

## SUPPLEMENTARY MATERIAL AND METHODS

### *Patients*

To enroll into the PAN longitudinal cohort, patients had to fulfill either two major criteria for disease (arteriographic abnormality, biopsy evidence of arterial wall inflammatory infiltrate, or neuropathy) or one major and one minor criterion (weight loss > 4 Kg, skin findings, testicular pain, myalgias, diastolic blood pressure > 90mm Hg, abnormal kidney function, or ischemic abdominal pain), or have biopsy proof of PAN limited to the skin. Healthy controls were recruited at Boston University. All patients were enrolled using protocols approved by the institutional review board and ethics committee of Boston University, which was the main center for the study; the approval numbers were: H-14969, H-24869, H-24992, and H-24998. Approvals were also obtained from each additional site, which were the following 8: University of Pennsylvania, University of Pittsburg, Johns Hopkins University, Mount Sinai Hospital in Toronto, McMaster University in Hamilton, University of Utah, Mayo Clinic and Cleveland Clinic. All patients gave written consent to participate in the study and also for the results of the study to be published without any patient identifiers.

Information on specific manifestations of vasculitis was recorded using versions of the Birmingham Vasculitis Activity Score (BVAS), as well as more detailed Medical History Forms designed for the VCRC studies (18). Overall disease activity during the prior 28 days was rated by physician global assessment (PGA), through which remission is indicated by PGA = 0 and active disease by PGA = 1-10, the BVAS, through which

remission is defined as BVAS=0, and by the VCRC Medical History Form with any active manifestation in the prior 28 days indicated active disease (non-remission).

Although many patients with active GCA will not have a specific manifestation available to record on the BVAS, there is an option for “other” that investigators were instructed to record. Patients with active asthma but no other manifestations were not regarded as having active EGPA. For a sample to be used, data from the PGA, VCRC Medical History Form, and BVAS had to be in agreement on whether the patient was in remission or had active disease at a particular visit. Treatment with immunosuppressive medications (yes/no) was recorded at each visit. For this study, glucocorticoids (usually prednisone) were used as one variable, all other immunosuppressive drugs were pooled as a second variable, and for a separate analysis both variables were pooled as a single dichotomous treatment variable.

### *Statistical Methods*

Mixed models provide the best assessment of how disease state affects marker concentration, but in clinical decision-making, an estimate of how marker concentration can be used to predict disease state is more widely used. Three types of logistic regression were used for the experimental markers with the strongest association with disease activity in mixed models. Stratified conditional logistic regression is the most rigorous approach and adjusts for different patient baselines, providing an odds ratio (OR) but not an area under a receiver operating characteristic curve (AUC-ROC).

Unadjusted logistic regression produces an AUC-ROC but does not account for different

patient baselines, nor for use of repeated measures more generally. In order to adjust for different patient baselines and calculate an AUC-ROC, we determined the mean during remission for each patient and calculated the difference from that mean for each data point during either remission or active disease.

For the J48 classification tree, when an independent cohort is not available, cross-validation within the dataset is a good way to estimate the actual performance of the classification tree, analogous to calculating a standard error. Cross-validation evaluates predictive models by partitioning the original sample into a training set to train the model and a test set to evaluate it. In 5-fold cross-validation the original sample is partitioned into 5 equal size subsamples. In each iteration of the model, one of the partitions (subsamples) is used as the test set. The validation results were averaged to estimate a final predictive model.

**Supplementary Table 1.** Concurrent use of any immunosuppressive drug (IS, including prednisone), or specifically prednisone, at the time of sample collection, separated by disease and by disease activity.

Disease	Remission					Active				
	Total	Any IS		Prednisone		Total	Any IS		Prednisone	
		Yes	No	Yes	No		Yes	No	Yes	No
<b>GCA</b>	104	102	2	94	10	61	46	15	51	10
<b>TAK</b>	50	47	3	35	15	30	26	4	21	9
<b>PAN</b>	44	41	3	35	9	26	26	0	23	3
<b>EGPA</b>	66	61	5	56	10	37	33	4	30	7

**Supplementary Table 2.** Mixed model analyses of active vs. inactive disease for the different types of vasculitides. Mixed effects models included biomarker concentration as the dependent variable, disease activity as a dichotomous independent variable, the patient as the random effect, with or without current use of prednisone and other immunosuppressive drugs (“Meds”) as independent dichotomous variables. Analyses with  $P < 0.1$  are shown with estimated beta-coefficients associating an increase (if  $> 0$ ) or decrease (if  $< 0$ ) in marker concentration with active disease, with 95% confidence intervals in parentheses. For non-transformed marker levels, beta coefficients represent absolute change, whereas for ln-transformed markers, the beta-coefficient multiplied by 2.72 represents fold-change.

Marker	GCA	GCA Meds	TAK	TAK Meds	PAN	PAN Meds	EGPA	EGPA Meds	LVV	LVV Meds
ACE	P=0.59	P=0.83	P=0.5 5	P=0.6 8	P=0.9	P=0.8 5	P=0.65	P=0.60	P=0.37	P=0.51
ln_ACE	P=0.49	P=0.91	P=0.3 4	P=0.4 6	P=0.5 4	P=0.6 0	-0.27 (-0.57 - 0.04) P=0.09	-0.32 (-0.64 - - 0.01) P=0.05	P=0.32	P=0.48
ln_BCA-1	0.23 (0.01 - 0.45) P=0.04	0.33 (0.10 - 0.56) P=0.005	P=0.2 1	P=0.2 9	P=0.4 5	P=0.6 3	0.27 (-0.01 - 0.55) P=0.06	0.34 (0.05 - 0.62) P=0.02	0.21 (0.03 - 0.38) P=0.02	0.24 (0.07 - 0.42) P=0.006
ln_CRP	0.35 (0.01 - 0.70) P=0.05	P=0.14	P=0.1 7	-0.47 (-1.02- 0.07) P=0.0 9	P=0.2 8	P=0.4 2	P=0.22	P=0.40	P=0.40	P=0.65
ESR	10.6 (5.3 - 15.8) P=0.000 1	10.3 (4.9 - 15.8) P=0.000 3	P=0.9 9	P=0.1 6	8.12 (1.6 - 14.6) P=0.0 2	8.53 (1.79 - 15.3) P=0.0 1	P=0.29	P=0.3	7.86 (3.76 - 12) P=0.000 2	7.69 (3.55 - 11.8) P=0.000 3
ln_ESR	P=0.21	P=0.3	P=0.9 3	P=0.9 9	P=0.1 0	P=0.1 1	P=0.34	P=0.19	P=0.24	P=0.28
ln_G-CSF	0.45 (0.03 - 0.87) P=0.04	0.39 (-0.04 - 0.83) P=0.08	P=0.9 1	P=0.9 7	P=0.6 4	P=0.4 5	0.53 (0.15 - 0.92) P=0.00 7	0.62 (0.23 - 1.02) P=0.002	P=0.21	P=0.26
ln_GM-CSF	0.31 (0.04 - 0.57) P=0.03	0.27 (-0.01 - 0.55) P=0.05	P=0.9 2	P=0.9 8	P=0.1 3	P=0.4 6	0.63 (0.21 - 1.06) P=0.00 4	0.75 (0.32 - 1.19) P=0.000 9	0.21 (0.02 - 0.39) P=0.03	0.19 (0.01 - 0.38) P=0.04
ln_IFNg	P=0.77	P=0.9	P=0.3 3	P=0.4	P=0.9 9	P=0.7 9	P=0.56	0.46	P=0.49	P=0.59
ln_IL-6	P=0.46	P=0.95	P=0.6 1	P=0.6 5	P=0.5 2	P=0.5 8	0.45 (0.02 - 0.88) P=0.04	0.49 (0.04 - 0.94) P=0.03	P=0.33	P=0.65
ln_IL-8	P=0.8	P=0.28	P=0.5 1	P=0.6 2	P=0.6 6	P=0.5 7	P=0.75	P=0.51	P=0.64	P=0.39
ln_IL-15	P=0.32	P=0.33	P=0.5 6	P=0.7 4	P=0.2 8	P=0.2 8	0.44 (0.07 - 0.81) P=0.02	0.58 (0.2 - 0.950) P=0.003	P=0.22	P=0.37

Marker	GCA	GCA Meds	TAK	TAK Meds	PAN	PAN Meds	EGPA	EGPA Meds	LVV	LVV Meds
In_IL-18	0.21 (-0.01 - 0.43) P=0.06	P=0.13	P=0.6 3	P=0.7	P=0.7 1	P=0.8 3	P=0.48	P=0.47	0.14 (0.02 - 0.25) P=0.02	0.14 (-0.02 - 0.31) P=0.09
In_IL-18BP	0.14 (0.00 - 0.29) P=0.05	P=0.19	P=0.2 5	P=0.2 7	P=0.3 2	P=0.4 1	P=0.39	P=0.26	0.16 (-0.01 - 0.32) P=0.06	0.11 (-0.00 - 0.23) P=0.05
In_IP-10	-0.26 (-0.47 - 0.05) P=0.02	-0.3 (-0.52 - 0.08) P=0.008	P=0.6 8	P=0.6 9	P=0.2 0	P=0.2 2	P=0.95	P=0.80	P=0.14	-0.18 (-0.37 - 0.01) P=0.06
In_MMP-3	P=0.89	P=0.31	P=0.2 4	P=0.3 5	-0.58 (-1.12 - -0.04) P=0.0 4	-0.68 (-1.24 - -0.13) P=0.0 2	P=0.73	P=0.45	P=0.51	P=0.84
NGAL	P=0.51	P=0.46	P=0.1 3	P=0.1 6	P=0.6 1	P=0.5 4	P=0.18	P=0.16	P=0.96	P=0.82
In_NGAL	P=0.37	P=0.37	P=0.5 1	P=0.5 9	P=0.4 2	P=0.4 3	P=0.59	P=0.53	P=0.66	P=0.52
Osteopontin	P=0.27	P=0.37	P=0.3 8	P=0.3 5	P=0.3	P=0.3 2	P=0.46	P=0.55	P=0.18	P=0.34
In_Osteopontin	P=0.11	P=0.13	P=0.2 4	P=0.2 1	P=0.4	P=0.3 7	P=0.91	P=0.86	0.20 (-0.01 - 0.4) P=0.06	P=0.11
In_PAI-1	P=0.97	P=0.85	P=0.2 3	P=0.2 9	P=0.7 6	P=0.7 7	P=0.99	P=0.54	P=0.52	P=0.51
PDGF-AB	P=0.84	P=0.55	P=0.2 7	P=0.3 9	P=0.9 2	P=0.7 6	711 (-67 - 1489) P=0.07	P=0.13	P=0.45	P=0.48
In_PDGF-AB	P=0.51	P=0.69	P=0.4	P=0.5 4	P=0.3 2	P=0.3 2	0.32 (-0.02 - 0.66) P=0.06	0.34 (-0.00 - 0.69) P=0.05	P=0.30	P=0.35
RANTES	P=0.17	P=0.12	P=0.8 3	P=0.9 1	P=0.6 8	P=0.5 7	P=0.97	P=0.98	P=0.40	P=0.38
In_RANTES	P=0.85	P=0.94	P=0.5 8	P=0.6 7	P=0.2 2	P=0.1 4	P=0.55	P=0.54	P=0.58	P=0.68
sICAM-1	P=0.99	P=0.53	P=0.4 7	P=0.5 7	P=0.3 3	P=0.2 5	P=0.46	P=0.25	P=0.78	P=0.42
In_sICAM-1	P=0.61	P=0.43	P=0.2 7	P=0.2 7	P=0.3 3	P=0.2 9	P=0.24	P=0.13	P=0.35	P=0.18
In_sIL-2R $\alpha$	0.47 (0.14 - 0.79) P=0.005	0.4 (0.06 - 0.73) P=0.02	P=0.1 4	P=0.1 5	P=0.3 4	P=0.2 8	0.60 (0.12 - 1.08) P=0.01	0.68 (0.18 - 1.18) P=0.008	P=0.33	P=0.32
sIL-6R	2.2 (-0.2 - 4.7) P=0.07	2.4 (-0.1 - 5.0) P=0.06 <sup>+</sup>	P=0.8 5	P=0.9 9	3.9 (-0.3 - 8.1) P=0.0 7	4.5 (0.1 - 8.9) P=0.0 5	P=0.43	P=0.33	P=0.30	P=0.37
In_sIL6R	P=0.39	P=0.2	P=0.8 9	P=1.0	P=0.1 9	P=0.1 4	P=0.68	P=0.54	P=0.59	P=0.63
sTNFR2	P=0.43	P=0.77	P=0.9 8	P=0.9 9	137 (-25 - 299) P=0.1	156 (-17 - 328) P=0.0 8	P=0.84	P=0.66	P=0.44	P=0.69
In_sTNFR2	P=0.34	P=0.63	P=0.4 4	P=0.3 7	P=0.4 9	P=0.3 8	P=0.42	P=0.77	P=0.62	P=0.89
TIMP-1	76 (28 - 124) P=0.002	78 (27 - 129) P=0.003	P=0.3 5	P=0.4 2	P=0.4 5	P=0.4 1	P=0.90	P=0.89	P=0.32	P=0.44

Marker	GCA	GCA Meds	TAK	TAK Meds	PAN	PAN Meds	EGPA	EGPA Meds	LVV	LVV Meds
In_TIMP-1	0.12 (0.02 - 0.21) P=0.02	0.13 (0.03 - 0.23) P=0.01	P=0.1 5	P=0.1 5	P=0.3 5	P=0.3 2	P=0.40	P=0.39	P=0.54	P=0.72

**Supplementary Table 3.** Mixed model analyses of active vs. inactive disease for subsets of patients with GCA (TAB/Angio = proven by temporal artery biopsy or angiography) or EGPA (ANCA-positive or ANCA-negative). Mixed effects models included biomarker concentration as the dependent variable, disease activity as a dichotomous independent variable, and the patient as the random effect. Analyses with  $P < 0.1$  are shown with estimated beta-coefficients associating an increase (if  $> 0$ ) or decrease (if  $< 0$ ) in marker concentration with active disease, with 95% confidence intervals in parentheses. For non-transformed marker levels, beta coefficients represent absolute change, whereas for ln-transformed markers, the beta-coefficient multiplied by 2.72 represents fold-change.

Marker	GCA (n=60)	GCA (TAB/Angio) (n=55)	EGPA (n=37)	EGPA ANCA-pos (n=18)	EGPA ANCA-neg (n=19)
ACE	P=0.59	P=0.86	P=0.65	P=0.88	P=0.58
In_ACE	P=0.49	P=0.55	-0.27 (-0.57 - 0.04) P=0.09	-0.11 P=0.60	-0.39 P=0.12
In_BCA-1	0.23 (0.01 - 0.45) P=0.04	0.26 (0.02 - 0.50) P=0.03	0.27 (-0.01 - 0.55) P=0.06	0.64 (0.27 - 1.00) P=0.001	-0.08 P=0.74
In_CRP	0.35 (0.01 - 0.70) P=0.05	P=0.21	P=0.22	P=0.46	P=0.22
ESR	10.6 (5.3 - 15.8) P=0.0001	9.2 (3.6 - 14.7) P=0.001	P=0.29	P=0.24	P=0.91
In_ESR	P=0.21	P=0.56	P=0.34	P=0.12	P=0.88
In_G-CSF	0.45 (0.03 - 0.87) P=0.04	0.50 (0.05 - 0.96) P=0.03	0.53 (0.15 - 0.92) P=0.007	0.41 P=0.14	0.66 (0.11 - 1.20) P=0.02
In_GM-CSF	0.31 (0.04 - 0.57) P=0.03	0.33 (0.04 - 0.63) P=0.03	0.63 (0.21 - 1.06) P=0.004	0.32 P=0.27	0.93 (0.22 - 1.64) P=0.01
In_IFNg	P=0.77	P=0.77	P=0.56	0.46	P=0.23
In_IL-6	P=0.46	P=0.70	0.45 (0.02 - 0.88) P=0.04	0.43 (-0.06 - 0.93) P=0.08	0.47 P=0.23
In_IL-8	P=0.8	P=0.71	P=0.75	P=0.39	P=0.30
In_IL-15	P=0.32	P=0.34	0.44 (0.07 - 0.81) P=0.02	0.46 (-0.03 - 0.94) P=0.07	0.45 P=0.15
In_IL-18	0.21 (-0.01 - 0.43) P=0.06	P=0.11	P=0.48	P=0.39	P=0.85

Marker	GCA (n=60)	GCA (TAB/Angio) (n=55)	EGPA (n=37)	EGPA ANCA-pos (n=18)	EGPA ANCA-neg (n=19)
In_IL-18BP	0.14 (0.00 - 0.29) P=0.05	0.14 (-0.02 - 0.29) P=0.08	P=0.39	P=0.92	P=0.49
In_IP-10	-0.26 (-0.47 - -0.05) P=0.02	-0.31 (-0.53 - -0.08) P=0.008	P=0.95	P=0.60	P=0.94
In_MMP-3	P=0.89	P=0.78	P=0.73	0.32 (-0.03 - 0.67) P=0.07	-0.18 P=0.44
NGAL	P=0.51	P=0.76	P=0.18	P=0.27	P=0.38
In_NGAL	P=0.37	P=0.52	P=0.59	P=0.38	P=0.98
Osteopontin	P=0.27	P=0.68	P=0.46	P=0.67	P=0.51
In_Osteopontin	P=0.11	P=0.21	P=0.91	P=0.86	P=0.95
In_PAI-1	P=0.97	P=0.39	P=0.99	P=0.54	P=0.58
PDGF-AB	P=0.84	P=0.98	711 (-67 - 1489) P=0.07	1120 (-104 - 2343) P=0.07	419 P=0.46
In_PDGF-AB	P=0.51	P=0.27	0.32 (-0.02 - 0.66) P=0.06	0.71 (-0.02 - 1.43) P=0.06	0.05 P=0.74
RANTES	P=0.17	P=0.23	P=0.97	P=0.56	P=0.53
In_RANTES	P=0.85	P=0.75	P=0.55	P=0.87	P=0.20
sICAM-1	P=0.99	P=0.89	P=0.46	P=0.72	P=0.19
In_sICAM-1	P=0.61	P=0.44	P=0.24	P=0.58	P=0.15
In_sIL-2R $\alpha$	0.47 (0.14 - 0.79) P=0.005	0.45 (0.10 - 0.81) P=0.01	0.60 (0.12 - 1.08) P=0.01	1.01 (0.14 - 1.87) P=0.02	0.23 P=0.43
sIL-6R	2.2 (-0.2 - 4.7) P=0.07	2.5 (-0.2 - 5.1) P=0.07	P=0.43	P=0.14	P=0.65
In_sIL6R	P=0.39	P=0.38	P=0.68	P=0.18	P=0.52
sTNFR2	P=0.43	P=0.93	P=0.84	P=0.50	P=0.39
In_sTNFR2	P=0.34	P=0.67	P=0.42	P=0.89	P=0.34
TIMP-1	76 (28 - 124) P=0.002	65 (15 - 115) P=0.01	P=0.90	P=0.94	P=0.44
In_TIMP-1	0.12 (0.02 - 0.21) P=0.02	0.10 (-0.00 - 0.12) P=0.06	P=0.40	P=0.83	P=0.11







