	3	3 - 6
<3	65	47%	16	70%	13	39%	7	50%	3	50%	26	41%	2	12%
≥3	74	53%	7	30%	20	61%	7	50%	3	50%	37	59%	15	88%
Hypertension	78	56%	6	26%	21	64%	7	50%	3	50%	41	65%	15	88%
Congestive heart failure	7	5%	0	0%	3	9%	0	0%	1	17%	3	5%	1	6%
h/o myocardial infarction	13	9%	1	4%	2	6%	1	7%	1	17%	8	13%	1	6%
Chronic lung disease	22	16%	2	9%	6	18%	1	7%	2	33%	11	17%	3	18%
Asthma	7	5%	1	4%	2	6%	0	0%	0	0%	4	6%	1	6%
COPD	15	11%	1	4%	5	15%	0	0%	1	17%	8	13%	2	12%
on home oxygen therapy	6	4%	0	0%	1	3%	0	0%	1	17%	4	6%	2	12%
Diabetes	31	22%	1	4%	9	27%	4	29%	1	17%	16	25%	3	18%
Type II diabetes (% of diabetes)	30	97%	1	100%	8	89%	4	100%	1	100%	16	100%	3	100%
Oral hypoglycaemic drugs	16	12%	0	0%	5	15%	2	14%	0	0%	9	14%	2	12%
Insulin therapy	11	8%	0	0%	6	18%	2	14%	0	0%	3	5%	0	0%
Chronic kidney disease	19	14%	2	9%	8	24%	3	21%	0	0%	6	10%	2	12%
Requiring RRT	2	2%	0	0%	1	3%	0	0%	0	0%	1	2%	1	6%
Chronic liver disease	8	6%	2	9%	3	9%	1	7%	0	0%	2	3%	1	6%
Lipid metabolism disorder	21	15%	4	17%	9	27%	1	7%	1	17%	6	10%	3	18%
h/o stroke	7	5%	0	0%	1	3%	1	7%	1	17%	4	6%	1	6%
Ischemic (% of stroke)	6	86%	0	0%	1	100%	1	100%	1	100%	3	75%	0	0%
Active malignancy	3	2%	0	0%	0	0%	0	0%	1	17%	2	3%	1	6%
h/o solid organ transplant	3	2%	0	0%	2	6%	0	0%	0	0%	1	2%	1	6%
h/o immunosuppressive therapy within past 3 months	13	9%	2	9%	4	12%	2	14%	0	0%	5	8%	3	18%
h/o smoking	33	24%	6	26%	14	42%	2	14%	2	33%	9	14%	2	12%
Current smoker	5	4%	1	4%	2	6%	0	0%	1	17%	1	2%	0	0%
<b>Outpatient medication</b>														
Total amount (Median, IQR)	2	1 - 3	1	0 - 2	3	2 - 5	1	0 - 2	5	2 - 8	2	1 - 4	2	1 - 3
ARB	24	17%	2	9%	6	18%	2	14%	0	0%	14	22%	2	12%
ACE-I	22	22%	3	13%	8	24%	1	7%	0	0%	10	16%	2	12%
Lipid lowering agents	25	25%	2	9%	11	33%	0	0%	1	17%	11	17%	3	18%

<b>Duration of hospital course* (days)</b>	20	9 - 48	7	4 - 10	14	9 - 17	20	13 - 28	38	24 - 71	46	32 - 75	28	16 - 46
Proning**	51	38%	-	-	-	-	-	-	2	33%	49	78%	13	76%
Mechanical ventilation**	69	50%	-	-	-	-	-	-	6	100%	63	100%	17	100%
RRT	46	33%	0	0%	1	3%	0	0%	1	17%	44	70%	15	88%
ECMO**	22	16%	-	-	-	-	-	-	-	-	22	35%	8	47%
ARDS	76	55%	0	0%	3	9%	7	50%	4	67%	62	98%	17	100%
Sepsis	41	29%	0	0%	2	6%	3	21%	2	33%	34	54%	12	71%
Thromboembolic event	32	23%	0	0%	1	3%	2	14%	1	17%	28	44%	8	47%
Cardiopulmonary resuscitation**	7	6%	0	0%	0	0%	0	0%	0	0%	7	12%	2	12%
<b>Outcome</b>														
Deceased (incl. DNI/DNR)	20***	14%	0	0%	1	3%	2	14%	0	0%	17	27%	-	-
DNI/DNR	3	2%	0	0%	1	3%	2	14%	0	0%	0	0%	-	-
Secondary DNI/DNR	4	3%	0	0%	0	0%	0	0%	0	0%	4	6%	4	24%
Requiring new oxygen therapy after discharge*	12	10%	0	0%	0	0%	1	10%	0	0%	11	24%	-	-
Requiring new RRT after discharge*	5	4%	0	0%	0	0%	0	0%	0	0%	5	11%	-	-

Data are shown in n (%) unless otherwise indicated. IQR – interquartile range, CCI – Charlson’s comorbidity index; CKD – chronic kidney disease; ACE-I – angiotensin-converting enzyme inhibitor, ARB - Angiotensin II receptor blockers, RRT – renal replacement therapy, ECMO – extracorporeal membrane oxygenation, DNI/DNR – do not intubate/do not resuscitate, i.e. patient’s wish not to receive mechanical ventilation, organ replacement therapy, or cardiopulmonary resuscitation - secondary DNR - secondary limitation of therapy in situation of probable unfavourable outcome and according to the presumed patient’s wish

\* deceased patients not included

\*\* patients with DNI/DNR not included

\*\*\* one patient died of non-COVID-19 related cause

**Supplementary Table 2. Baseline, treatment and outcome characteristics of patient cohort with COVID-19 at Charité - University hospital Berlin.** Patients are stratified according to the maximum grade on WHO ordinal scale.



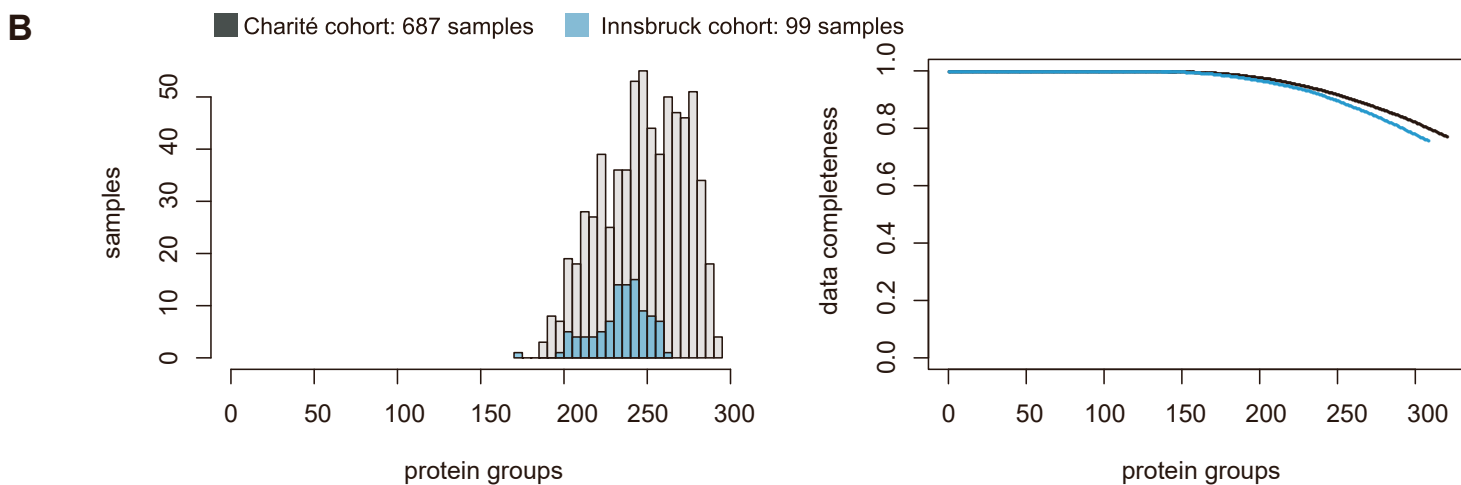
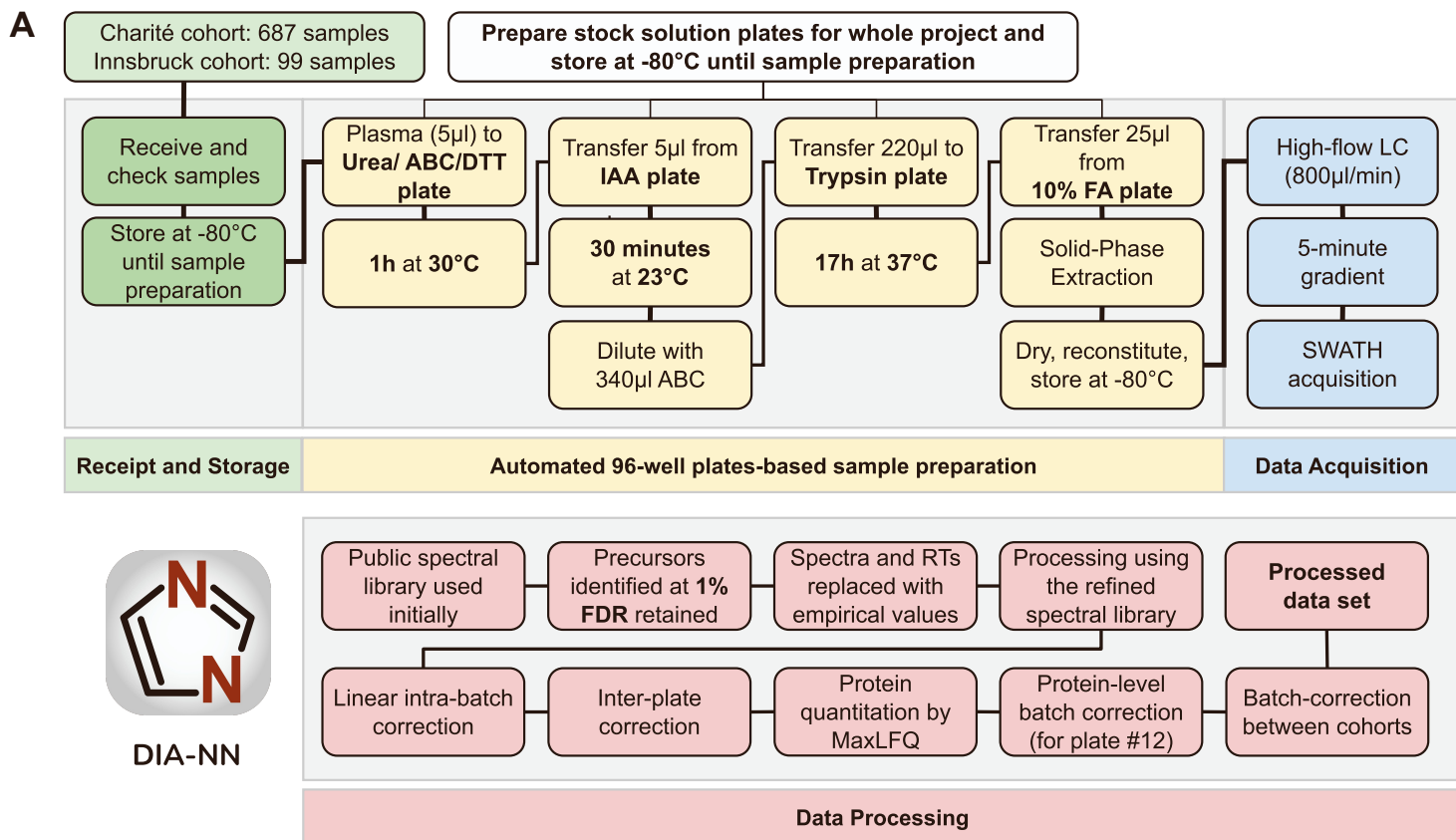


Figure S1. **Plasma proteomics workflow.** **A** The schematic of the 96-well plates-based sample preparation workflow (Messner et al., 2020), followed by mass spectrometry and raw data processing. The workflow results in normalised and batch-corrected protein quantities. Imputation of missing values is not performed per se, but might be required for certain downstream analyses. All statistical tests in the present work were applied without imputation, while imputation was performed for machine learning (Methods). **B** Distribution of the numbers of quantified protein groups across different samples in two cohorts (left) and the data completeness plotted against the number of protein groups (right).

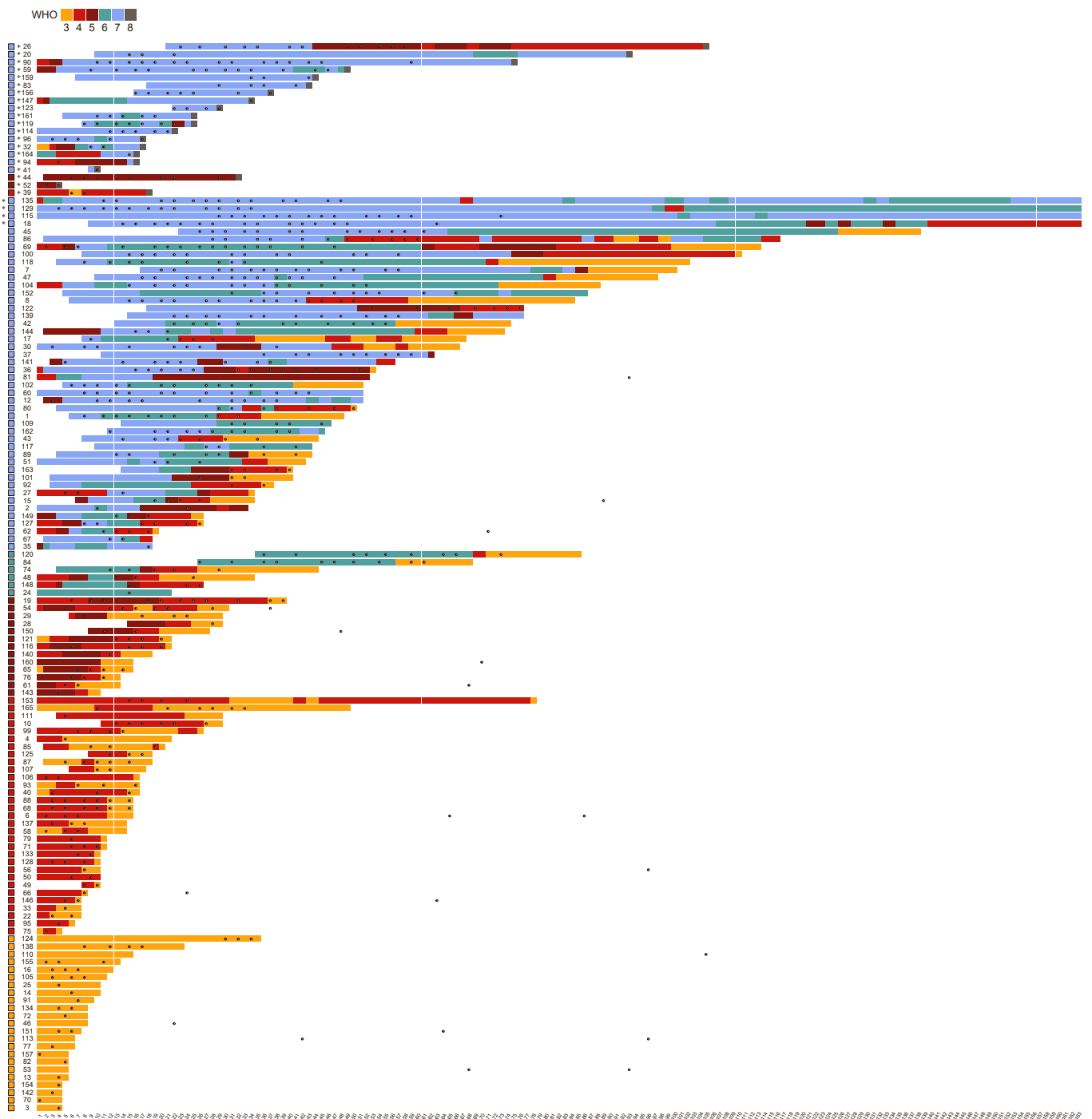


Figure S2. Disease trajectories from hospital admission onward. Patient IDs are given on the y-axis, number of days since admission on the x-axis, WHO severity grade is color-coded, starting with the day the patient was admitted to Charite or transferred from another hospital. Proteomic samples (including follow-up visits after discharge) are indicated with white points.

+ deceased  
 \* still in hospital on 30 August 2020

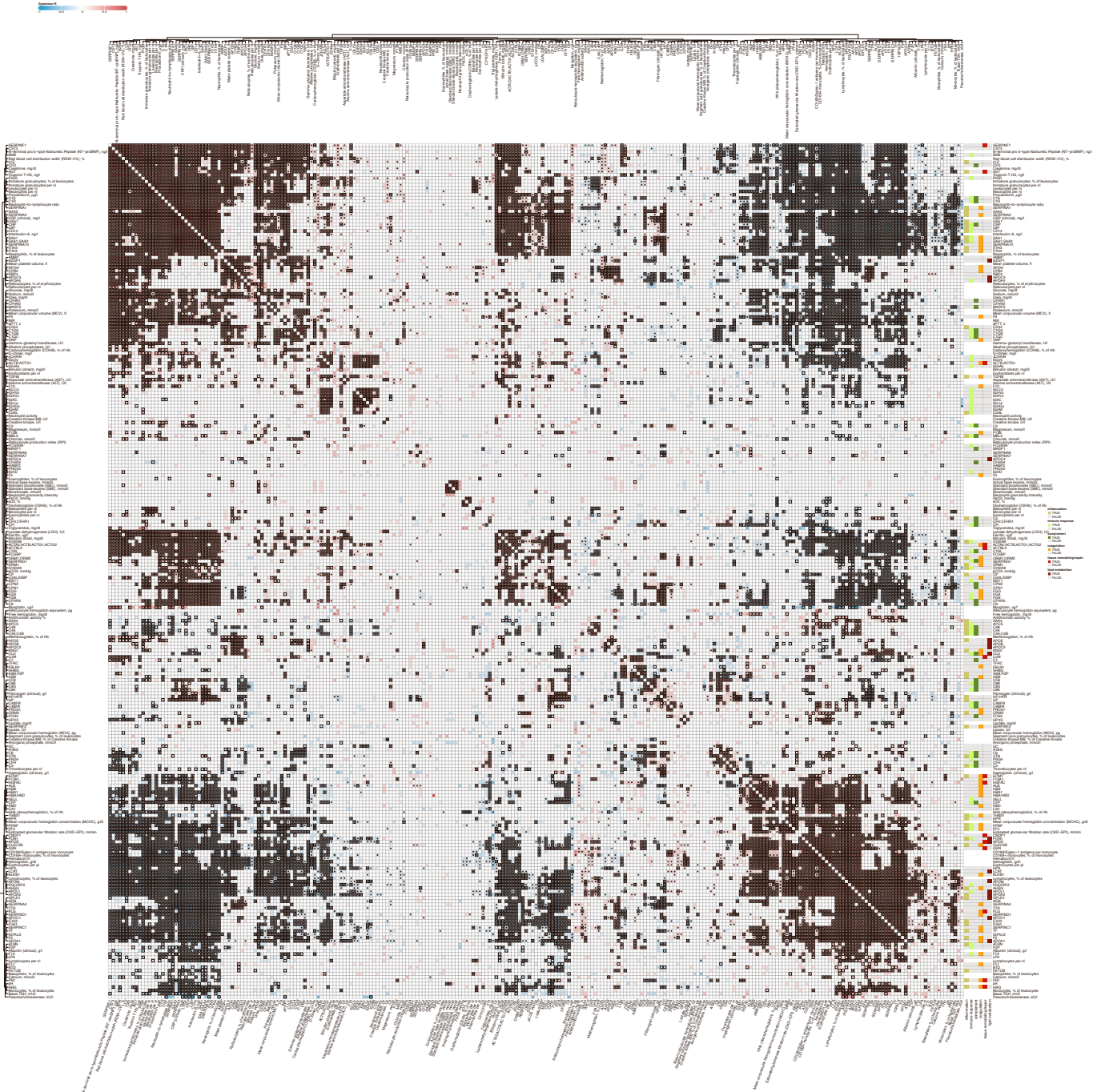


Figure S3. Map of all correlations between omics measurements

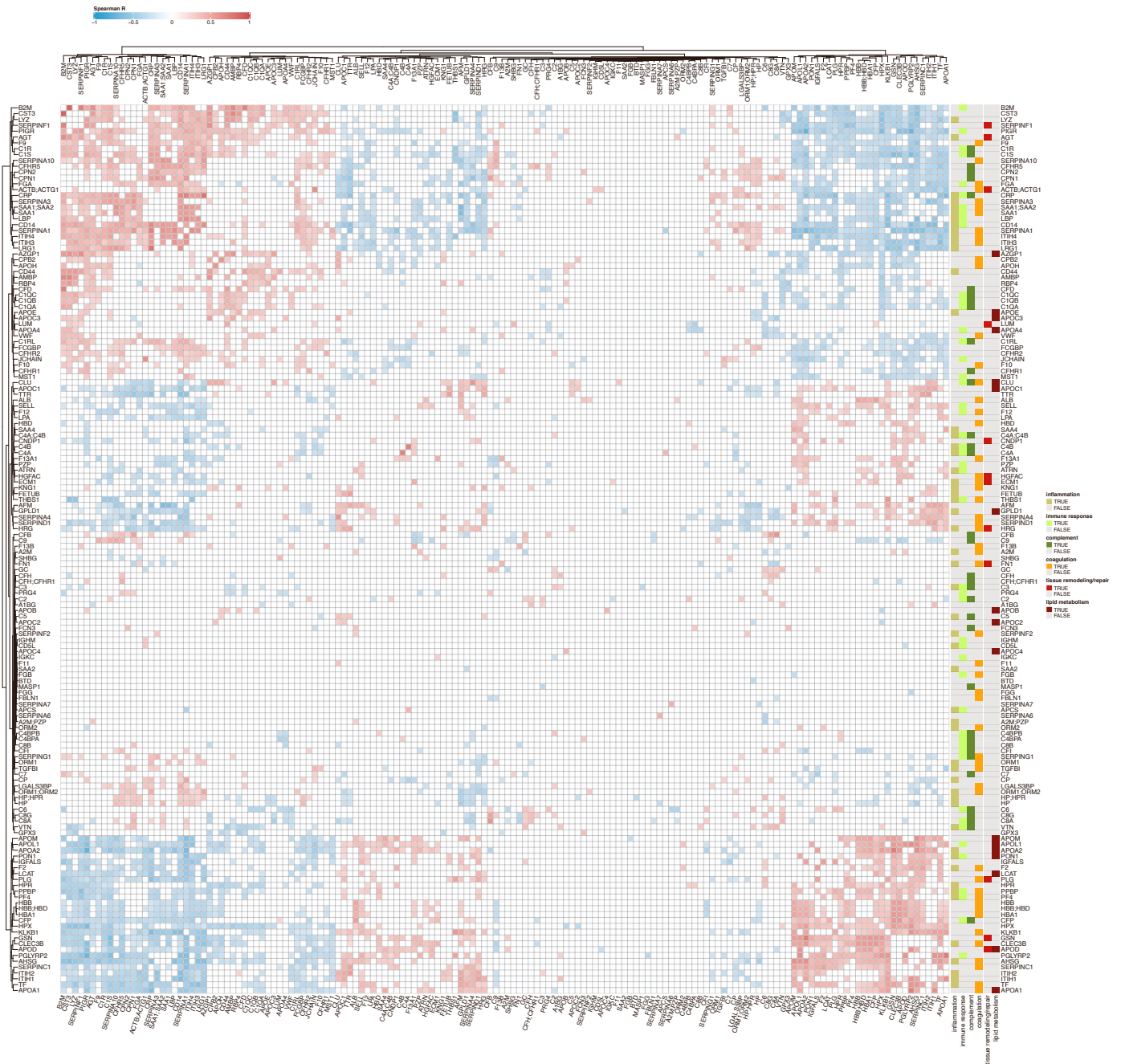
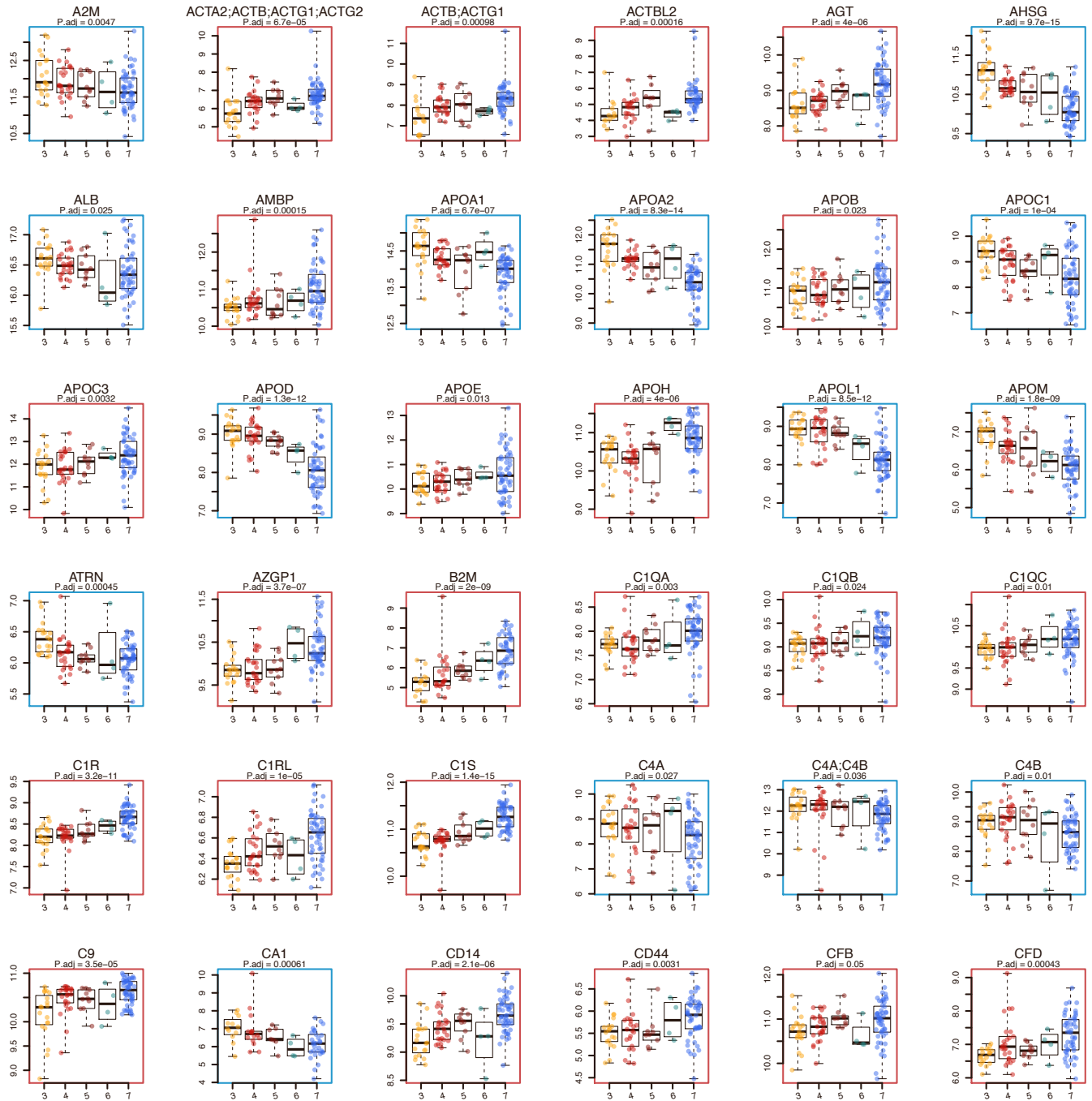


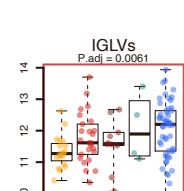
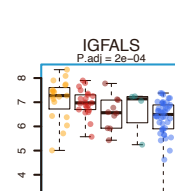
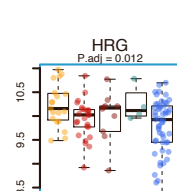
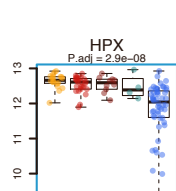
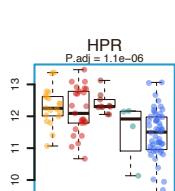
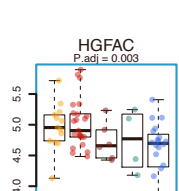
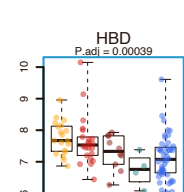
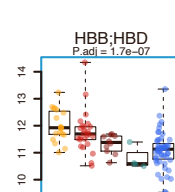
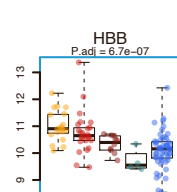
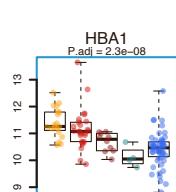
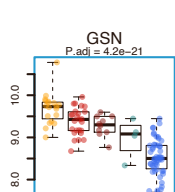
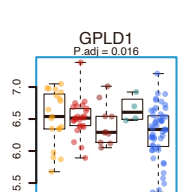
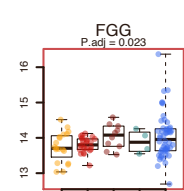
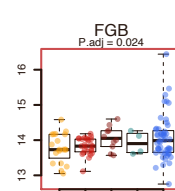
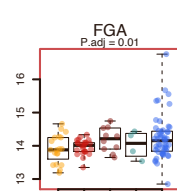
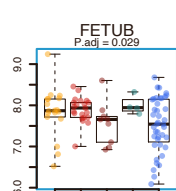
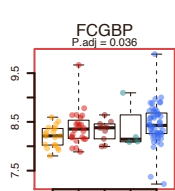
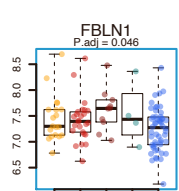
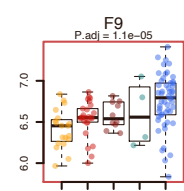
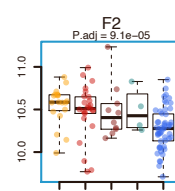
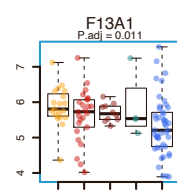
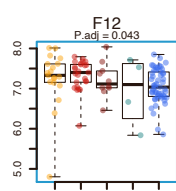
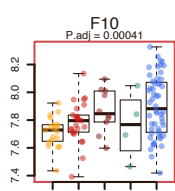
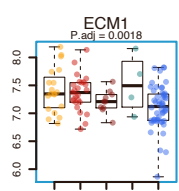
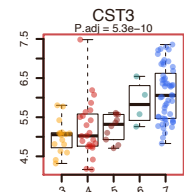
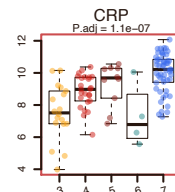
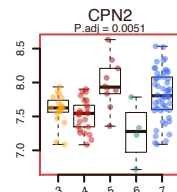
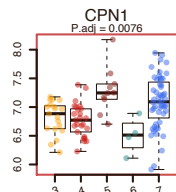
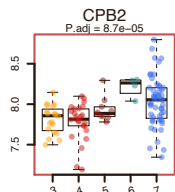
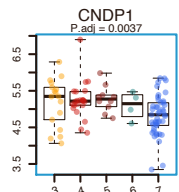
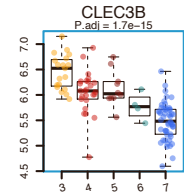
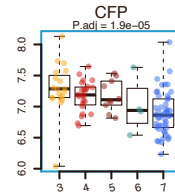
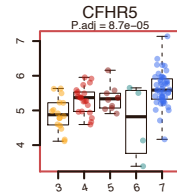
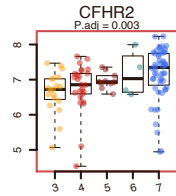
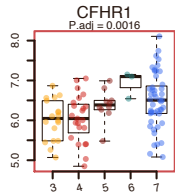
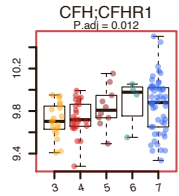
Figure S4. Map of COVID-19-specific protein-protein correlations

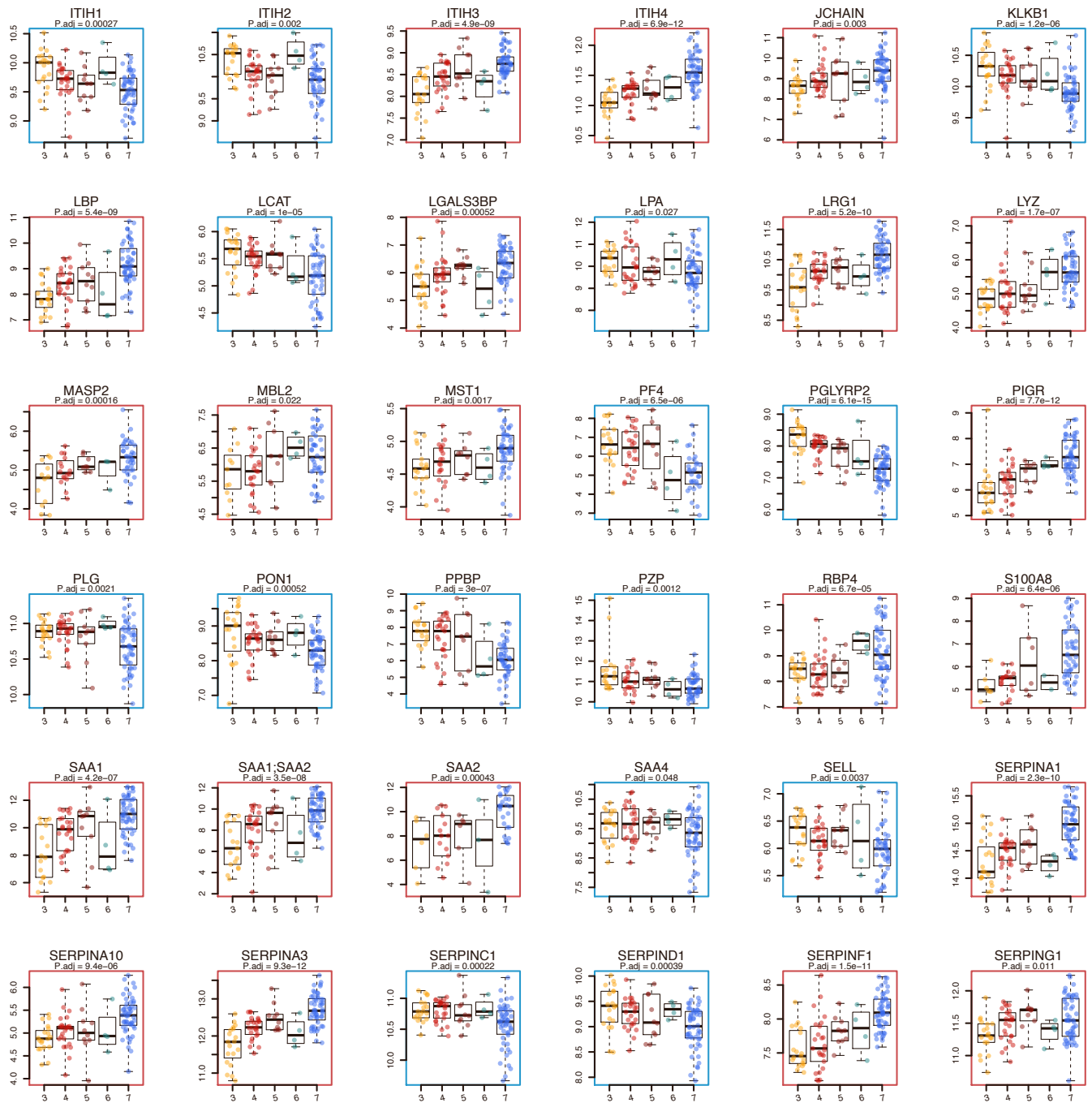




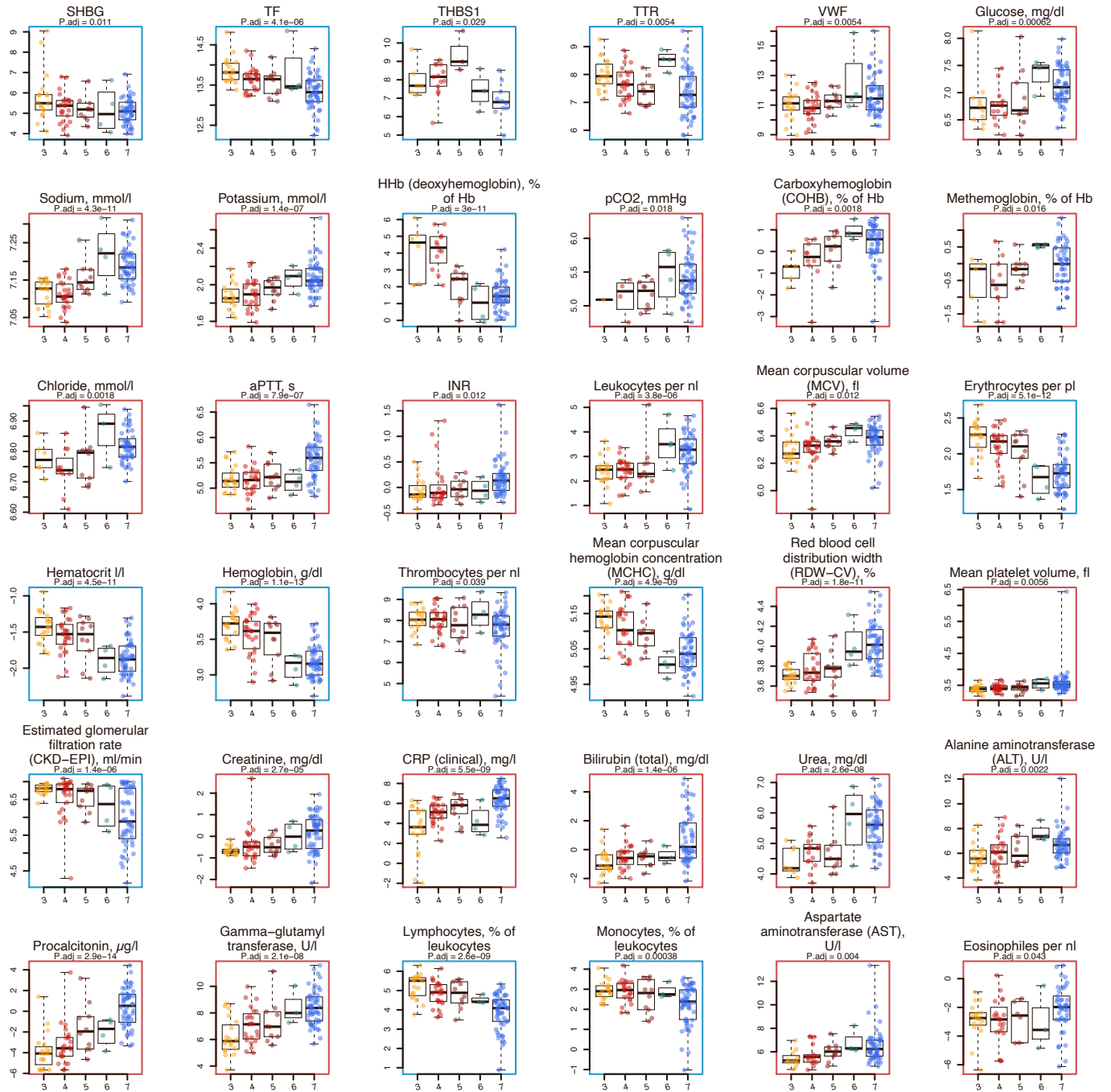
Figure S6 (following 5 pages). Omics features significantly regulated depending on COVID-19 severity











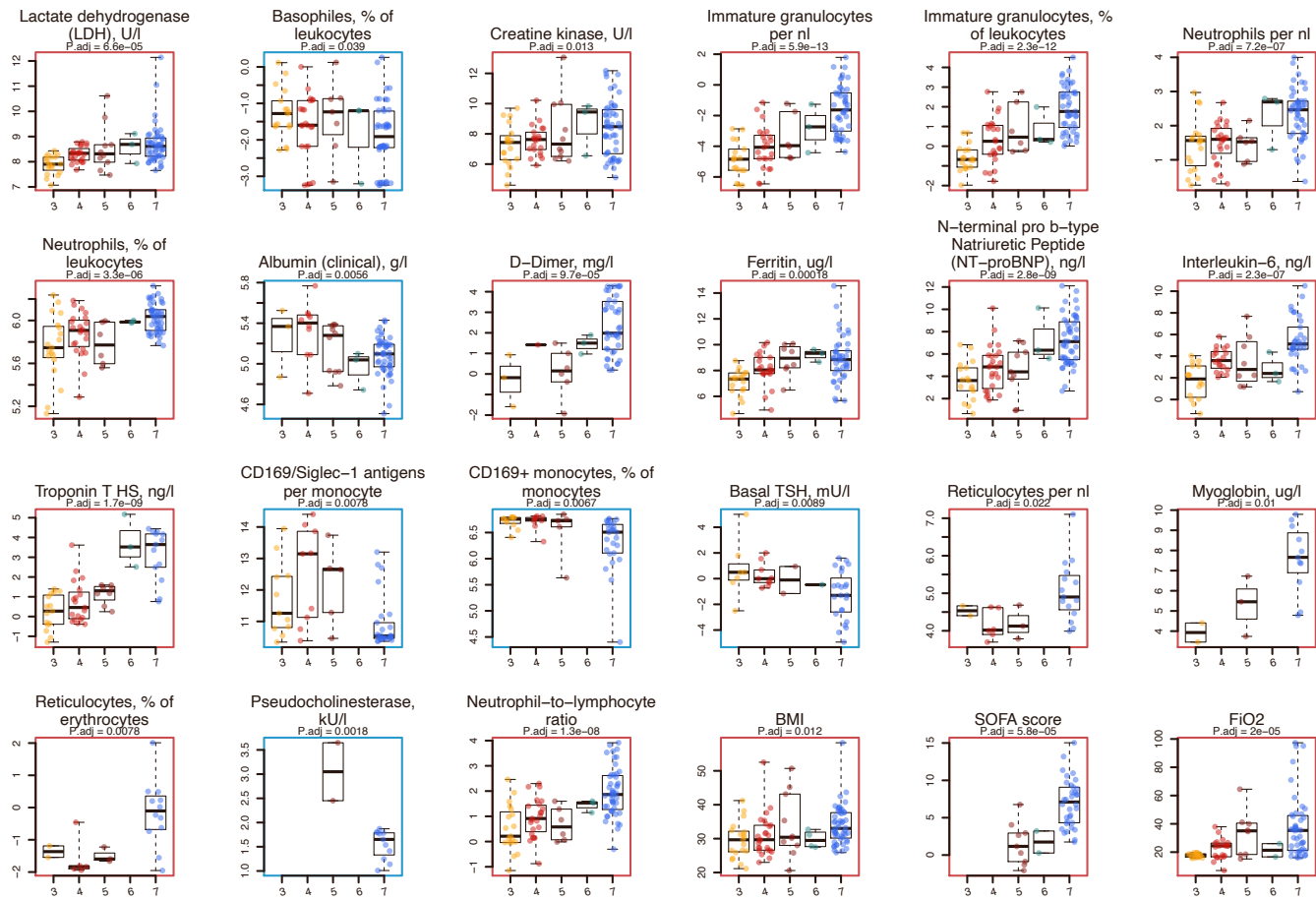


Figure S7. Omics features significantly regulated upon RRT

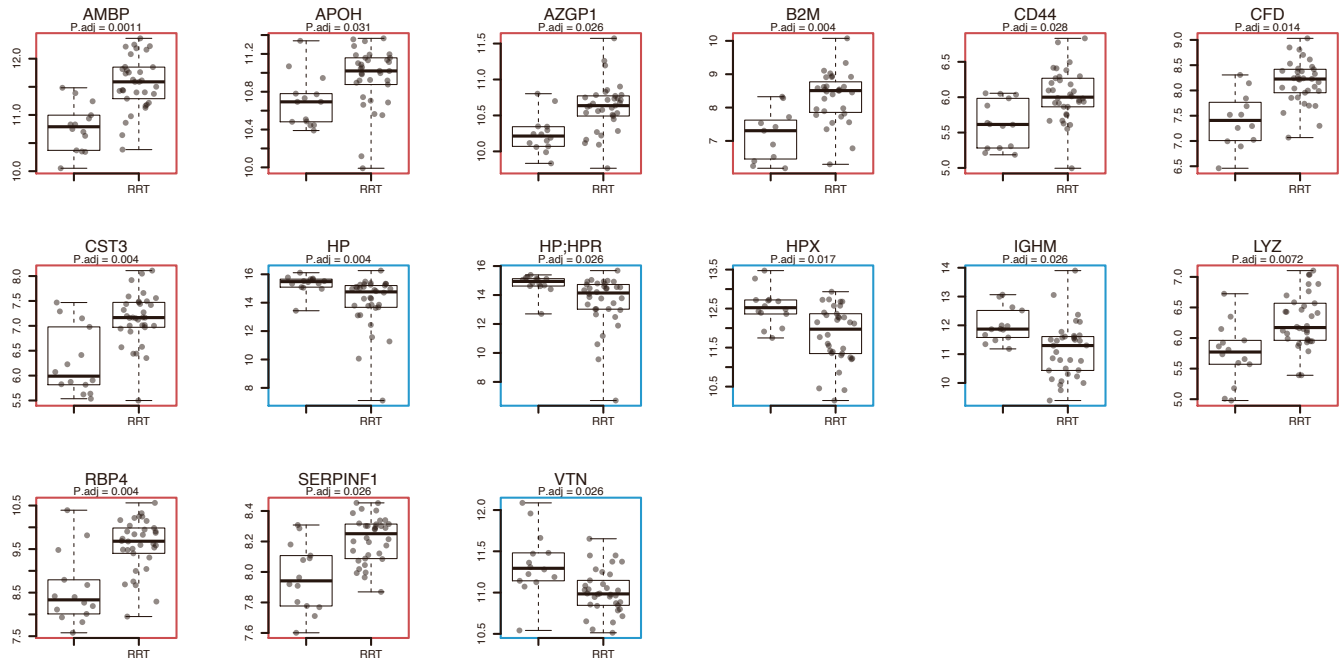


Figure S8. Omics features significantly regulated upon ECMO

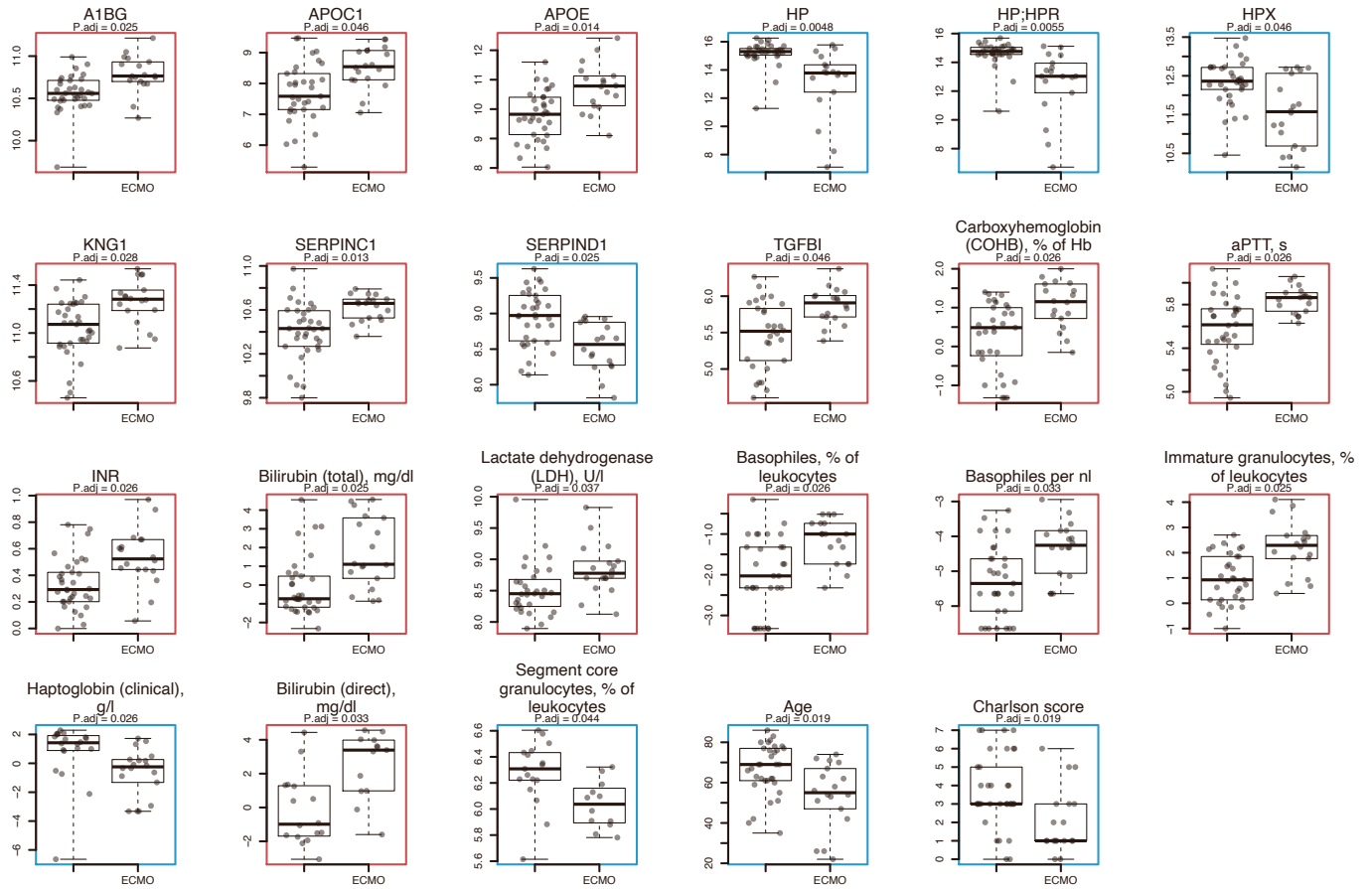
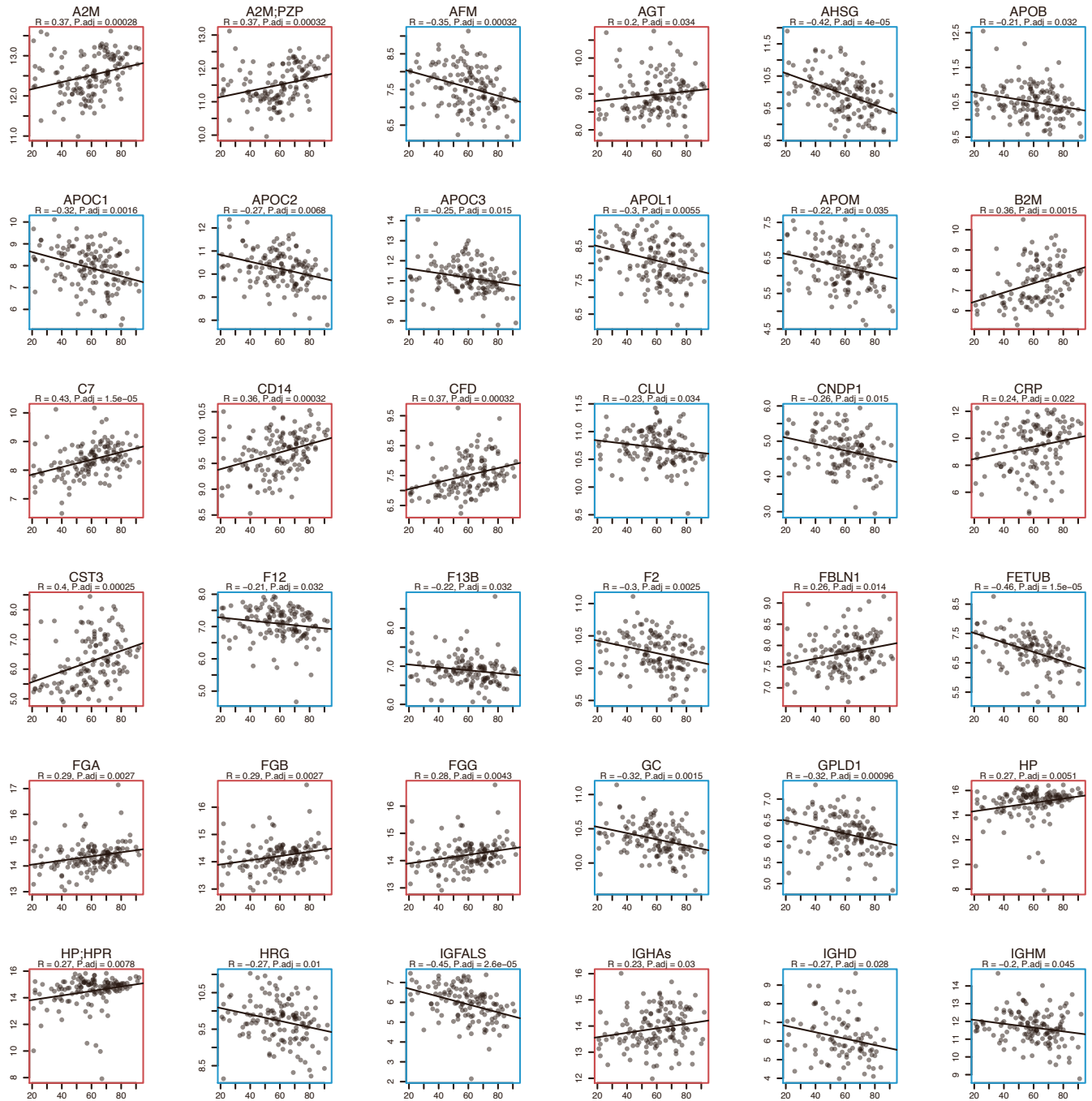
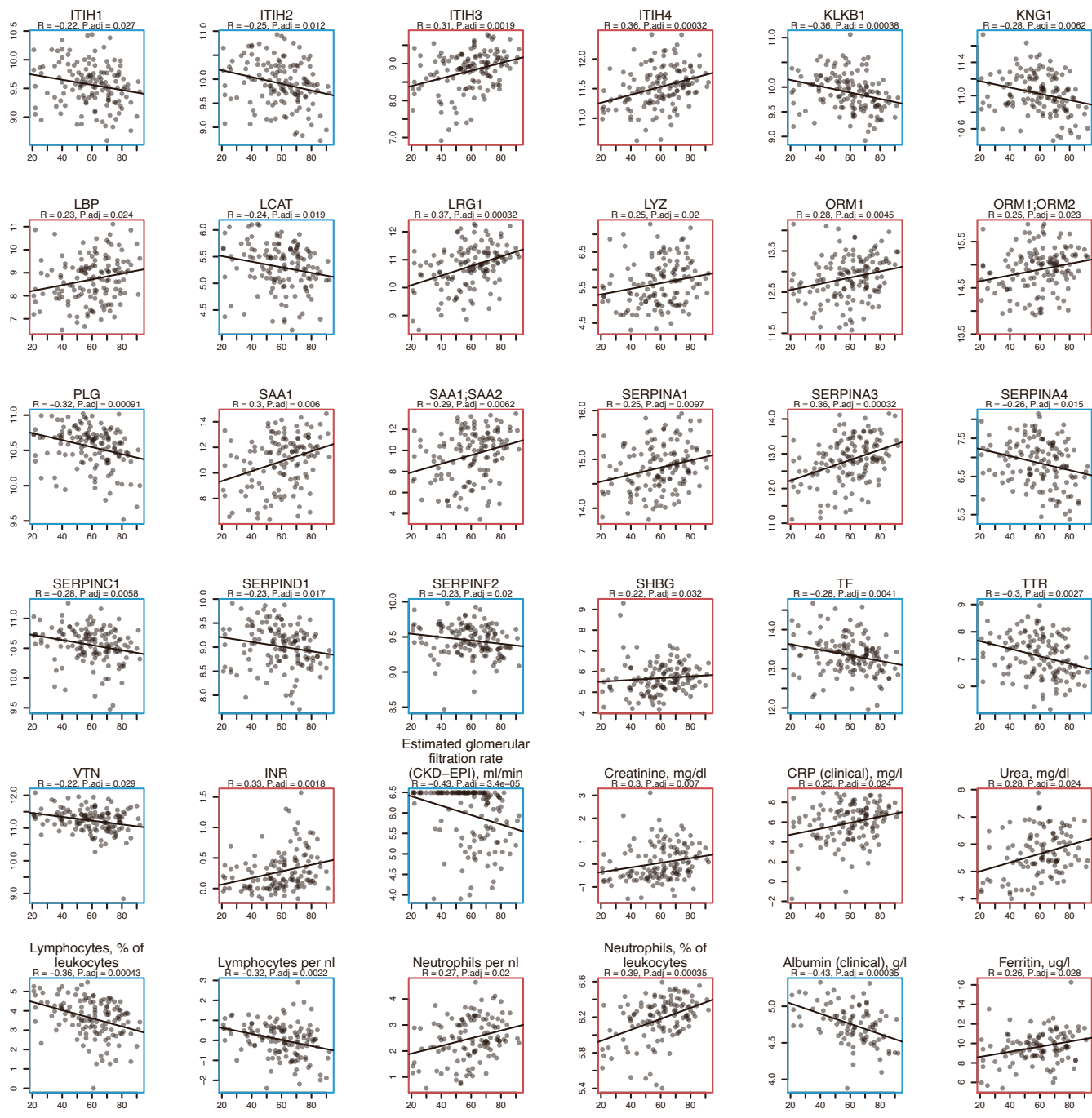
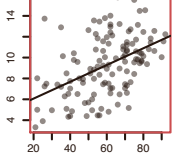


Figure S9 (following 3 pages). Omics features changing with age - test without accounting for the WHO grade as a covariate

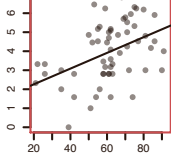




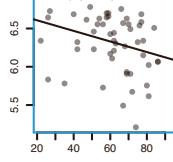
N-terminal pro b-type  
Natriuretic Peptide  
(NT-proBNP), ng/l  
R = 0.47, P,adj = 8.5e-06



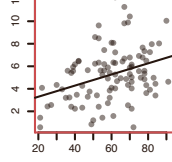
Creatine Kinase MB, % of  
Creatine Kinase  
R = 0.42, P,adj = 0.011



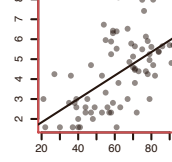
Antithrombin activity %  
R = -0.37, P,adj = 0.033



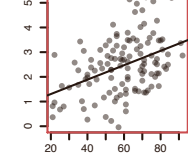
Interleukin-6, ng/l  
R = 0.31, P,adj = 0.02



Troponin T HS, ng/l  
R = 0.58, P,adj = 7.7e-05



Neutrophil-to-lymphocyte  
ratio  
R = 0.39, P,adj = 0.00033



Charlson score  
R = 0.79, P,adj = 2e-24

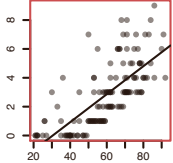
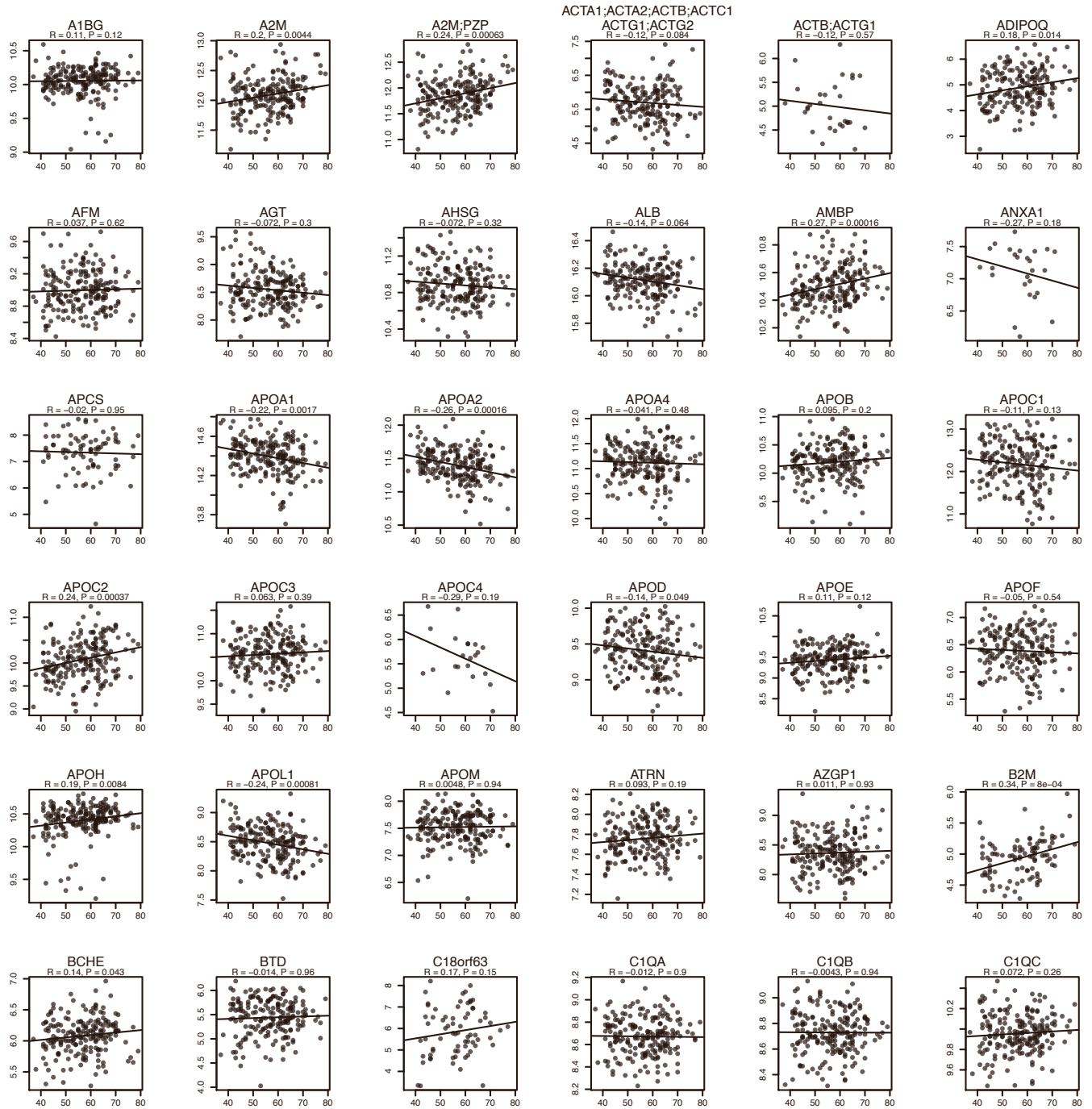
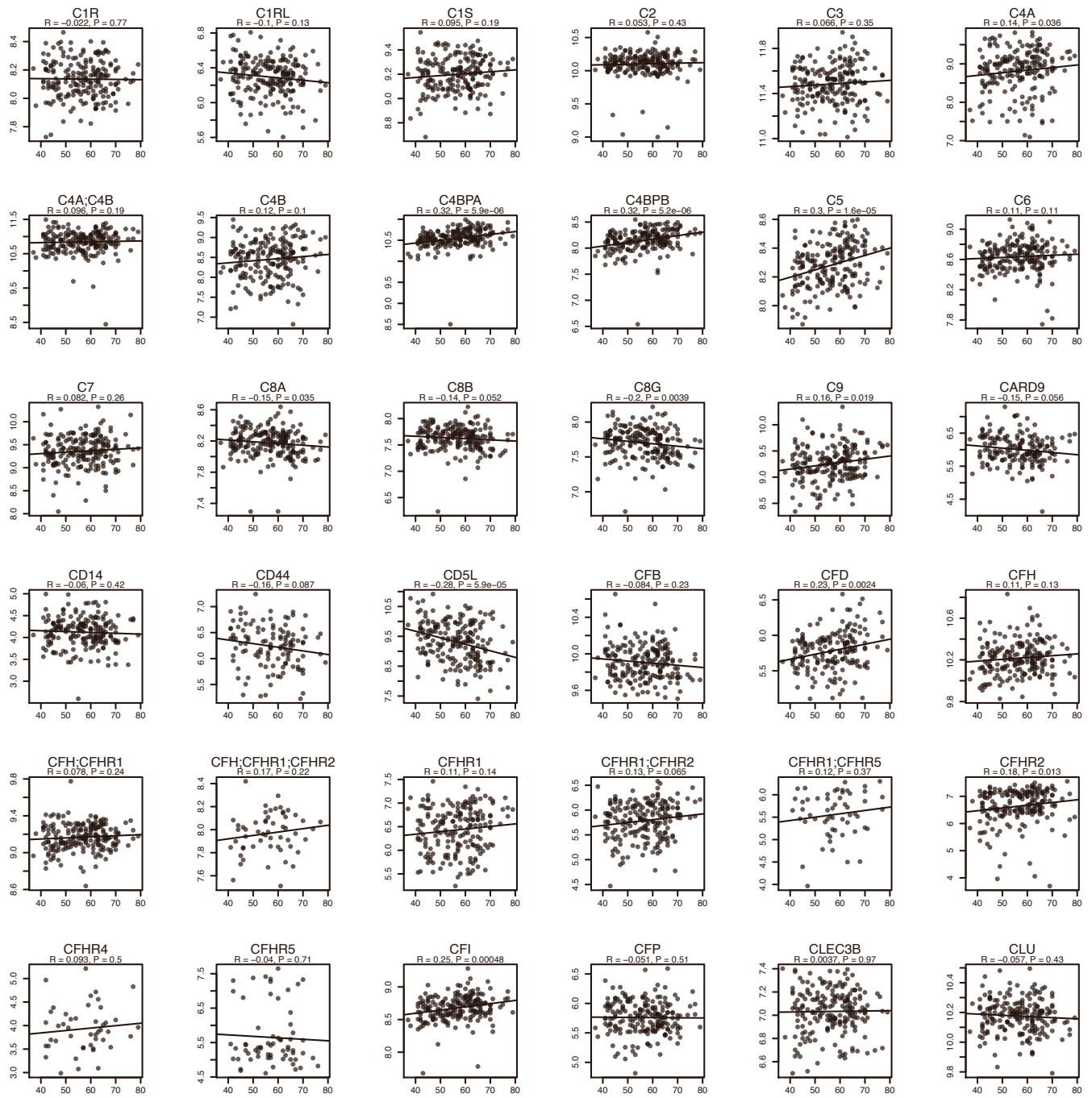
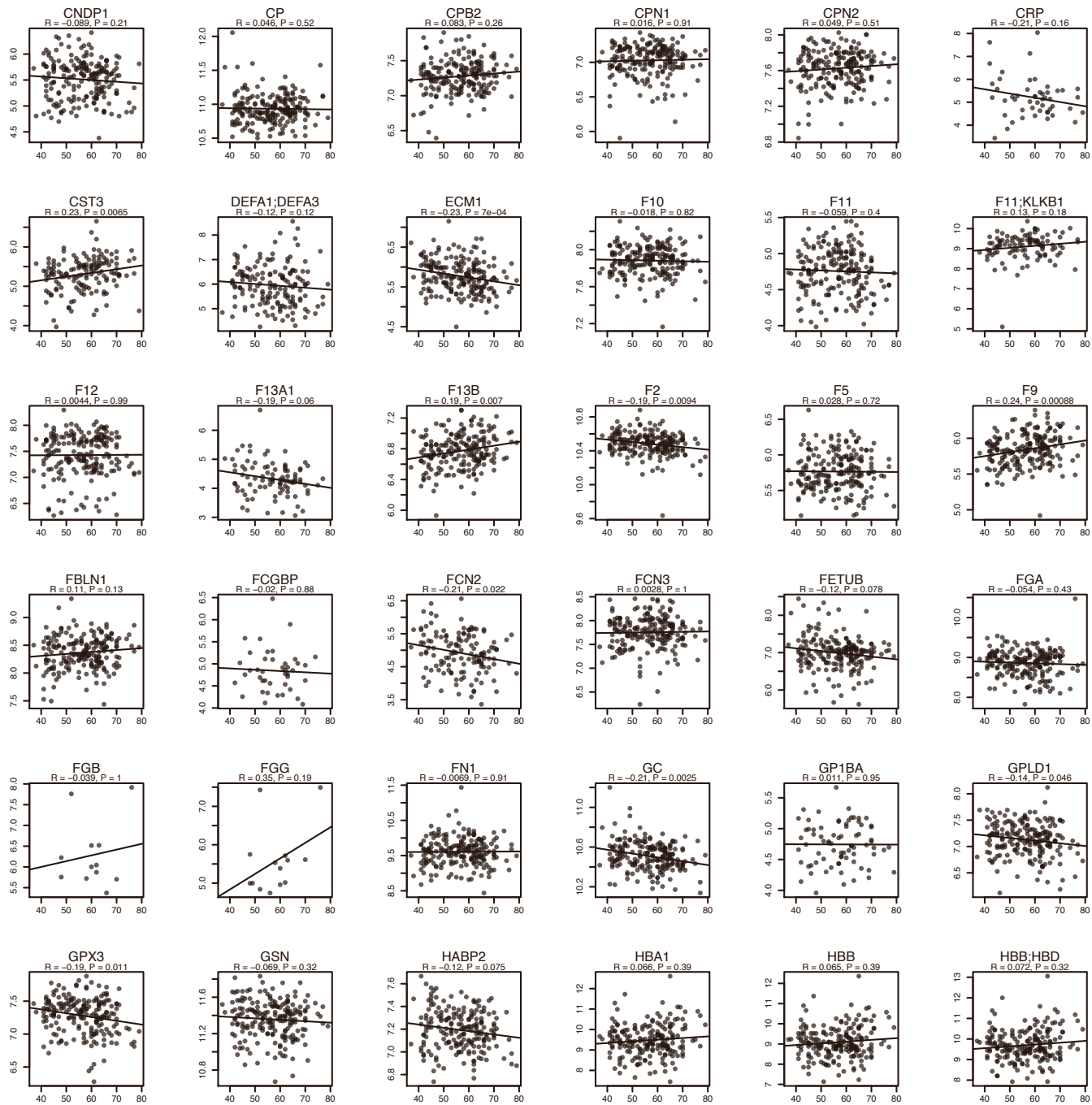


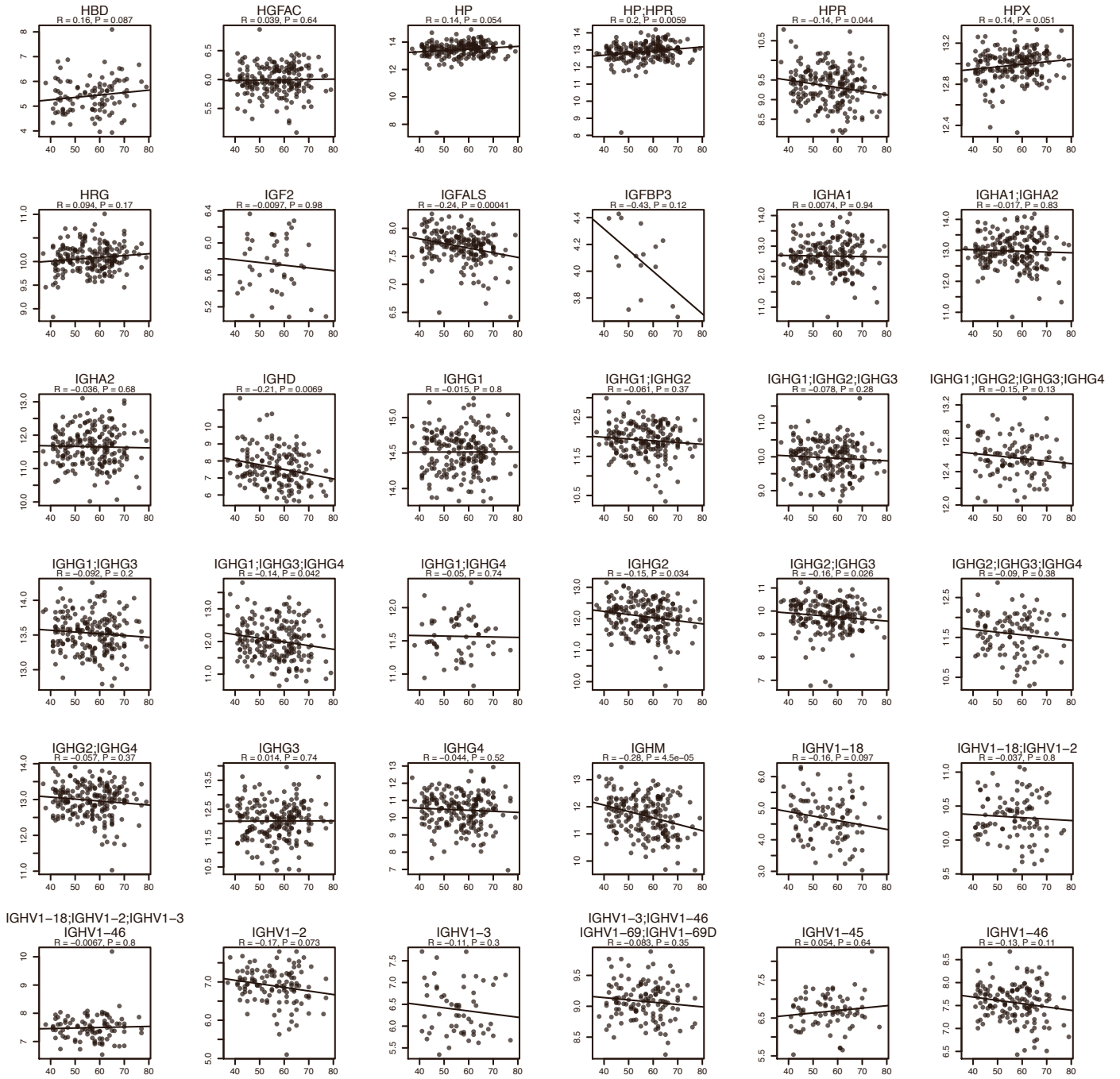
Figure S10 (following 9 pages). Plasma protein levels vs age in general population based on Generation Scotland cohort

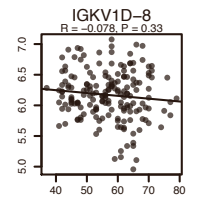
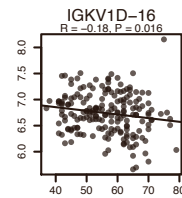
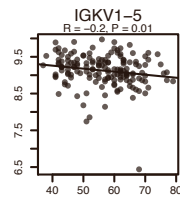
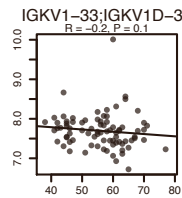
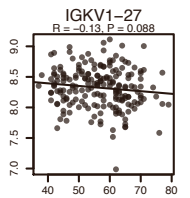
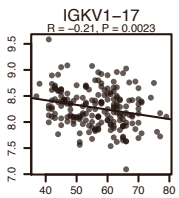
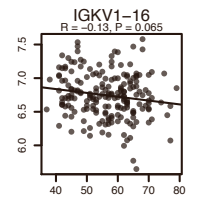
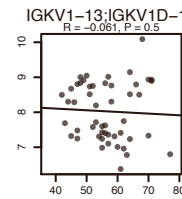
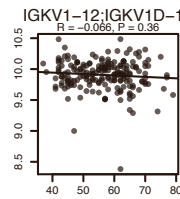
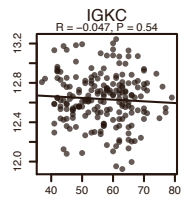
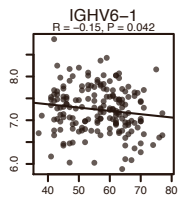
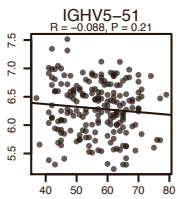
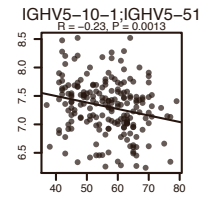
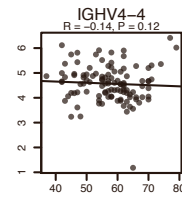
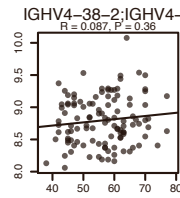
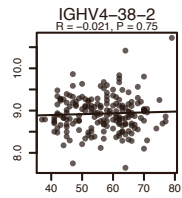
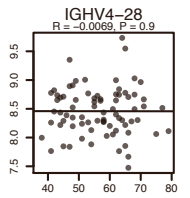
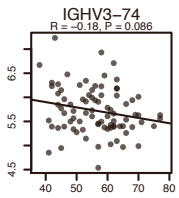
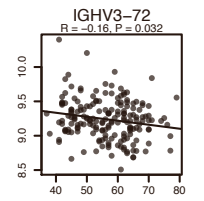
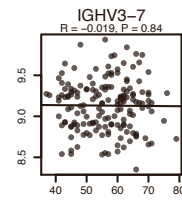
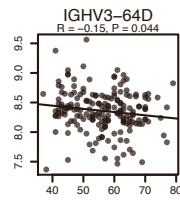
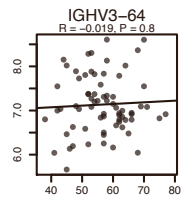
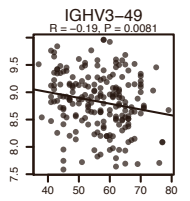
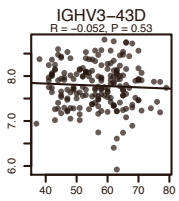
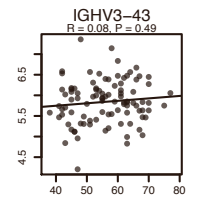
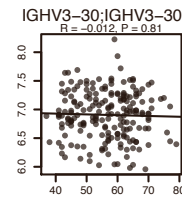
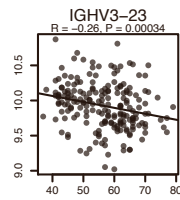
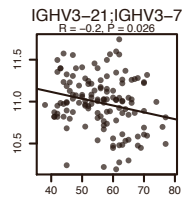
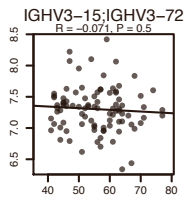
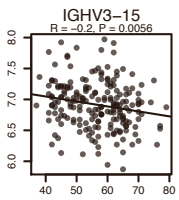
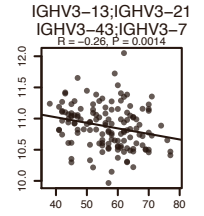
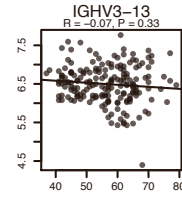
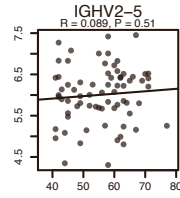
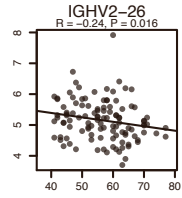
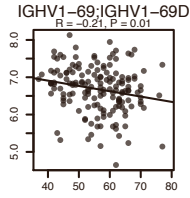
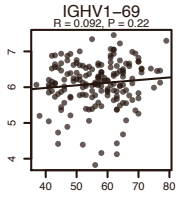


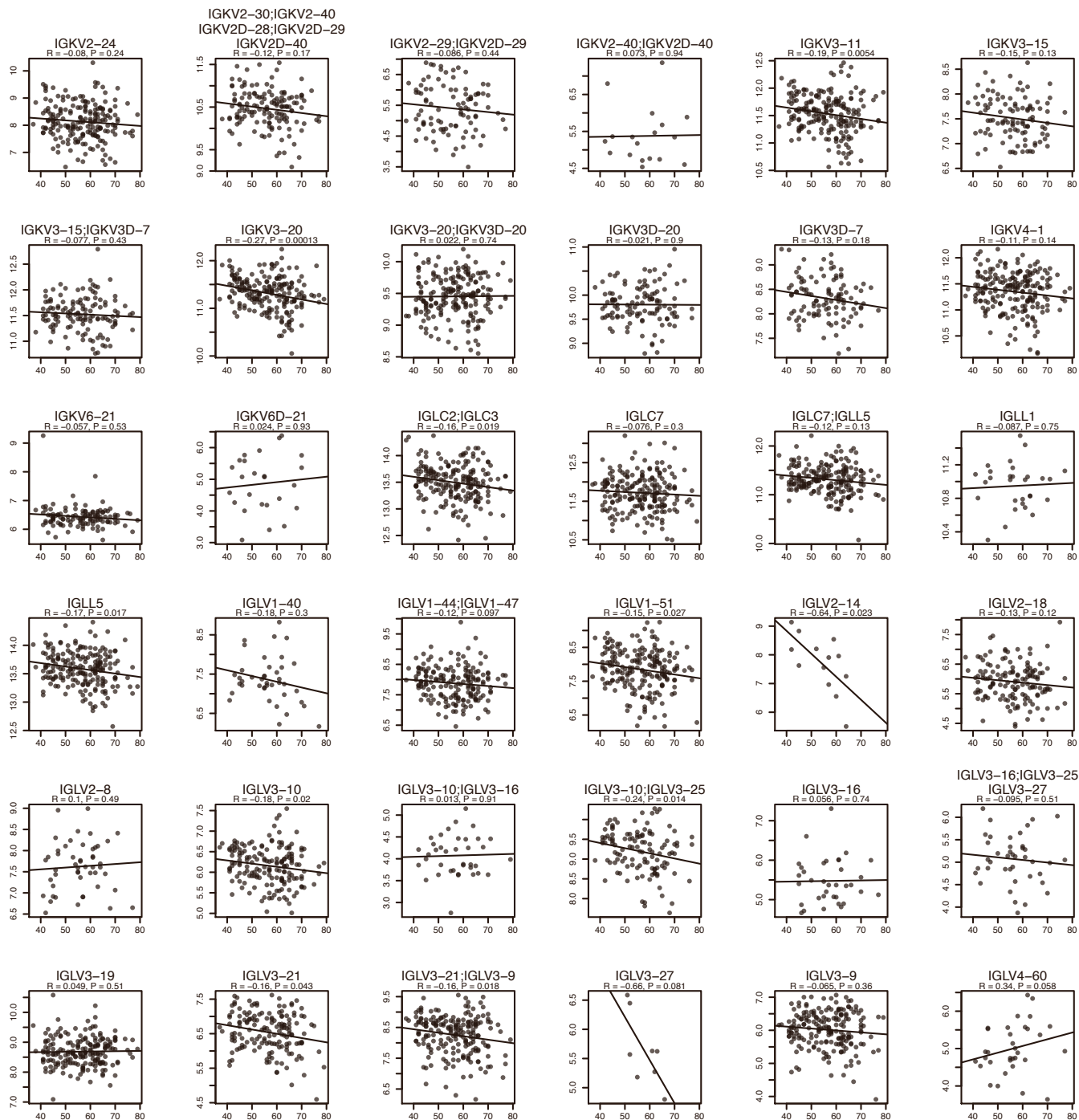


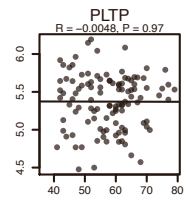
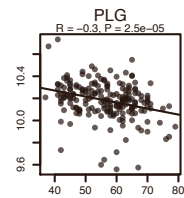
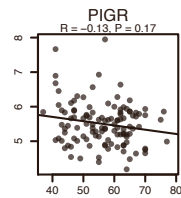
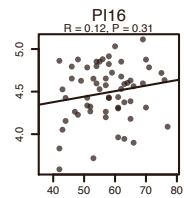
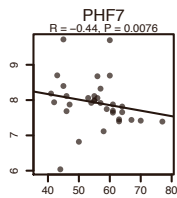
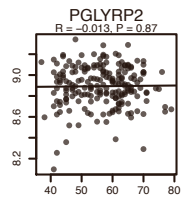
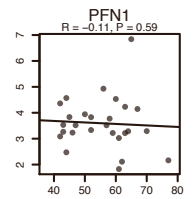
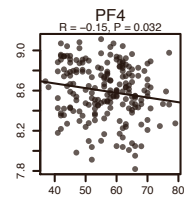
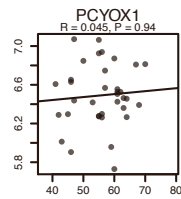
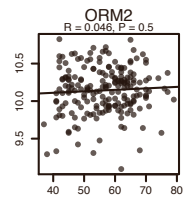
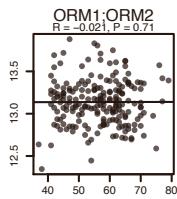
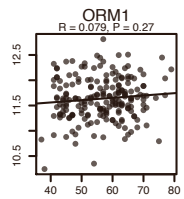
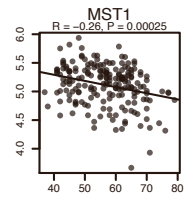
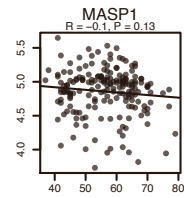
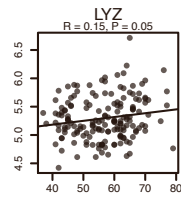
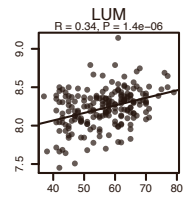
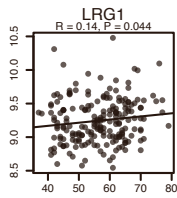
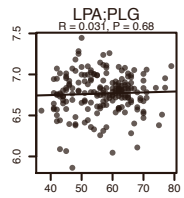
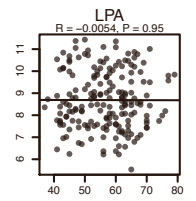
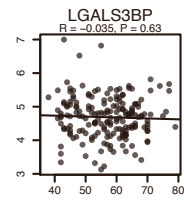
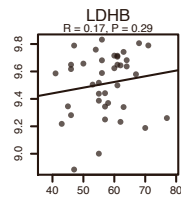
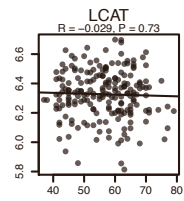
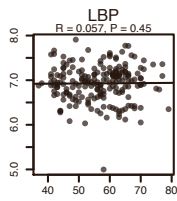
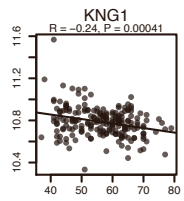
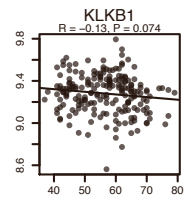
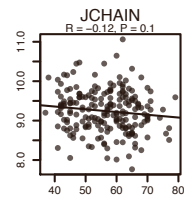
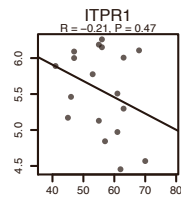
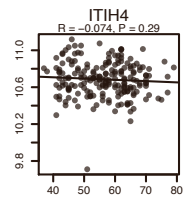
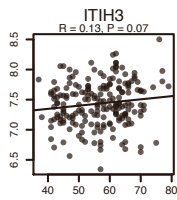
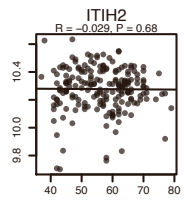
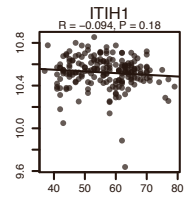
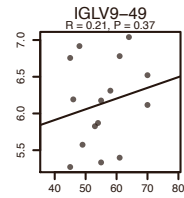
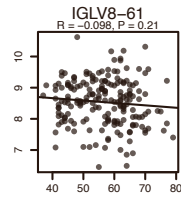
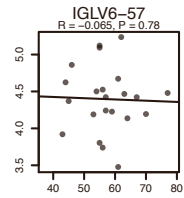
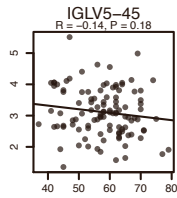
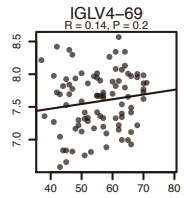




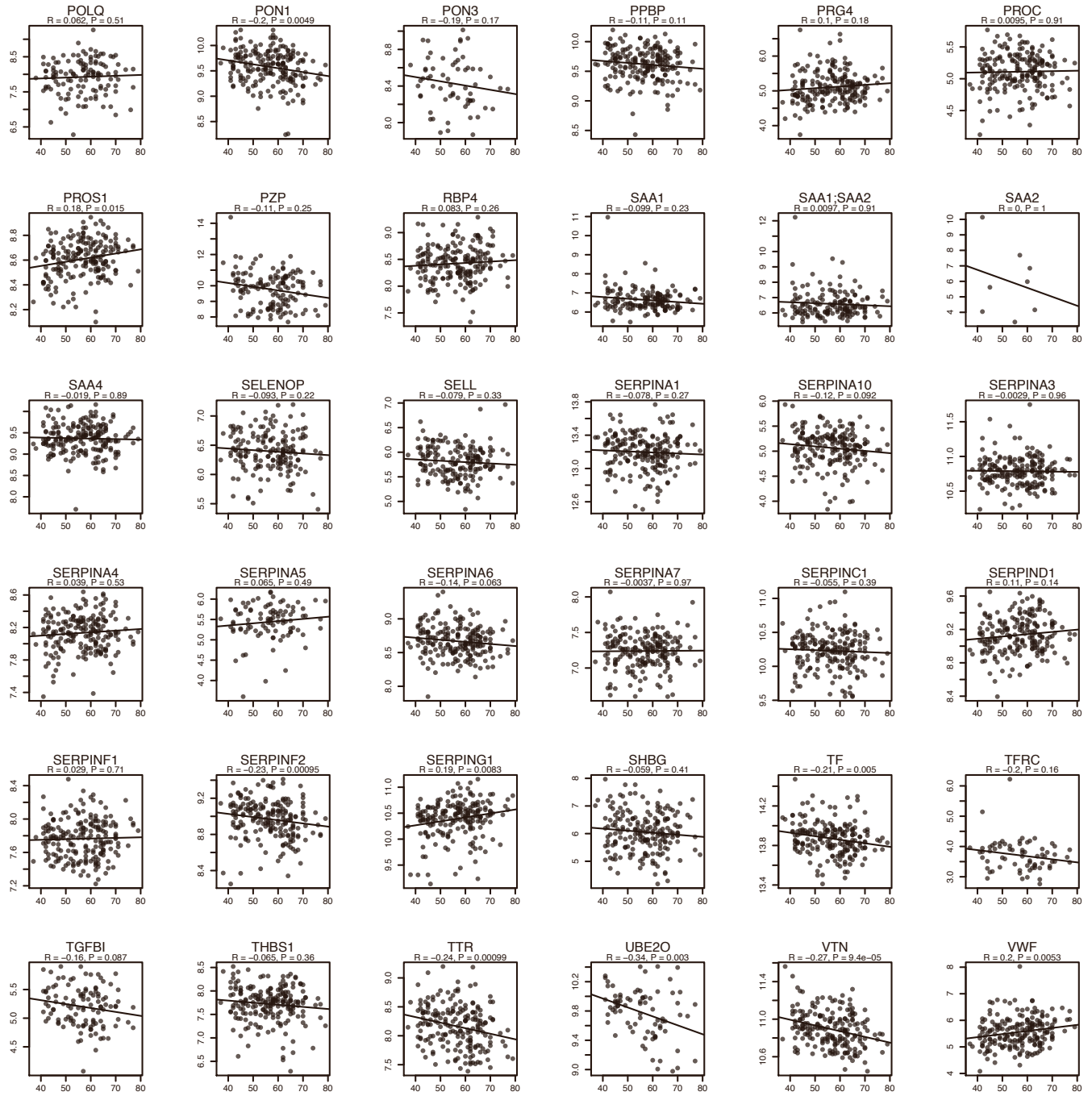












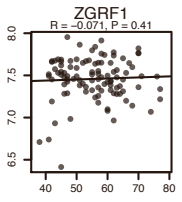
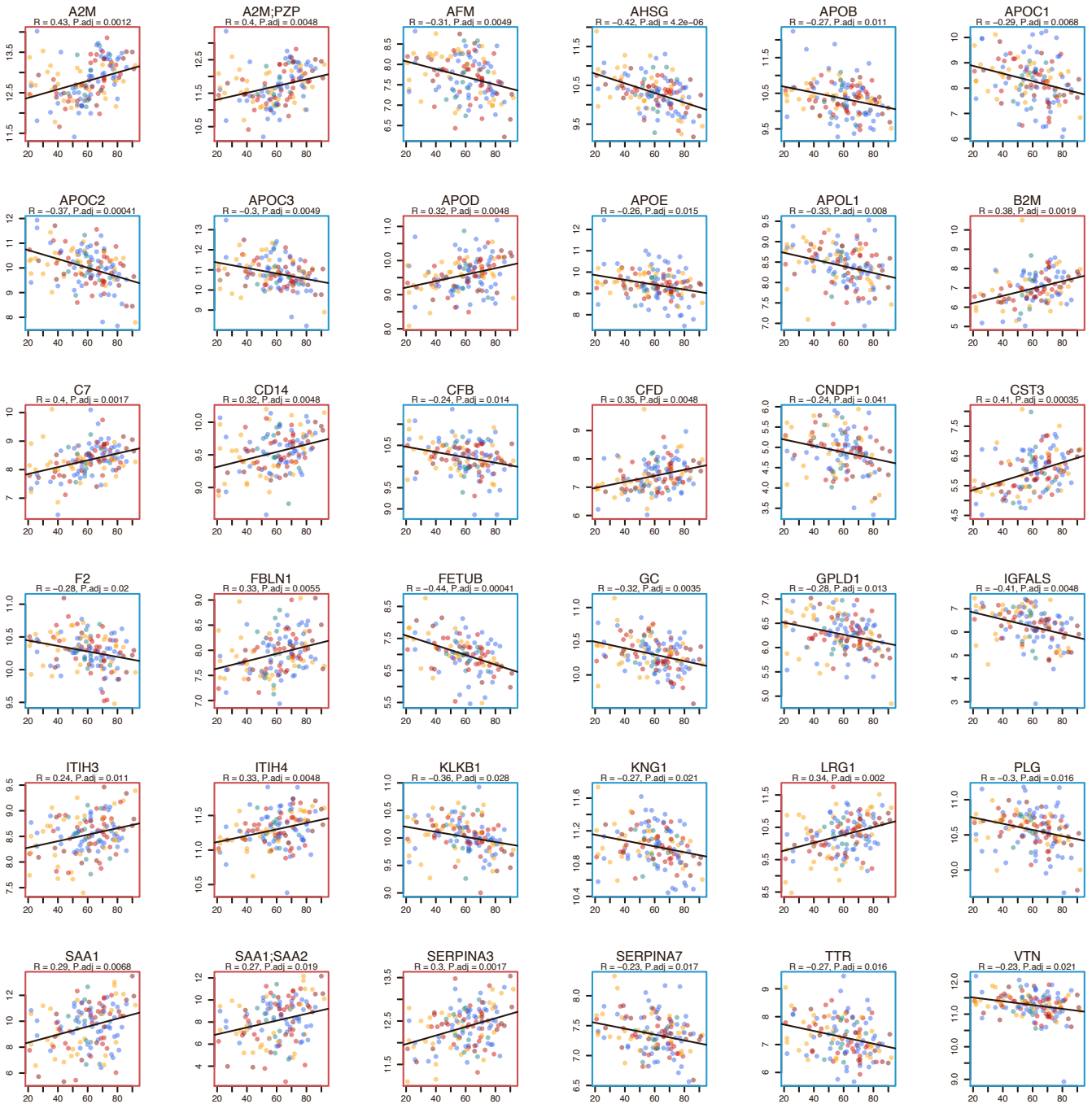
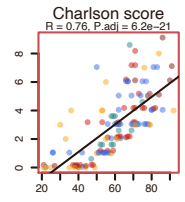
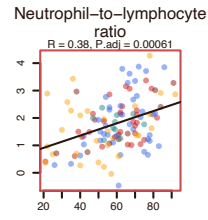
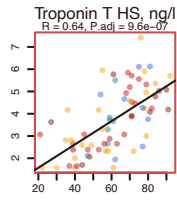
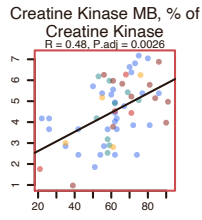
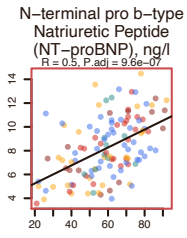
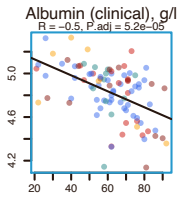
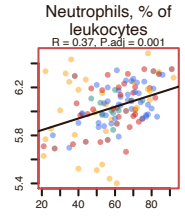
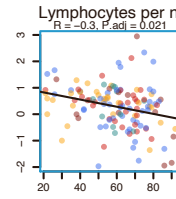
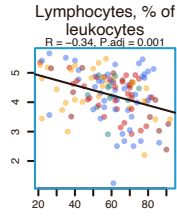
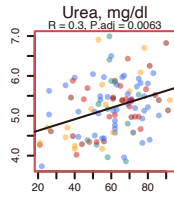
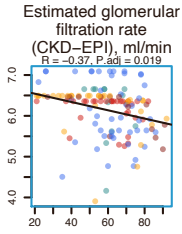
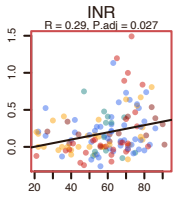




Figure S11 (following 2 pages). Omics features significantly regulated depending on age





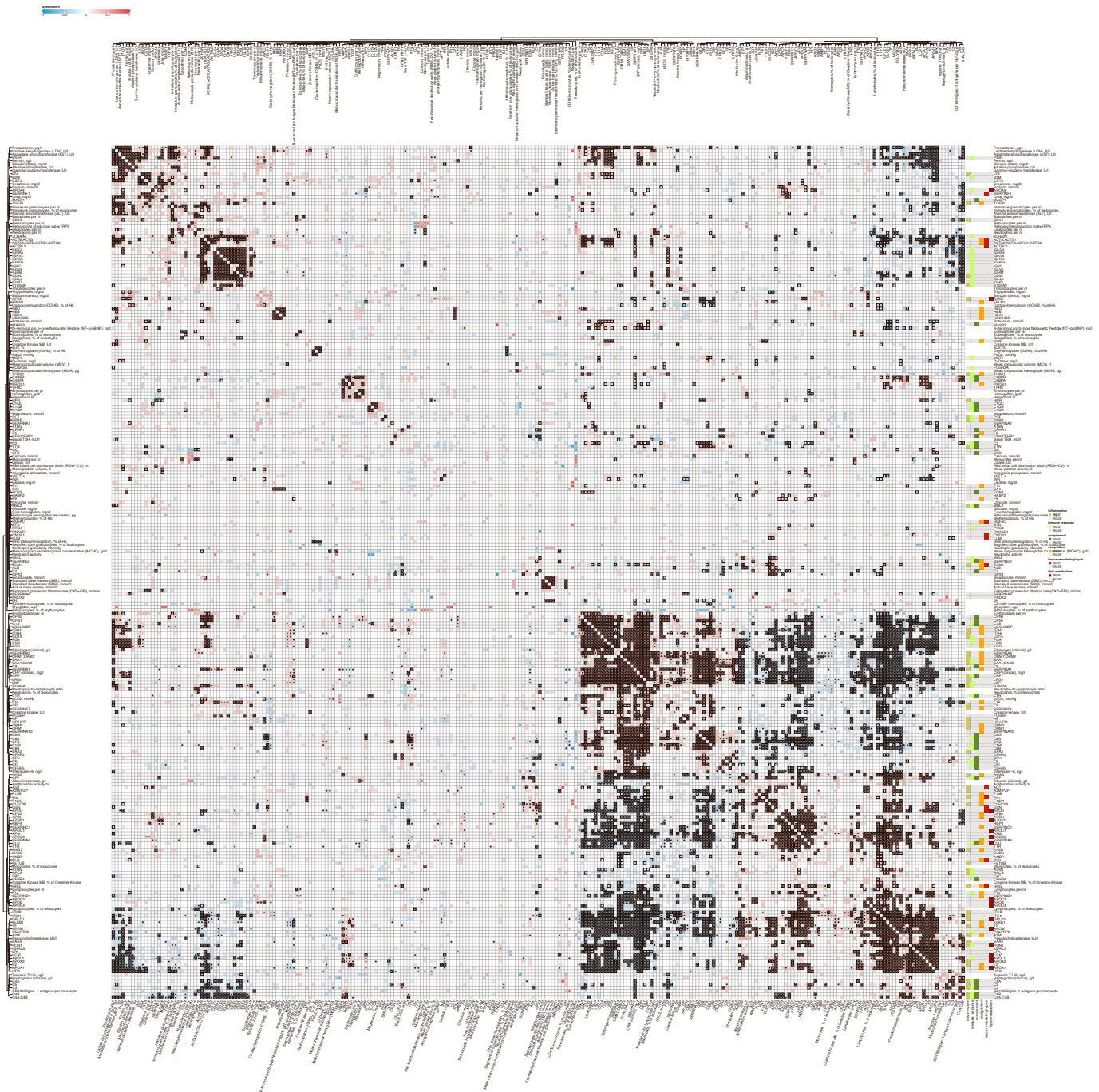


Figure S12. Map of correlations between dynamic changes in omics measurements during the peak period of the disease

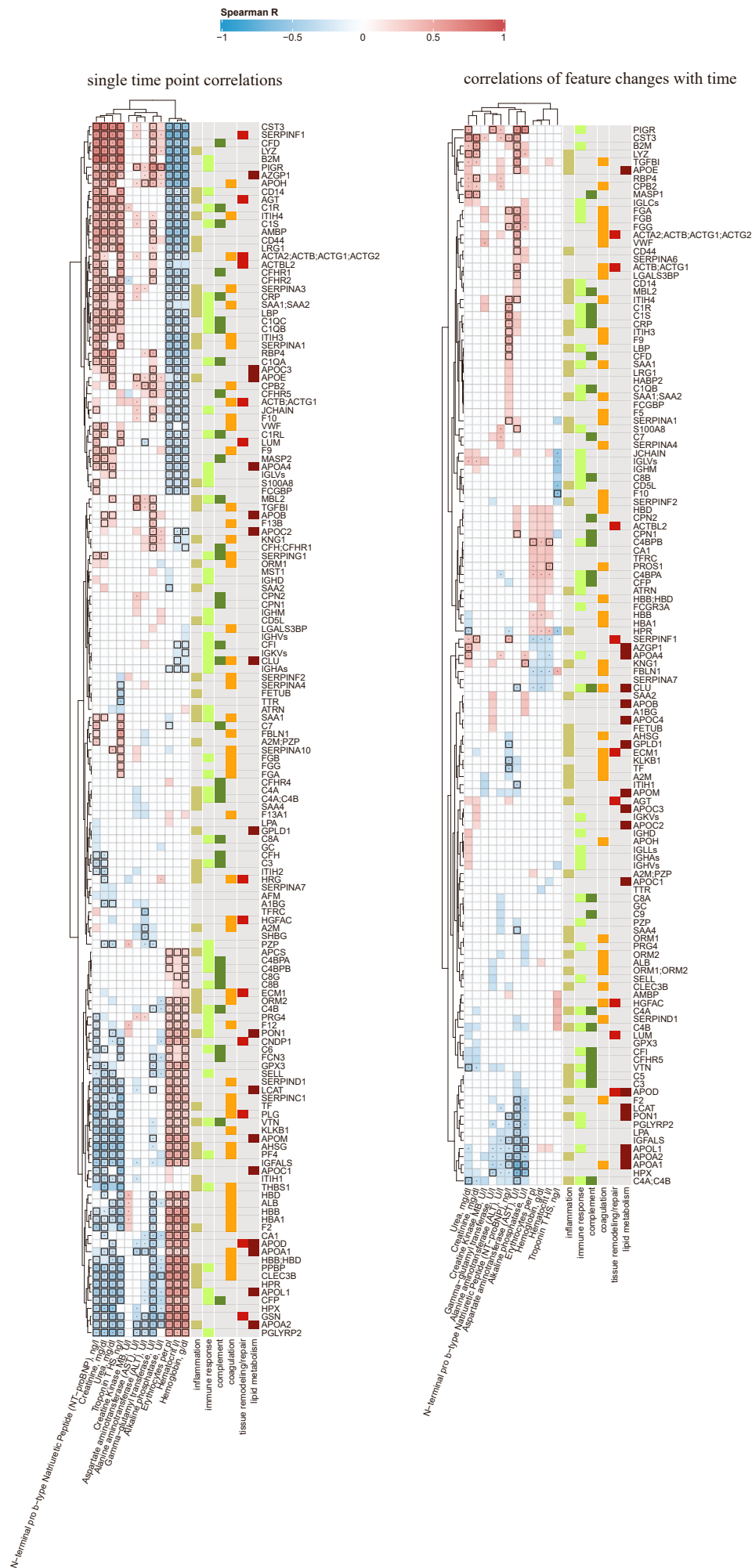
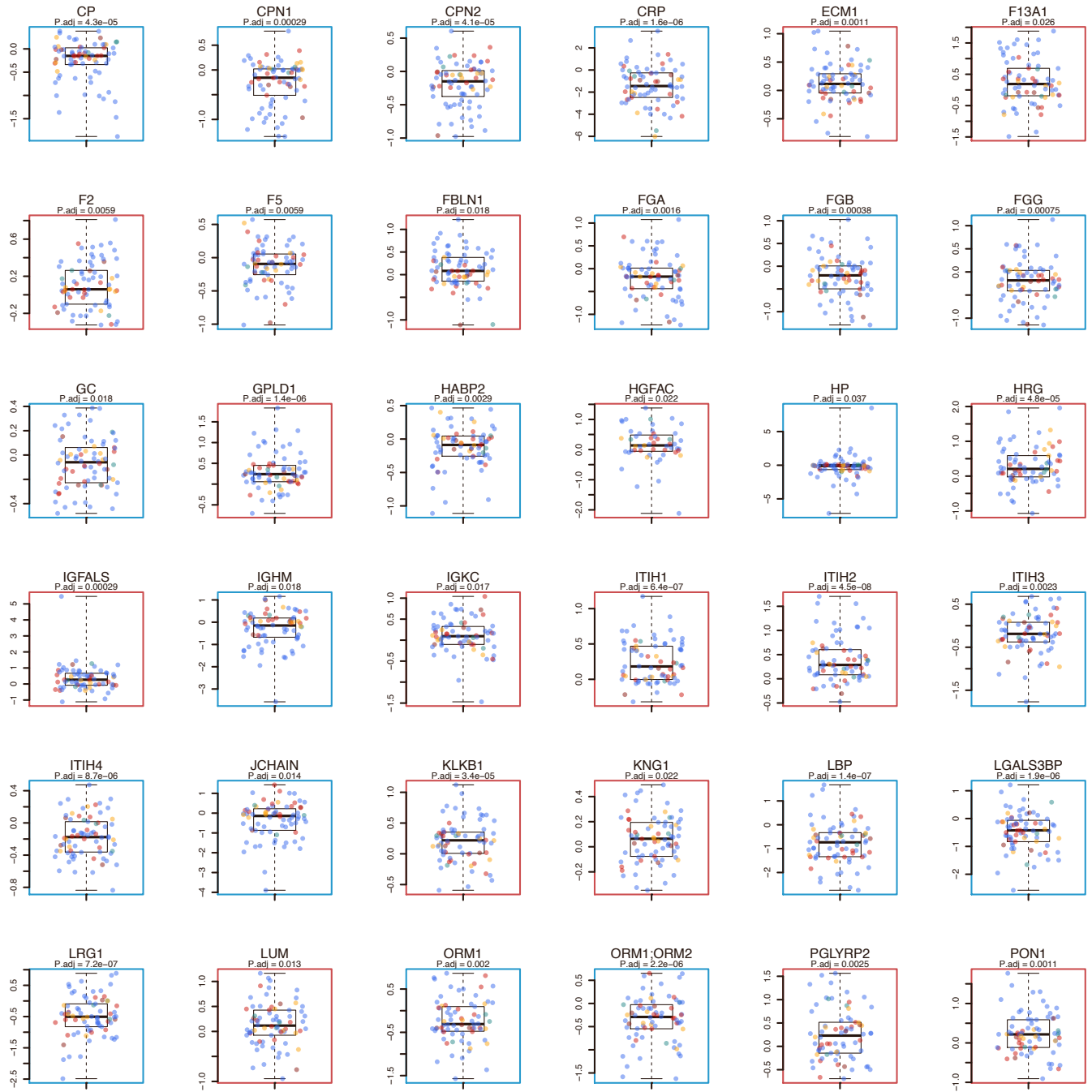
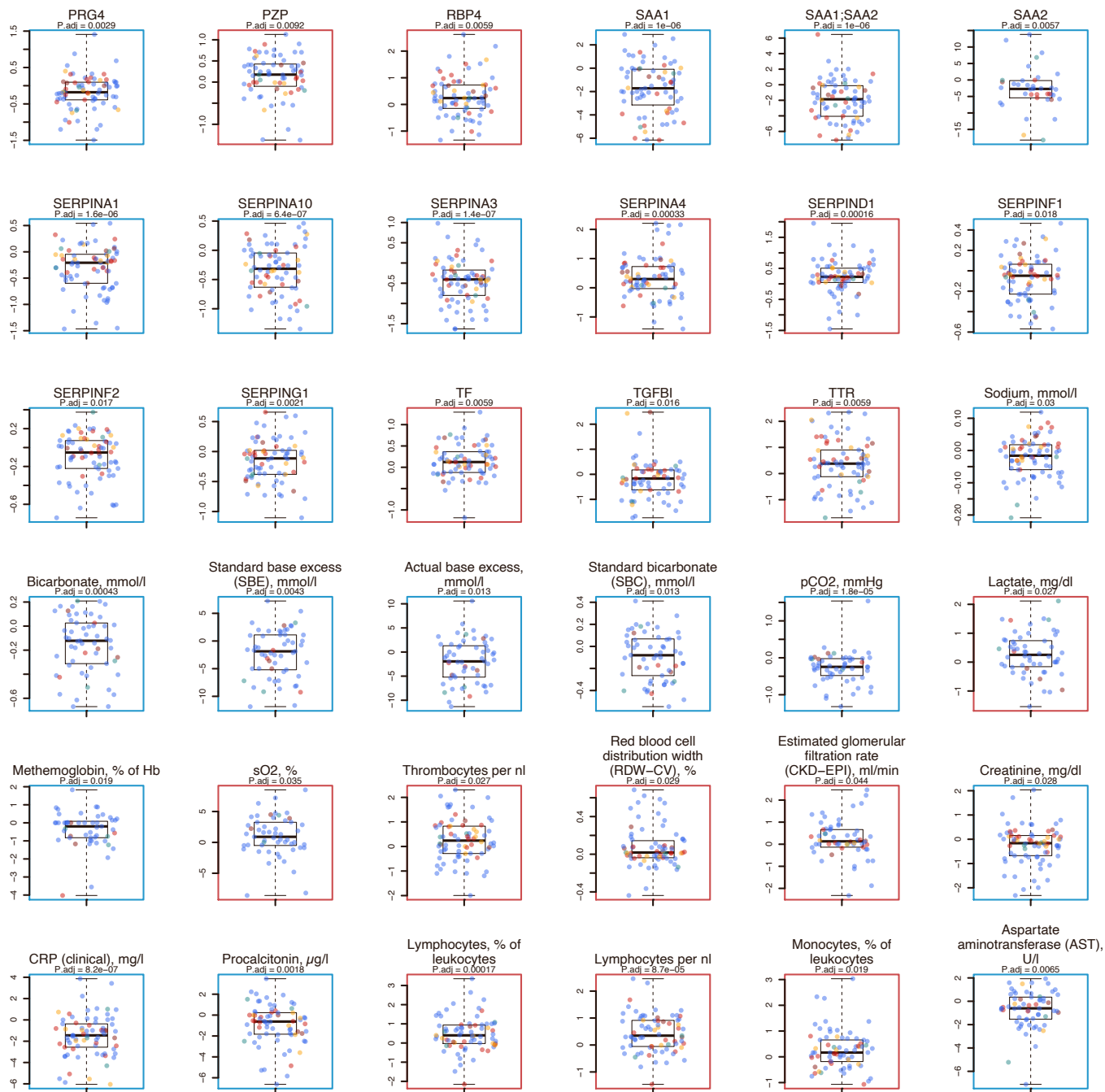


Figure S13. Covariation of organ function markers and plasma proteins

Figure S14 (following 4 pages). Omics features changing during the peak of the disease









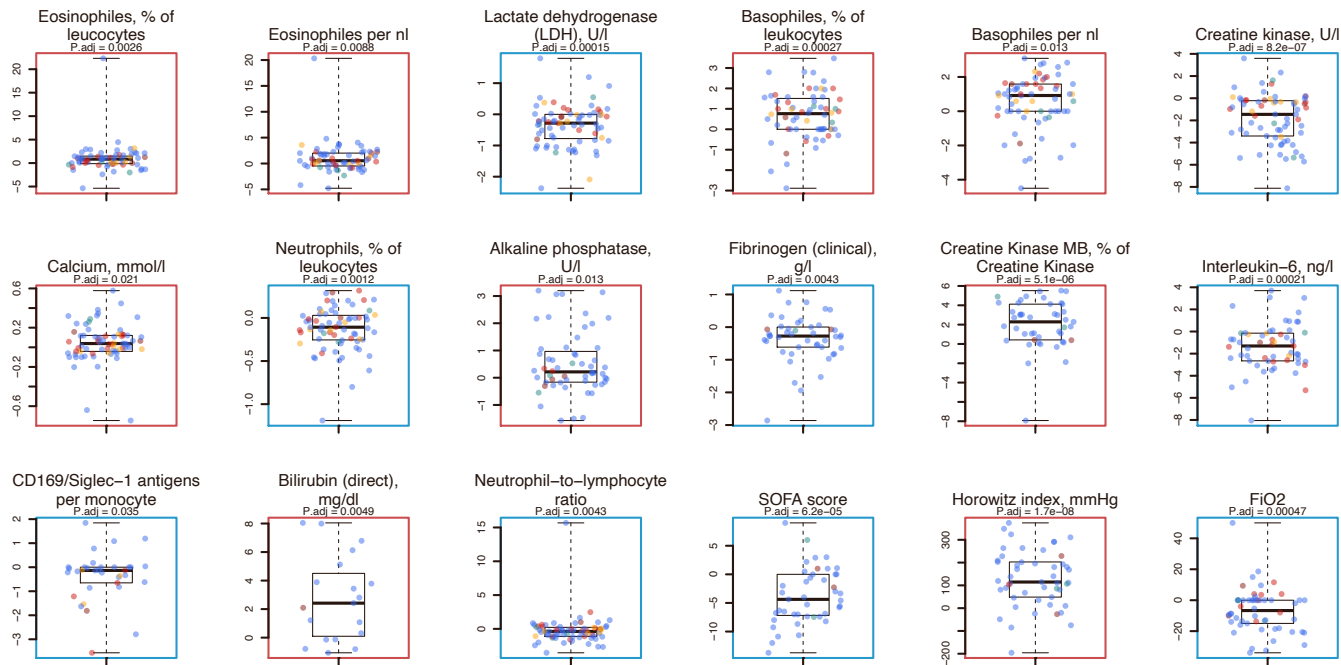




Figure S15. Omics features differentially changing during the peak of the disease depending on the severity

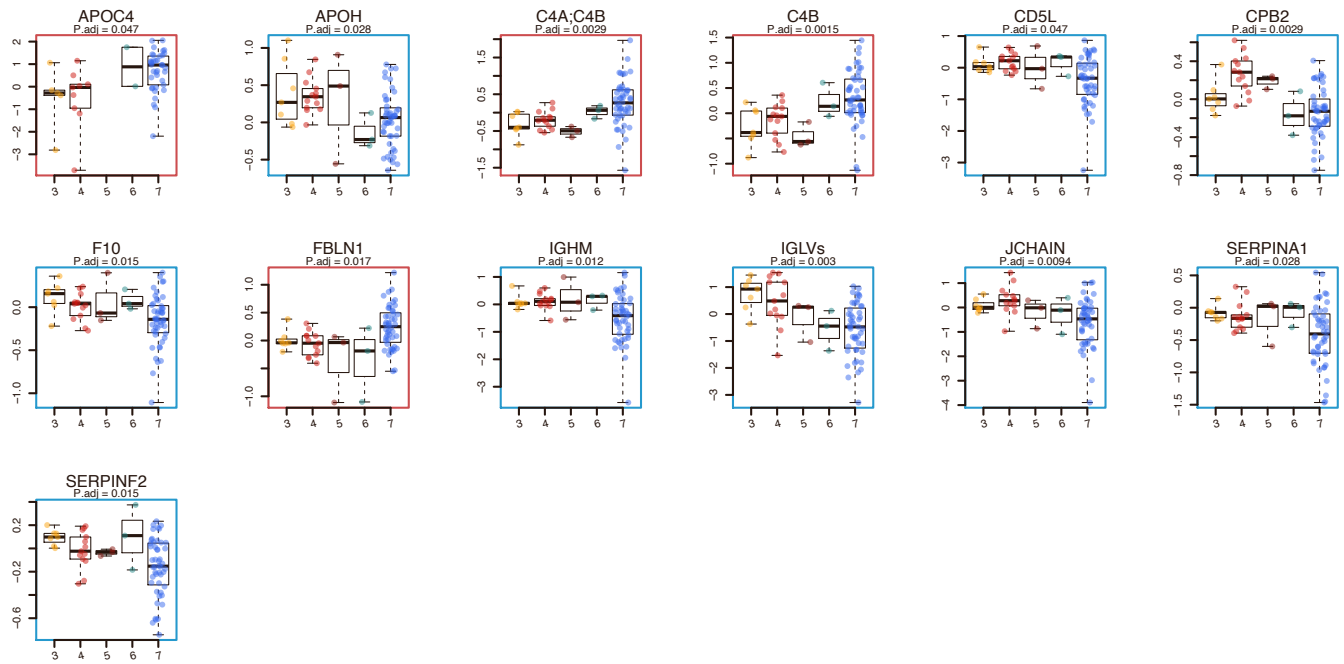
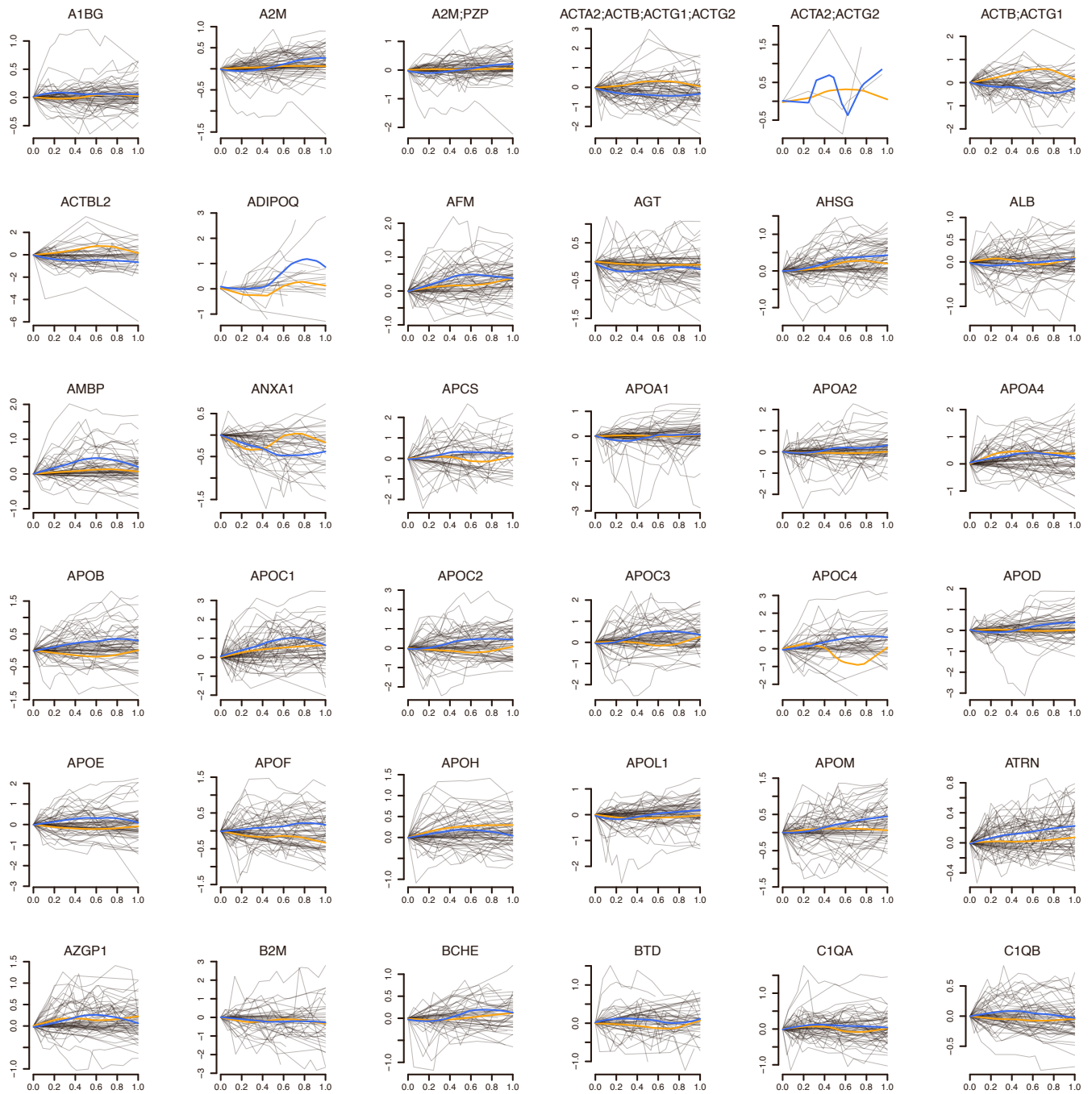
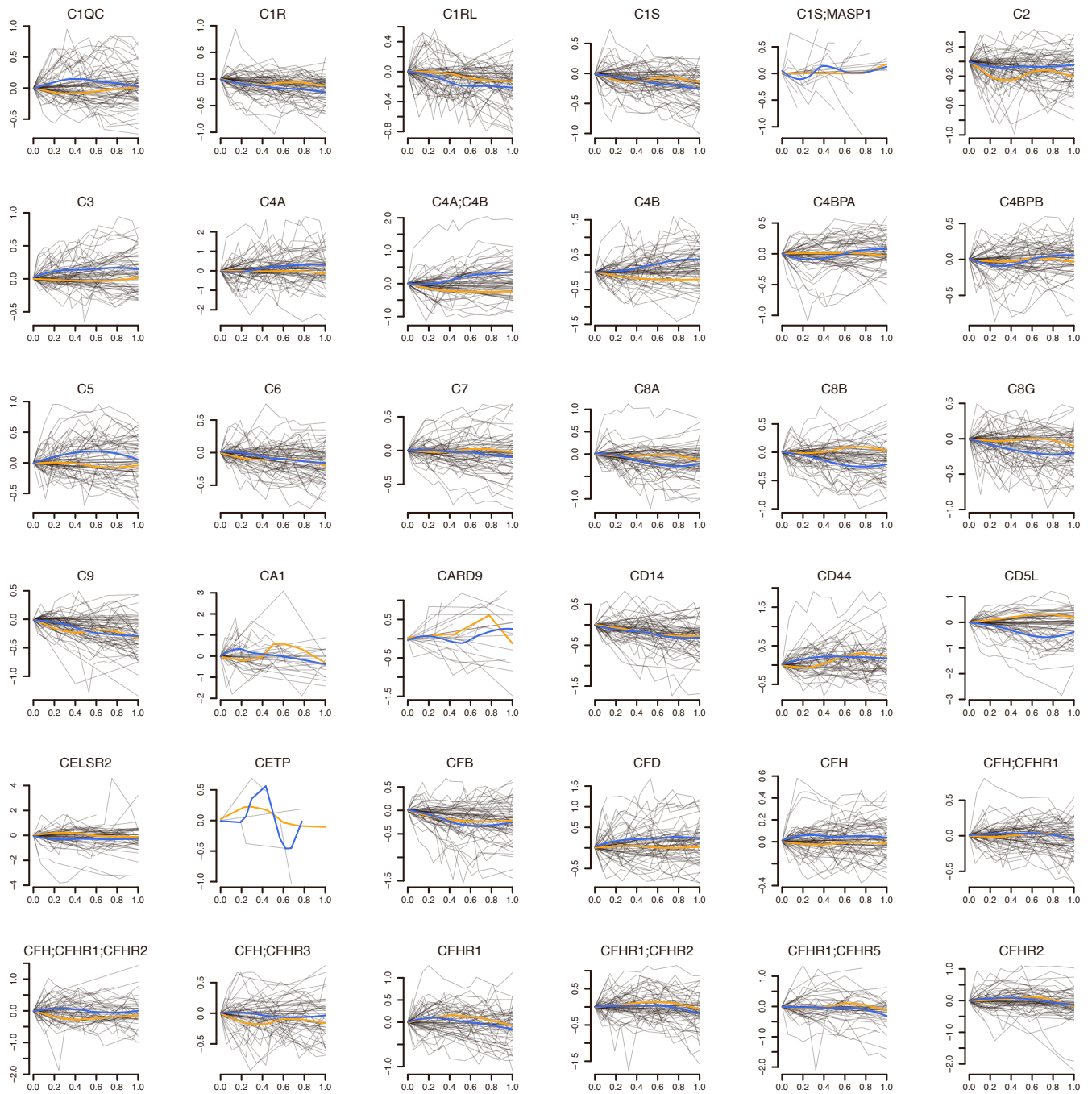
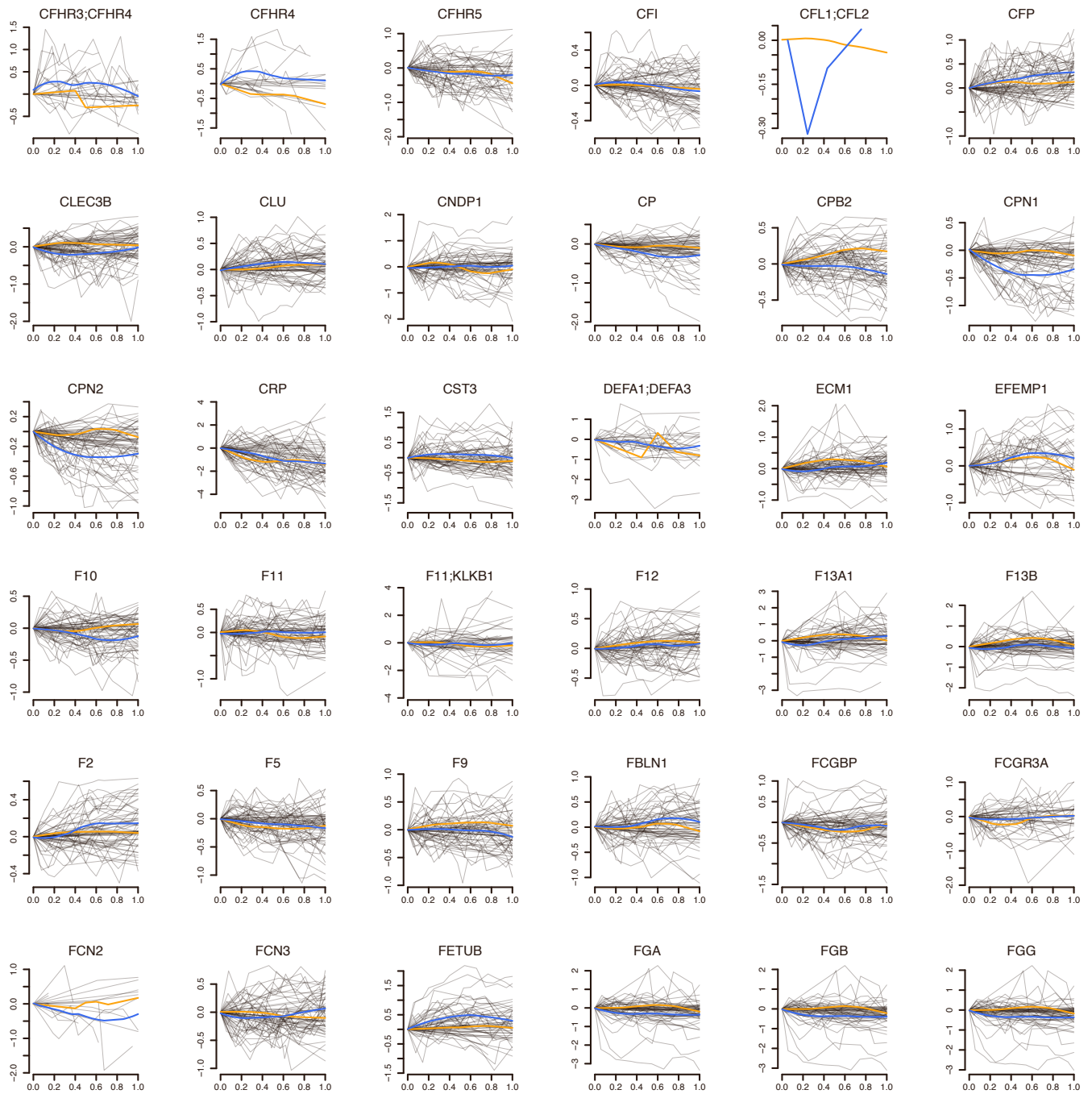
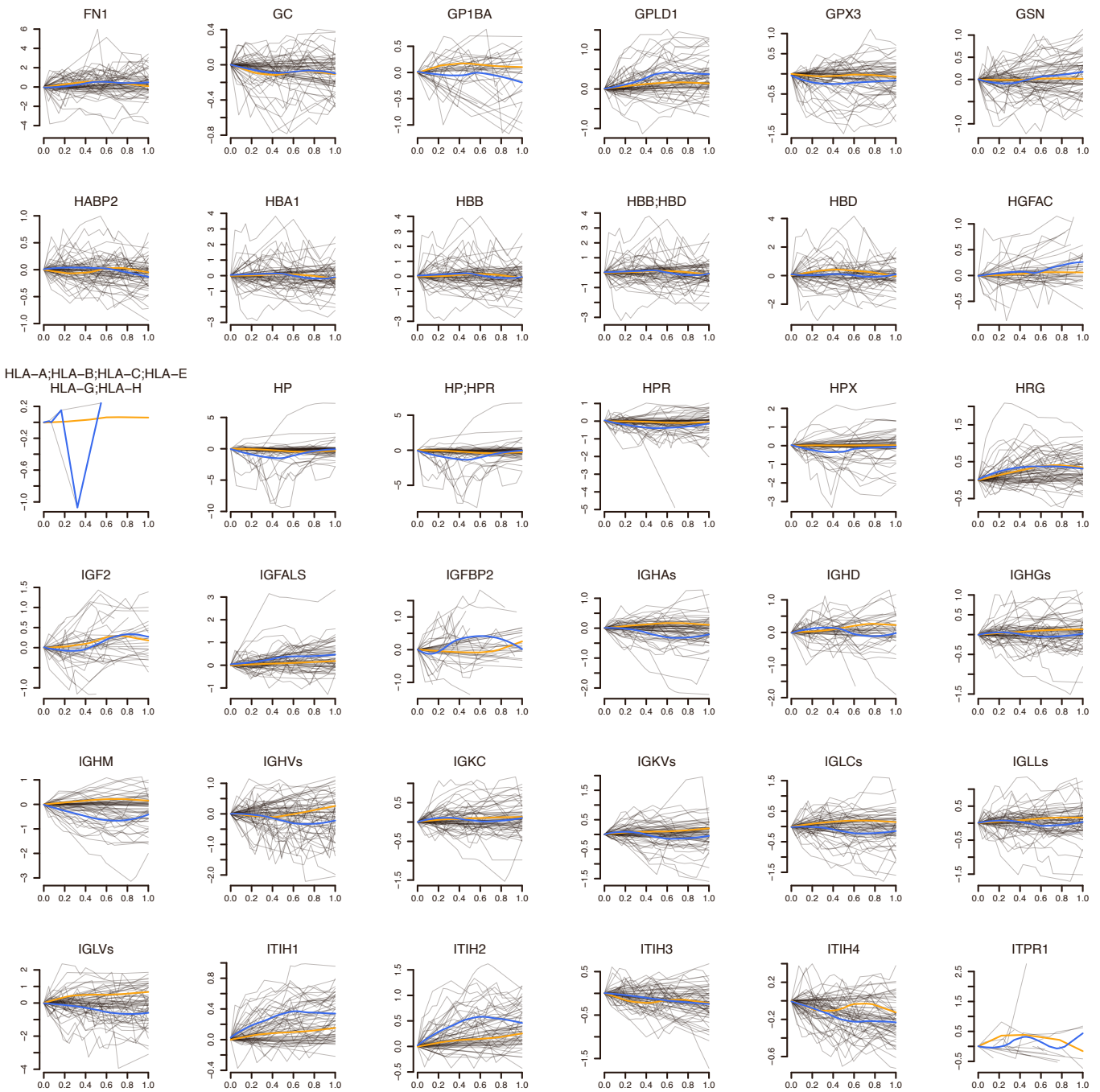


Figure S16 (following 9 pages). Trajectories at the peak of the disease

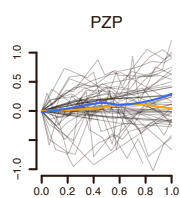
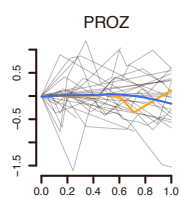
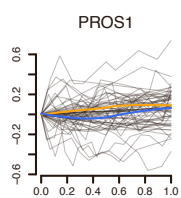
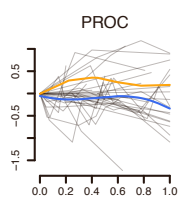
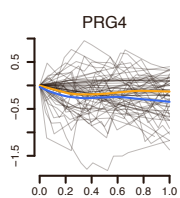
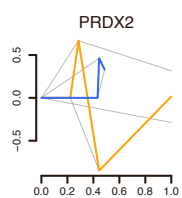
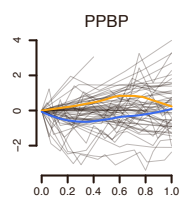
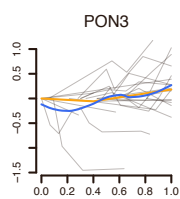
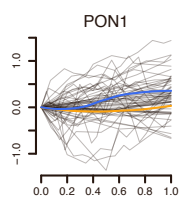
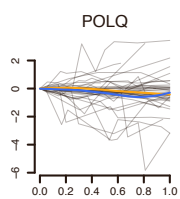
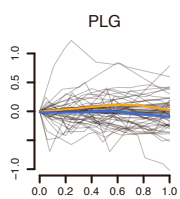
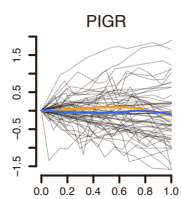
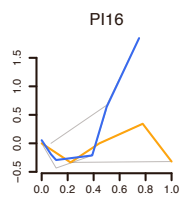
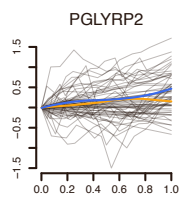
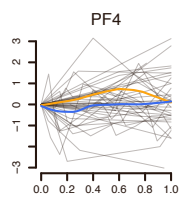
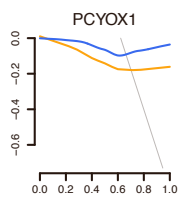
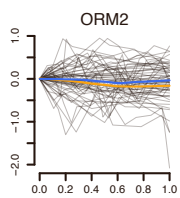
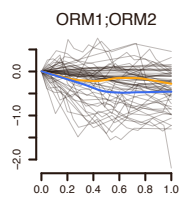
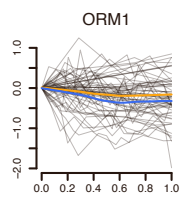
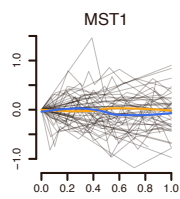
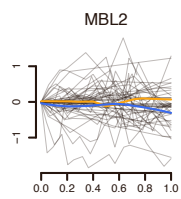
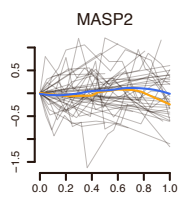
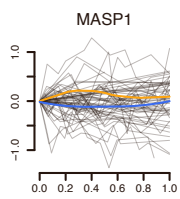
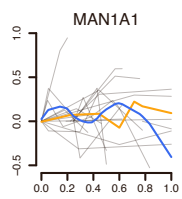
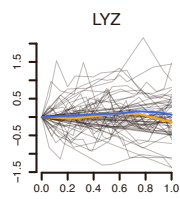
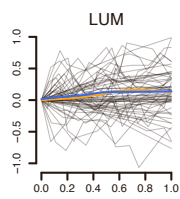
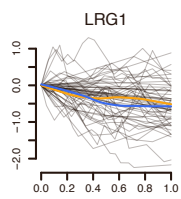
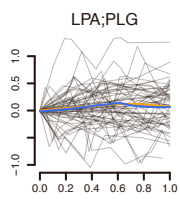
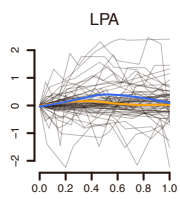
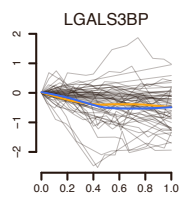
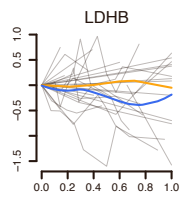
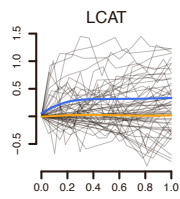
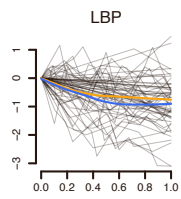
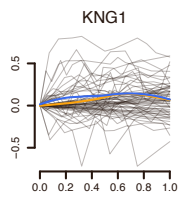
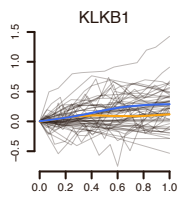
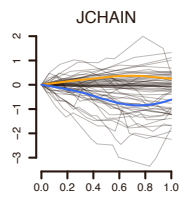


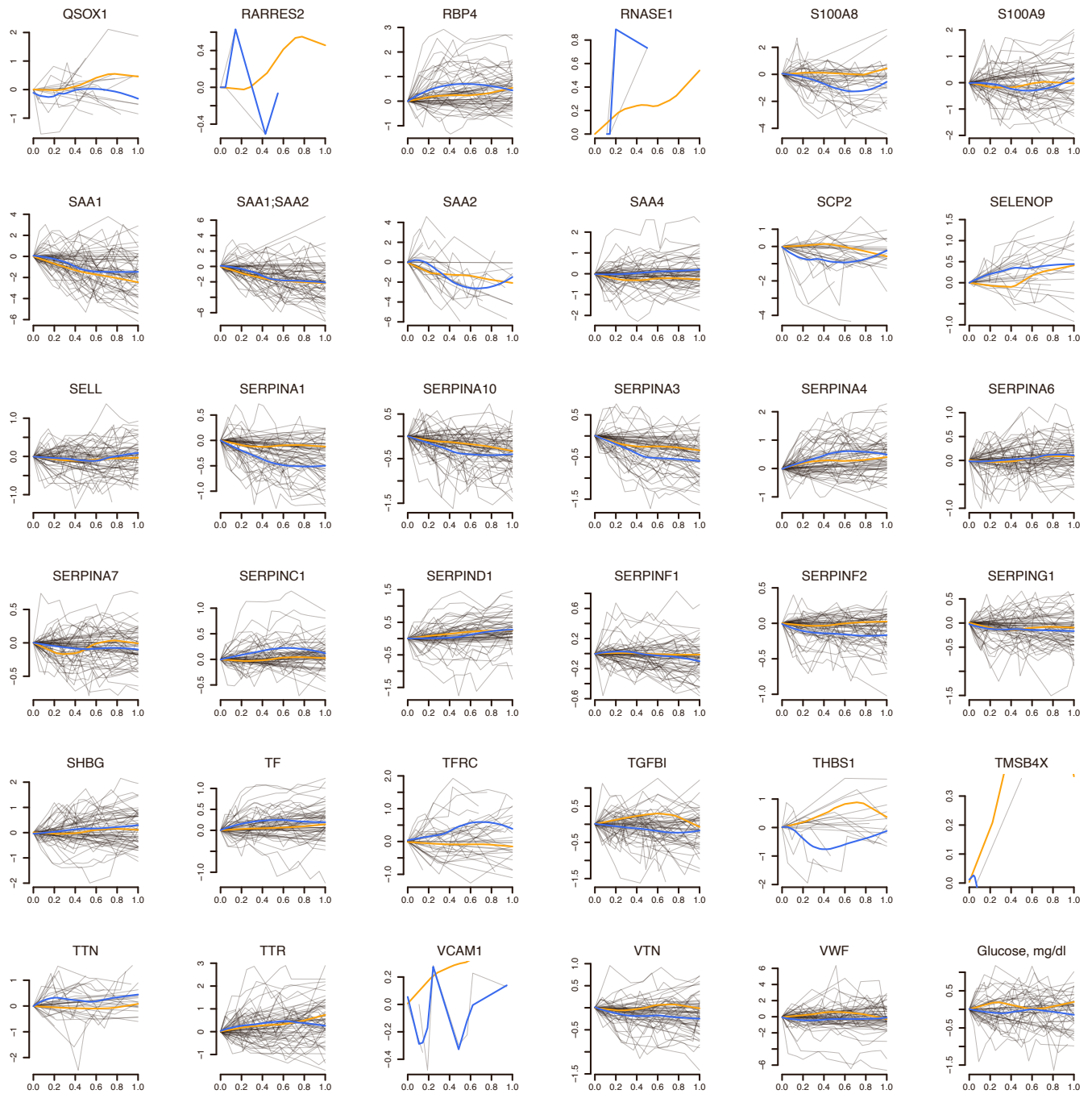




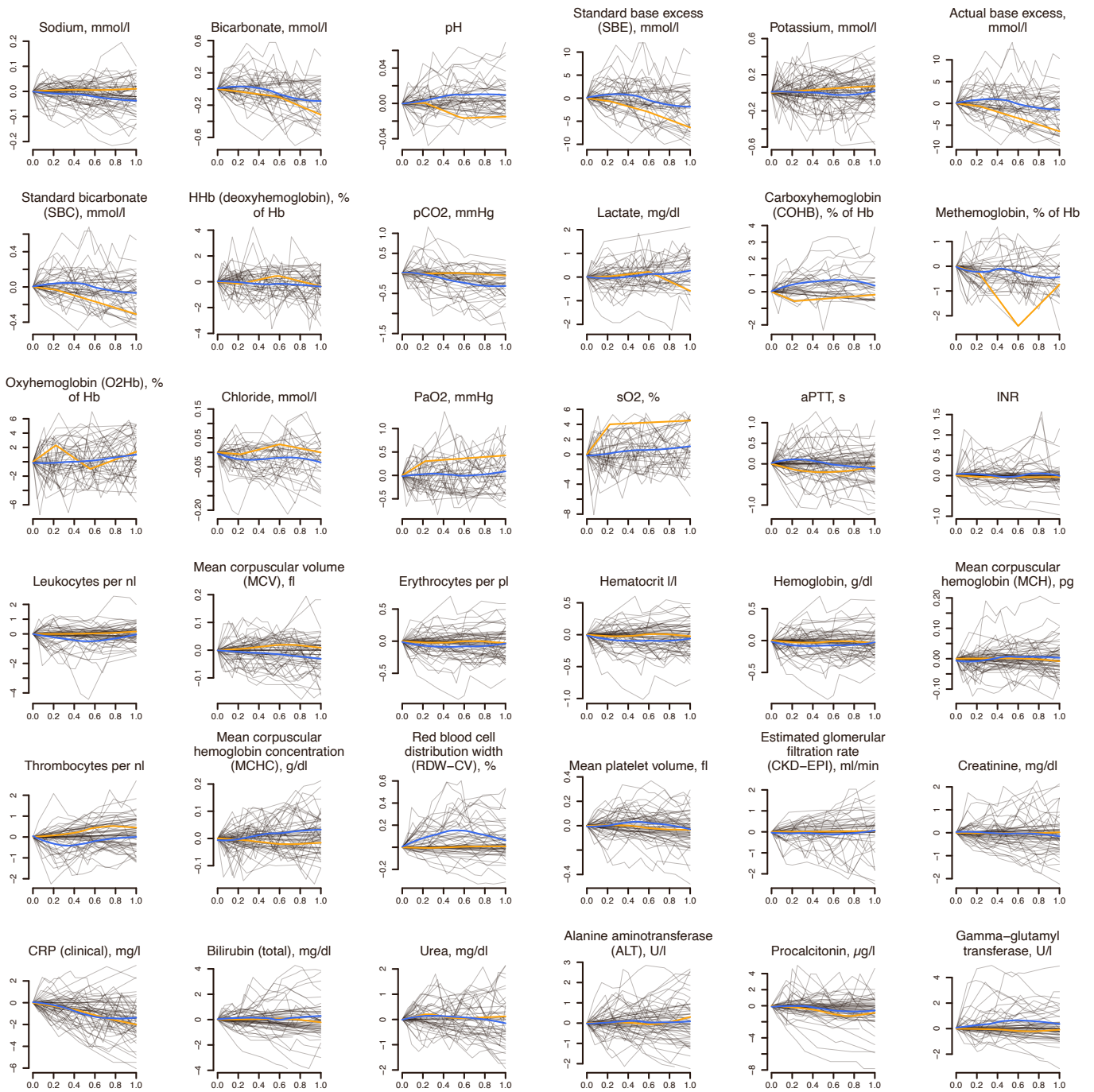


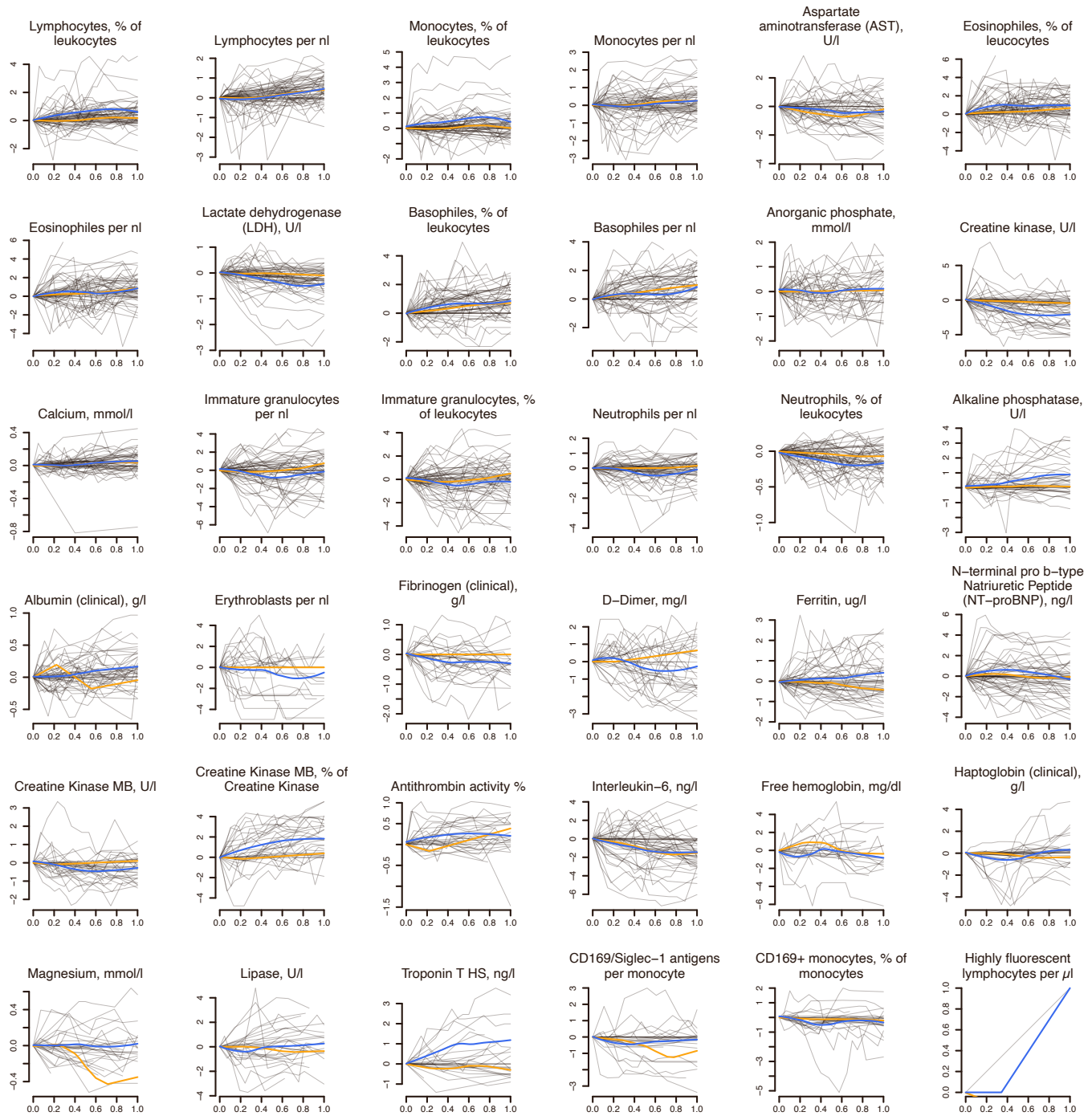












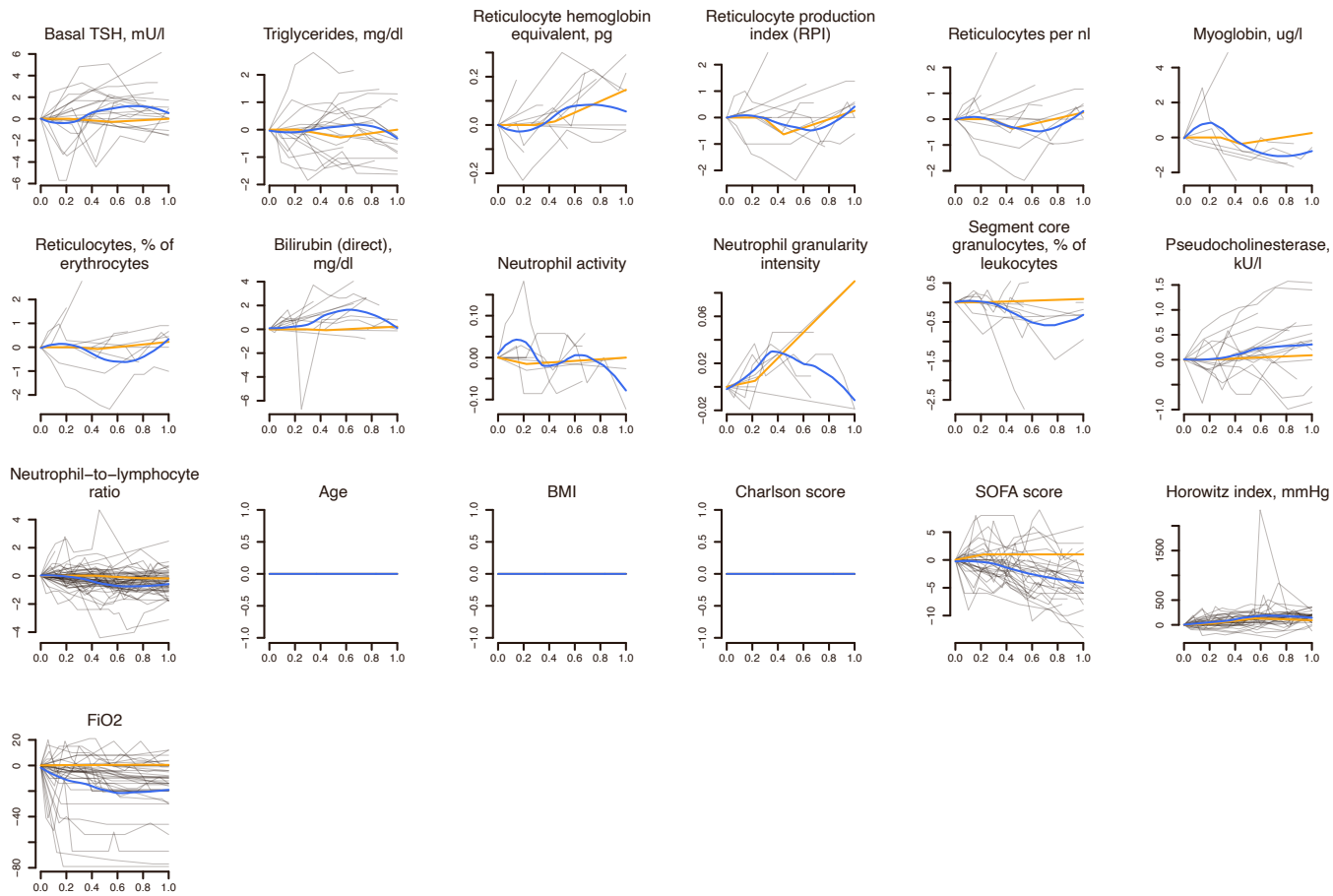


Figure S17. Omics features predictive of future disease worsening

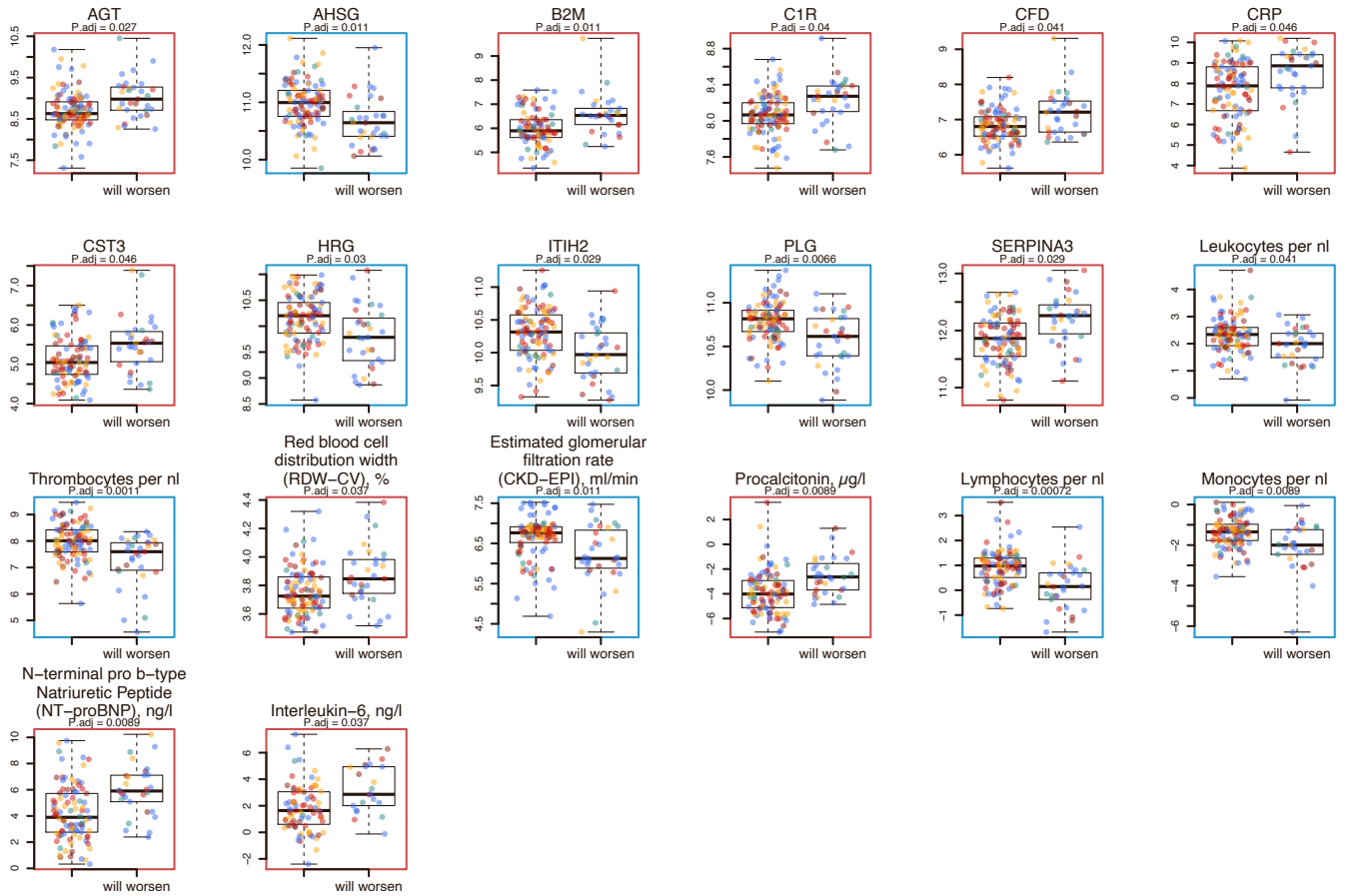


Figure S18 (following 2 pages). Omics features predictive of the remaining time in hospital for patients at WHO = 3

