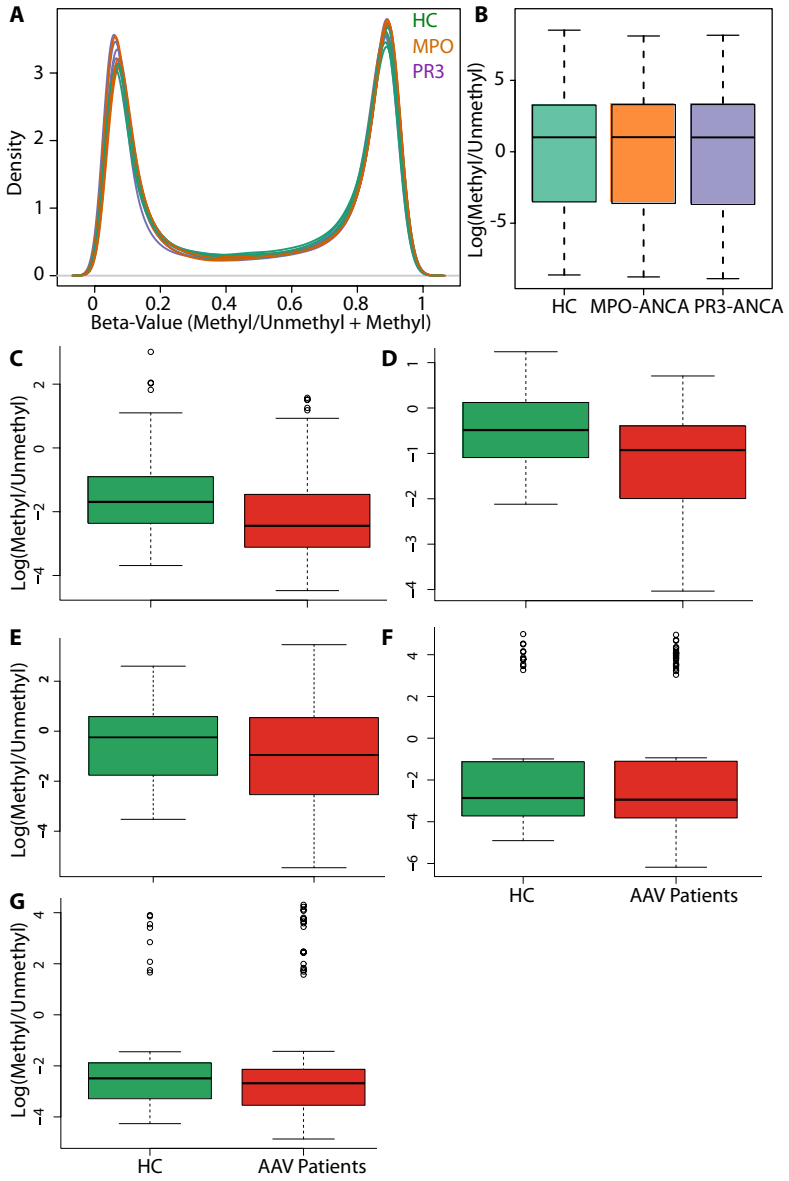
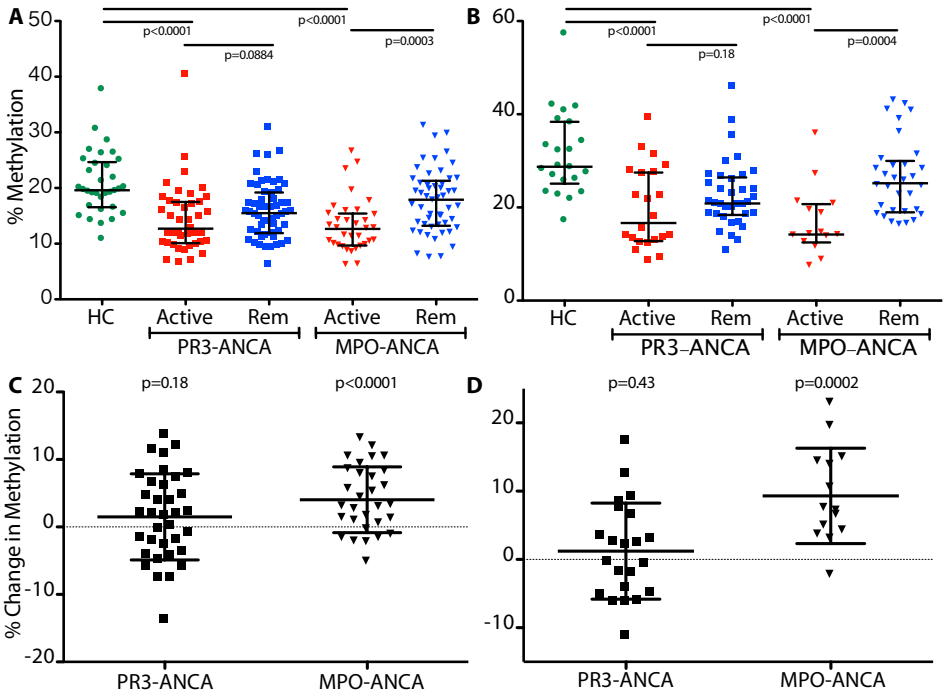
Supplementary Materials:

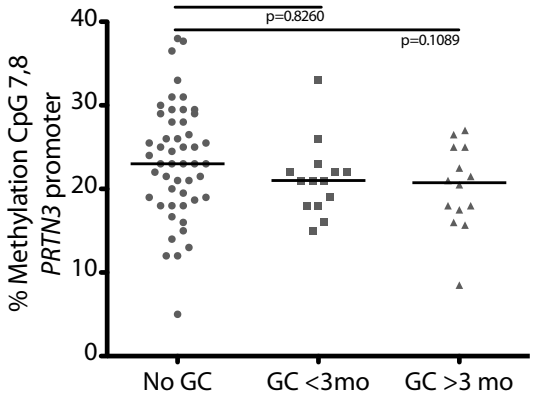


Supplemental Figure 1. Epigenome-wide DNA methylation in patients with AAV. Genome-wide DNA methylation (**A**) beta-value (methylated signal/(methylated signal+unmethylated signal)) and (**B**) Mean M value (log(methylated signal/unmethylated signal)) at 485,512 CpGs for 4 healthy controls (green), 4 MPO-ANCA active patients (orange) and 6 PR3-ANCA active patients (purple). Gene-specific median methylation at all CpG dinucleotides in healthy controls (left, green) compared to AAV patients (right, red) at (**C**) *PRTN3*, (**D**) *MPO*, (**E**) *ELANE*, (**F**) *LTF* and (**G**) *BPI*. For each graph, the line represents the

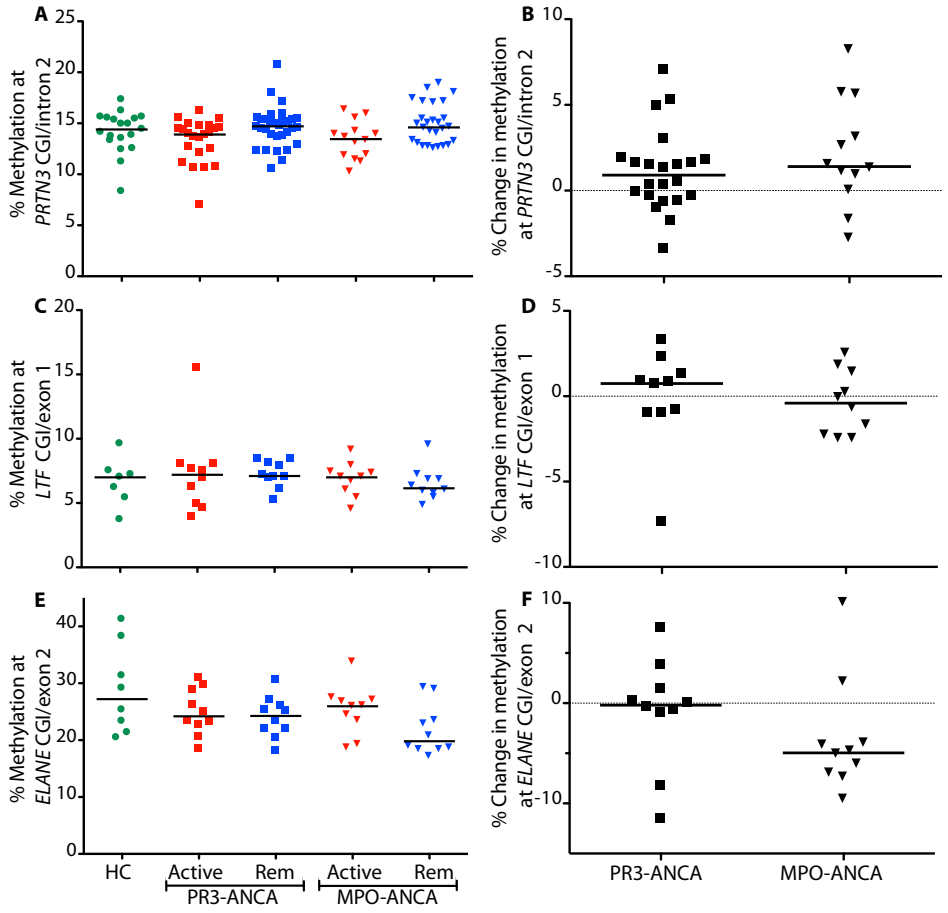
median, the box the first and third quartiles, and the whiskers represent the maximum and minimum (A, B, D) values or 1.5 interquartile range (C, E, F).



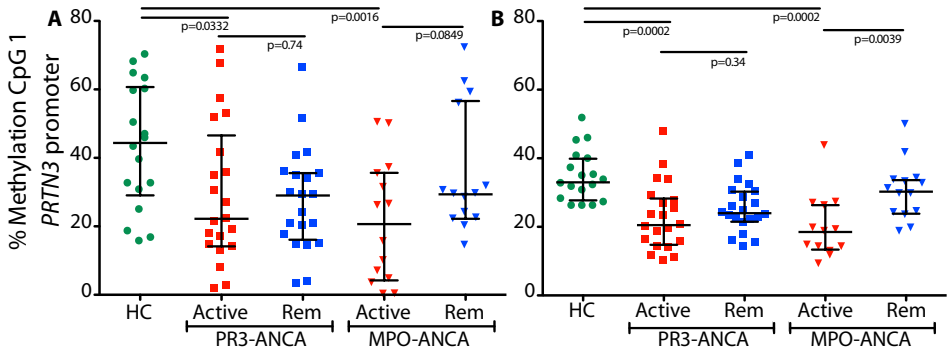
Supplemental Figure 2. DNA methylation at additional loci within *PRTN3* and *MPO*. Cross-sectional methylation at (**A**) *PRTN3* CGI/exon 5 and (**B**) *MPO* CGI/exon 7. Healthy controls (green circles); PR3-ANCA patients (squares); MPO-ANCA patients (triangles); active patients are red and patients in remission are blue; bars shown are median with interquartile range; $p<0.0125$ is considered significant after accounting for multiple testing. Mean longitudinal methylation change from disease activity to remission at (**C**) *PRTN3* CGI/exon 5: PR3-ANCA patients 1.49%, MPO-ANCA patients 4.36%; and (**D**) *MPO* CGI/exon 7: PR3-ANCA patients 1.22%, MPO-ANCA patients 9.31%. Error bars are standard deviation; p-values shown are as different from zero, where $p<0.025$ is significant after accounting for multiple testing.



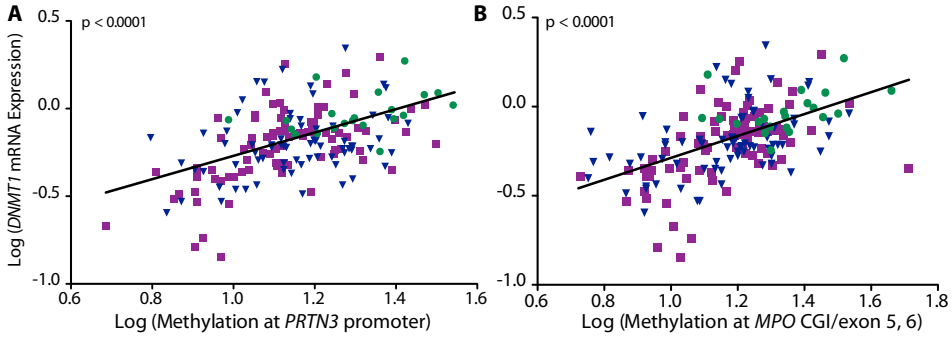
Supplemental Figure 3. Role of glucocorticoid therapy in DNA methylation. (**A**) DNA methylation at CpG 7, 8 of the *PRTN3* promoter for all samples collected from active patients not prescribed glucocorticoid therapy (GC) (circles); active patients prescribed GC for less than or equal to three months (squares) and patients prescribed GC for more than three months (triangles). Bars shown are median DNA methylation; $p<0.05$ is considered significant.



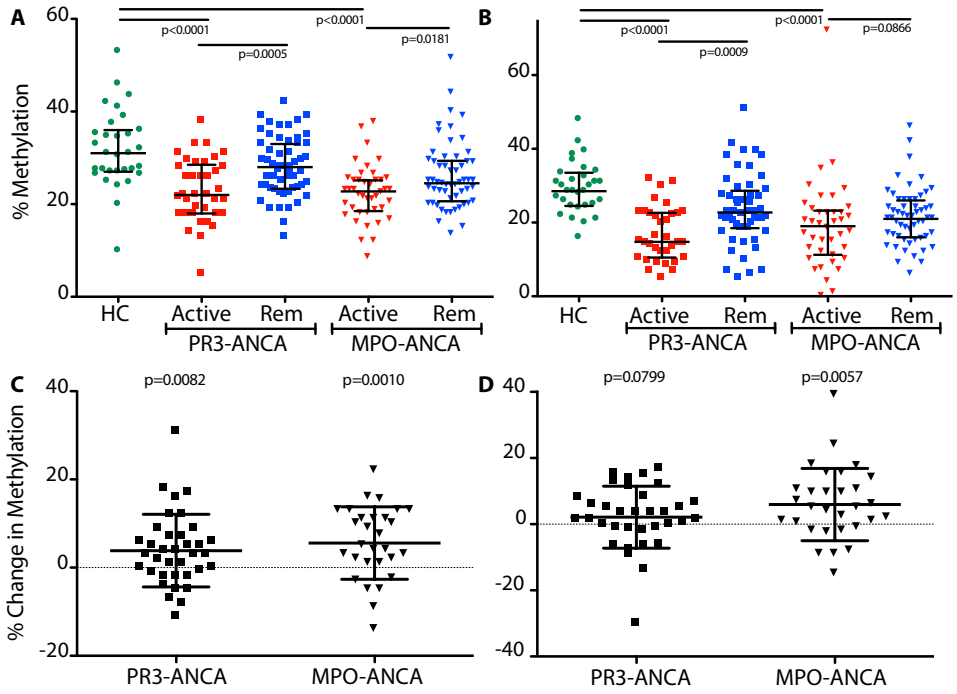
Supplemental Figure 4. DNA methylation at loci within additional granulocyte genes. Green circles are healthy controls; squares are PR3-ANCA patients; triangles are MPO-ANCA patients; active patients are red and patients in remission are blue. (**A**) Cross-sectional and (**B**) longitudinal methylation at CGI/intron 2 in *PRTN3*. (**C**) Cross-sectional and (**D**) longitudinal methylation at a CGI/exon 1 in lactotransferrin (*LTF*). (**E**) Cross-sectional and (**F**) longitudinal methylation at a CGI and exon 2 in elastase (*ELANE*). Bars are median methylation (**A,C,E**) or median longitudinal methylation change from disease activity to remission (**B,D,F**).



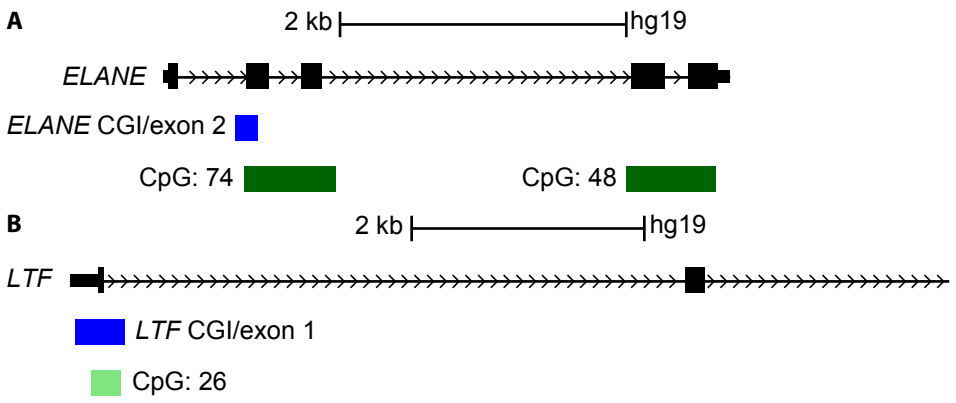
Supplemental Figure 5. DNA methylation platform comparison. Bisulfite sequencing compared to MassARRAY. (**A**) Cross-sectional methylation at CpG 1 *PRTN3* promoter for (**A**) bisulfite sequencing and (**B**) MassARRAY. Green circles are healthy controls; squares are PR3-ANCA patients; triangles are MPO-ANCA patients; active patients are red and patients in remission are blue. Bars are median and interquartile range for all three graphs; p<0.0125 is considered significant, accounting for multiple testing.



Supplemental Figure 6. Correlation of DNA methylation and mRNA expression at *DNMT1*. Healthy controls (green circles); MPO-ANCA patients (blue triangles) and PR3-ANCA patients (purple squares). Log transformed correlation between methylation at the (**A**) *PRTN3* promoter and *DNMT1* expression (n=179; r= 0.4858) and (**B**) correlation between methylation at *MPO* CGI/exon 5-6 and *DNMT1* expression (n=177; r= 0.5464).



Supplemental Figure 7. DNA methylation changes at individual CpGs within the *PRTN3* promoter and *MPO* CGI/exons 5-6. Green circles are healthy controls; squares are PR3-ANCA patients; triangles are MPO-ANCA patients; active patients are red and patients in remission are blue. Bars shown are median with interquartile range; p<0.0125 is significant after accounting for multiple testing. Cross-sectional methylation at (**A**) CpG 7, 8 *PRTN3* promoter and (**B**) CpG 38 *MPO* CGI/exons 5-6. Mean longitudinal methylation change from disease activity to remission at (**C**) CpG 7, 8 *PRTN3* promoter: PR3-ANCA patients 3.85%, MPO-ANCA patients 5.57% and (**D**) CpG 38 *MPO* CGI/exons 5-6: PR3-ANCA patients 2.11%, MPO-ANCA patients 5.95%. For longitudinal graphs, p-values shown are as different from zero where p<0.025 is significant after accounting for multiple testing, bars are mean and standard deviation.



Supplemental Figure 8. Amplicon locations within *ELANE* and *LTF*. (**A**) Amplicon shown covering part of a CGI and exon 2 within the *ELANE*. (**B**) Amplicon shown covering a CGI and exon 1 within the *LTF*. Gene is shown in black, amplicon in blue, CGIs in green.

Sample	Age	Sex	Race	mRNA Expression		
				PRTN3	***MPO***	***DNMT1***
1	47	M	W	NA	NA	NA
2	57	M	W	16.05	105.72	1.22
3	52	M	W	NA	NA	NA
4	66	F	A	NA	NA	NA
5	52	F	W	NA	NA	NA
6	22	F	W	2.09	33.12	1.84
7	56	F	W	28.29	66.92	0.75
8	51	F	W	NA	NA	NA
9	59	F	W	NA	NA	NA
10	69	M	W	19.56	66.98	0.84
11	67	M	W	1.85	38.93	1.21
12	65	M	W	51.72	102.3	0.81
13	51	F	W	28.64	29.89	1.18
14	59	F	B	9.69	33.14	0.71
15	58	F	W	NA	NA	NA
16	57	F	W	5.56	38.14	0.97
17	57	F	W	14.79	77.65	0.9
18	54	M	W	45.4	118.73	1.49
19	22	M	A	NA	NA	NA
20	22	M	W	8.07	25.14	0.79
21	58	F	W	11.29	42.73	0.87
22	26	M	B	2.46	25.03	1.03
23	22	M	A	NA	NA	NA
24	58	F	W	26.67	24.77	0.7
25	56	F	W	1.81	28.46	0.86
26	77	M	W	15.06	34.61	0.84
27	69	M	W	13.74	58.12	0.56
28	56	M	W	10.71	35.89	NA
29	64	F	W	NA	NA	NA
30	56	M	W	33.21	175.38	0.76
31	47	M	W	50.53	156.82	0.92
32	57	F	W	NA	NA	0.85

Supplemental Table 1. Healthy individual demographics. Age, gender, race and mRNA expression of *PRTN3*, *MPO* and *DNMT1* for each of 32 healthy controls.

Patient	Sample	Diagnosis	Age	Sex	Race	Serotype	Disease Status *=new onset	BVAS	ANCA Titer		mRNA Expression			WBC Ct	PMN Ct	Therapy
									PR3	MPO	*PRTN3*	*MPO*	*DNMT1*	($x10^9$cells/L)		
1	1a	MPA	23	F	W	MPO	Active	18	2.2	47.6	4.90	70.31	NA	5.9	4	MMF
	1b		26				Remission	0	2	21.4	1.65	26.16	0.58	5.8	NA	MMF
	1c		29				Active	6	2.1	29.5	3.18	10.78	0.52	5.9	NA	None
	1d		29				Remission	2	NA	NA	4.00	35.03	0.39	5.6	3.8	MMF
2	2a	Lim	53	F	W	MPO	*Active	10	3.4	147.1	28.47	115.91	1.32	6.5	4.5	CYIV
	2b		55				Remission	0	4.5	72.6	12.75	65.72	0.66	NA	NA	AZA
3	3a	Lim	57	F	B	MPO	Active	12	2.7	85.8	NA	NA	NA	11.3	NA	MPD; RITUX
	3b		58				Remission	0	3.2	3.5	3.97	42.60	2.17	2.7	1.7	CS
	3c		60				Remission	0	3.6	139.2	3.62	19.85	0.46	NA	NA	None
4	4a	Lim	78	M	W	MPO	*Active	12	3.6	35.9	23.56	36.52	0.29	8.9	7.4	MPD
	4b		78				Remission	0	NA	NA	30.23	110.52	0.66	NA	NA	MMF
	4c		80				Remission	0	NA	NA	186.72	741.66	0.86	NA	NA	None
5	5a	EGPA	62	M	W	MPO	*Active	24	5.9	21.5	211.86	581.61	0.43	13.2	11.7	CS
	5b		66				Remission	0	3.1	5.9	NA	NA	NA	6.6	5.2	MMF; CS
6	6a	MPA	68	M	W	MPO	Remission	0	3.1	27.2	23.68	247.81	0.59	NA	NA	MMF
	6b		69				Active	3	2.1	53	110.45	633.26	1.1	6	NA	RITUX; MMF
7	7a	Lim	87	M	W	MPO	Remission	0	1.9	70.4	35.66	45.86	1.35	6.1	2.4	RITUX
	7b		88				Active	6	2.1	97.1	41.63	223.74	0.81	5.9	2.7	None
	7c		88				Remission	0	NA	NA	46.72	144.44	0.9	5.4	NA	RITUX
8	8a	MPA	58	M	B	MPO	*Active	22	3.6	36.6	12.22	83.60	0.35	11.3	10.1	MPD
	8b		58				Remission	0	NA	NA	378.77	2400.50	0.93	12.2	9.3	CYIV
9	9a	MPA	17	M	W	MPO	Active	6	NA	NA	336.62	2070.72	1.19	6.4	4.6	CS; CYIV; RITUX
	9b		17				Remission	0	NA	NA	11.97	143.00	1.39	4.9	2.7	RITUX; AZA

	9c		19				Remission	0	NA	NA	18.46	171.66	1.29	4.9	NA	RITUX; AZA
10	10a	MPA	46	M	W	MPO	Active	5	3	32.6	1005.43	670.70	0.48	7.3	6.7	CS; CYPO
	10b		47				Remission	0	2.2	4.6	82.56	202.39	0.78	NA	NA	None
11	11a	Lim	72	M	W	MPO	Active	6	1.9	72	577.54	1913.73	0.73	9.3	8.2	CS; CYIV
	11b		75				Remission	0	2.9	35.1	19.08	101.04	0.61	5.1	3.4	None
12	12a	MPA	59	F	W	MPO	*Active	8	1.6	34.4	151.86	631.38	NA	NA	NA	CS; CYPO
	12b		60				unclear	2	1.5	16.5	2.69	58.03	0.55	5.3	NA	MMF
	12c		63				Remission	0	2.5	21.2	3.52	82.41	0.36	NA	NA	None
13	13a	Lim	51	M	W	MPO	Active	6	3.4	60.6	18.47	89.13	0.5	9.8	7.5	MMF; CyA
	13b		56				Remission	0	13.3	76.2	42.07	50.62	0.52	NA	NA	None
14	14a	MPA	37	F	W	MPO	Active	0	2.7	20.1	742.25	2129.74	0.47	10.2	9.1	CS; CYIV
	14b		40				Remission	0	2.7	21.7	44.60	174.36	0.47	5.6	NA	MMF
15	15a	GPA	74	M	W	MPO	Active	3	1.6	24.6	43.55	68.94	NA	3.8	NA	MPD
	15b		75				Remission	0	NA	NA	22.55	96.26	0.61	6.2	3.9	MMF
16	16a	MPA	26	F	W	MPO	*Active	16	2.6	42.7	61.45	86.23	0.58	10.9	7.8	None
	16b		27				Remission	0	2	28	12.07	68.88	0.6	11.6	NA	None
17	17a	MPA	53	F	W	MPO	Active	10	3	119.3	26.16	94.92	0.29	18	15.8	MPD; CYIV
	17b		54				Remission	0	2.2	10.5	112.28	338.63	0.44	10.4	NA	CS; MPD; CYIV; RITUX
18	18a	MPA	57	M	B	MPO	*Active	20	3	140.1	252.54	366.86	0.25	15.4	NA	CS; RITUX; PLEX
	18b		57				Remission	0	NA	NA	33.33	68.49	0.84	NA	NA	CS
19	19a	GPA	59	F	W	MPO	*Active	3	NA	NA	740.67	2033.02	0.34	14	12.5	CS
	19b		60				Remission	0	1.9	2.9	134.41	243.99	0.55	5.1	NA	CS; CYIV
	19c		61				Remission	0	NA	NA	132.54	312.36	NA	9.1	5.3	RITUX
20	20a	Lim	60	F	B	MPO	Active	6	1.7	3.4	NA	NA	NA	9.6	6.5	RITUX
	20b		60				Remission	0	1.4	3.6	0.08	47.30	0.55	10.9	7.9	RITUX
21	21a	MPA	69	M	W	MPO	*Active	12	1.8	108	103.07	342.52	0.64	9.6	7	None
	21b		69				Active	16	0.7	64.9	19.91	86.63	0.85	3.8	2	CS; RITUX
	21c		69				Remission	0	NA	NA	183.38	626.70	0.58	10.4	7.9	CS; RITUX
22	22a	GPA	80	M	W	MPO	Active	6	2.8	45	12.83	150.77	0.6	10	NA	None

	22b		80				Remission	0	NA	NA	41.43	411.60	0.71	NA	NA	RITUX
23	23a	GPA	22	F	W	MPO	Active	3	1.7	9.4	31.68	115.42	0.6	5.2	3.4	CS; MMF; belumimab
	23b		23				Remission	0	1.3	11.6	22.34	41.05	0.34	6.9	5.6	CYIV; RITUX
24	24a	GPA	33	F	U	MPO	Active	12	4.3	57.9	10.25	74.86	0.36	6.6	NA	CS
	24b		34				Remission	0	3.7	2.8	0.07	36.96	0.65	5.3	3.7	None
25	25a	EGPA	51	M	W	MPO	*Active	24	2.7	85.6	2488.70	2171.77	0.51	18.1	NA	CS
	25b		52				Remission	0	2.4	6.9	38.33	137.39	0.87	5.4	2.9	AZA
26	26a	GPA	48	F	U	MPO	Active	6	2.4	15.9	1795.83	9560.15	0.47	11.7	9.6	CS; CYIV
	26b		48				Remission	1	6.1	21.2	48.85	832.22	0.64	5.7	3.5	CS; CYIV
27	27a	GPA	24	F	W	MPO	*Active	8	1.4	7	73.76	448.45	0.51	18.6	14.9	CS
	27b		25				Remission	0	1.4	2.1	2.89	43.01	0.62	11.5	8.7	CS
28	28a	MPA	72	M	W	MPO	Active	6	1.5	62.4	407.32	1199.96	NA	6.3	5.6	CS; MMF
	28b		73				Remission	0	NA	NA	23.98	123.94	0.62	NA	NA	MMF
29	29a	MPA	33	M	W	MPO	Active	8	NA	NA	55.13	317.00	0.57	NA	NA	None
30	30a	MPA	80	M	W	MPO	Active	8	NA	NA	674.09	213.60	0.32	NA	NA	CS; AZA
	30b		81				Remission	0	1.6	3.6	26.67	135.30	0.61	8	6	CYIV
31	31a	Lim	83	M	W	MPO	Active	15	1.7	51.5	176.18	588.15	0.42	8.8	NA	RITUX
32	32a	MPA	47	M	H	MPO	Remission	0	2.3	3.5	16.17	216.50	0.60	4.2	2.2	AZA
	32b		48				Remission	0	4.6	18.7	13.81	123.64	0.48	7	NA	None
	32c		49				Remission	0	2.6	17.5	23.58	290.17	0.65	8	NA	None
33	33a	Lim	51	M	W	MPO	Remission	1	NA	NA	163.38	305.40	0.67	6.6	4.4	AZA
	33b		52				Remission	0	1.5	35.7	133.98	187.97	0.75	7.8	NA	None
	33c		54				Remission	0	NA	NA	99.93	238.48	0.92	NA	NA	None
34	34a	MPA	21	F	W	MPO	Active	6	1	53	NA	NA	NA	6	3.2	None
	34b		25				Remission	0	2.4	86.9	25.17	87.33	1.28	5.7	3.6	MMF
	34c		33				Remission	0	2.1	51.5	NA	NA	NA	8.9	NA	None
	34d		38				Remission	0	NA	NA	21.23	91.73	0.78	NA	NA	None
35	35a	Lim	23	F	W	MPO	Remission	0	4.6	12.4	4.88	15.78	0.59	7.6	NA	None
	35b		25				Remission	0	2.2	12.4	9.09	35.53	0.44	NA	NA	None

36	36a	Lim	67	M	W	MPO	Remission	0	2.5	92.3	6.33	110.12	NA	NA	NA	None
37	37a	MPA	42	F	W	MPO	Remission	0	2.2	10.8	166.44	421.52	0.5	NA	NA	CS
38	38a	MPA	56	F	W	MPO	Remission	0	1.5	36	13.75	69.36	1.64	6.8	4.7	None
39	39a	GPA	51	F	W	MPO	Remission	0	1.3	4.8	NA	NA	NA	6.1	NA	None
40	40a	Lim	66	F	B	MPO	Remission	0	NA	NA	NA	NA	NA	6.2	NA	None
41	41a	MPA	55	F	A	PR3	Active	6	78.8	2.3	NA	NA	NA	6	NA	MMF
	41b		57				Remission	0	21.4	1.3	5.28	39.88	0.73	4.6	NA	MMF
	41c		59				Active	0	40	1	0.33	39.58	0.96	6.2	3.6	MMF
42	42a	GPA	47	M	W	PR3	Active	19	107.7	2.6	9.82	38.18	0.21	22.6	20.4	CYIV; CS; PLEX
	42b		49				Remission	0	NA	NA	30.34	120.19	0.54	9.3	6.4	CS
	42c		49				Remission	0	NA	NA	18.11	67.88	0.73	8.2	5.6	CS
43	43a	MPA	53	M	W	PR3	Remission	0	145	1.6	NA	NA	NA	4.7	3.6	CYIV; CS
	43b		54				Active	12	165	2.3	NA	NA	NA	6.4	NA	AZA
44	44a	MPA	74	F	W	PR3	Active	0	22.5	2.7	NA	NA	NA	2.3	1.8	CYIV; CS
	44b		79				Remission	0	114.8	3.4	48.75	179.32	0.87	7.2	4.6	AZA
	44c		83				Remission	0	NA	NA	20.43	32.43	1.35	6.3	NA	None
45	45a	GPA	34	M	B	PR3	*Active	13	136.2	3.1	34.91	61.88	0.48	19.5	NA	MPD; PLEX
	45b		41				Remission	0	40	3.5	9.97	26.05	NA	8.6	NA	MMF; CyA; CS
46	46a	GPA	50	F	B	PR3	*Active	21	104.8	3.4	683.67	2008.83	0.33	16	14.6	HD; MPD; PLEX
	46b		59				Remission	0	29.3	5.7	4.23	23.75	0.47	6.6	5.1	AZA
	46c		60				Remission	0	NA	NA	NA	NA	NA	7.2	4.9	None
47	47a	GPA	70	M	W	PR3	Active	0	123.7	3	32.81	62.24	NA	5.2	NA	RITUX
	47b		71				Remission	0	85.5	1.5	43.15	39.83	1.19	7.8	3	None
	47c		71				Remission	0	NA	NA	67.66	86.44	1.94	7.8	NA	RITUX
48	48a	MPA	64	M	W	PR3	Active	1	148.3	5	9.81	52.94	0.66	4.3	2.5	AZA
	48b		65				Remission	0	67.8	2.4	12.27	70.84	0.71	4.9	3	None
	48c		66				Active	1	161.7	3.5	0.08	45.86	0.69	NA	NA	None
	48d		67				Active	7	147.9	1.9	0.16	7.19	0.5	7.2	NA	CS; AZA
	48e		67				Remission	0	36.7	2.6	20.77	184.16	0.81	4.8	NA	CS; RITUX

49	49a	MPA	71	F	W	PR3	Active	2	NA	NA	55.84	899.21	NA	8.8	NA	CS; MMF
	49b		72				Remission	0	NA	NA	67.62	445.37	0.76	9.7	6.1	CS; MMF
50	50a	GPA	32	F	W	PR3	Remission	0	50.3	4	42.44	62.88	0.87	3.6	2.3	AZA
	50b		33				Active	6	69.9	5	17.08	22.33	1.01	NA	NA	AZA
51	51a	GPA	19	M	W	PR3	Remission	0	NA	NA	685.64	297.81	0.40	NA	NA	CS; AZA; CyA
	51b		20				Active	6	2.3	1.7	1849.11	2760.90	0.40	13.5	11.8	CS; AZA
52	52a	MPA	53	F	W	PR3	Active	3	108.1	2.4	4.88	27.08	0.78	7.6	5.1	MMF
	52b		54				Remission	0	50.6	2.4	5.71	81.44	0.42	6.5	4.6	MMF; RITUX
53	53a	GPA	57	F	W	PR3	Active	9	102.4	3.2	76.19	481.00	0.29	9.7	8.9	CS
	53b		58				Remission	0	111.4	1.4	17.16	63.65	1.57	6.6	4.2	None
54	54a	GPA	50	M	W	PR3	Active	3	16.1	2.5	26.03	196.25	0.43	9.2	8.1	CS; CYIV; RITUX; MMF
	54b		52				Remission	0	12.8	1.1	11.28	29.81	0.78	6.5	4.6	RITUX; AZA
	54c		53				Active	4	11.5	0.9	5.42	75.76	0.58	6.3	4.7	None
	54d		54				Remission	0	5	1.5	6.61	56.19	0.72	NA	NA	RITUX
55	55a	MPA	69	M	W	PR3	Remission	0	83.7	2.7	13.63	78.93	0.82	6.1	4.5	MMF
	55b		72				Active	7	124.6	2.3	30.13	373.99	0.6	5.7	3.7	CS; MMF
	55c		73				Remission	0	NA	NA	55.99	175.44	0.44	NA	NA	RITUX
56	56a	GPA	56	M	W	PR3	Remission	0	20.4	2.2	11.81	69.28	NA	4.4	2.5	RITUX; MMF
	56b		57				Active	6	59.6	2	6.20	61.76	0.58	5.2	3	MMF
	56c		59				Active	6	84.1	1.1	5.43	60.07	0.72	NA	NA	MMF
	56d		59				Remission	0	27.8	1.9	4.92	52.04	1.06	5.6	3.5	RITUX
57	57a	MPA	58	F	W	PR3	*Active	8	157.3	1.9	7.47	131.35	0.55	13.6	NA	CS
	57b		60				Remission	0	28	1.5	0.36	77.42	0.71	5	2.8	RITUX
58	58a	MPA	65	M	W	PR3	*Active	18	149.9	1.4	329.28	471.68	0.43	1.4	NA	MPD; PLEX
	58b		66				Remission	0	26	1.2	14.97	165.41	0.73	8.6	5.9	RITUX
	58c		67				Active	1	27.7	1.7	82.16	193.62	0.46	8.6	5.6	None
	58d		67				Remission	0	7.6	1.9	16.96	83.91	0.67	6.8	4.3	RITUX
59	59a	GPA	36	M	W	PR3	Active	5	92.1	2.4	568.03	2001.14	0.44	8.8	7.8	MPD

	59b		38				Remission	0	33	1.6	27.39	102.28	0.62	7	4.7	None
	59c		39				Remission	0	15.5	1.4	9.02	92.43	0.61	11.2	8.9	None
60	60a	MPA	29	F	W	PR3	Active	12	121.4	1.5	35.65	79.95	0.67	10.8	NA	CYIV
	60b		29				Remission	0	NA	NA	8.38	34.27	0.52	6.1	4.5	AZA
	60c		30				Remission	0	104.5	1.9	4.43	53.07	0.91	3.8	NA	AZA
61	61a	MPA	45	F	B	PR3	Active	4	NA	NA	14.53	176.10	NA	NA	NA	CS; MTX
	61b		45				Active	0	92.9	2.1	4.43	33.32	1.04	9.6	7.5	CS; RITUX
	61c		47				Remission	0	109.9	1.9	2.49	40.21	0.48	7.6	6	RITUX
62	62a	GPA	37	M	W	PR3	Active	0	70.2	2.2	30.66	92.71	0.57	NA	NA	None
	62b		38				Remission	0	47.6	1.5	13.34	154.49	0.71	8.3	5.7	None
63	63a	GPA	73	F	W	PR3	Active	0	3.3	1.5	90.61	203.09	0.69	5.8	NA	CS; CYPO
	63b		74				Remission	0	2.6	4.6	6.91	43.46	1.22	6.7	4.7	AZA
64	64a	GPA	51	M	W	PR3	*Active	7	NA	NA	2207.36	5354.39	0.45	26.6	NA	CS
	64b		52				Remission	0	NA	NA	NA	NA	NA	11.3	6.9	CS; RITUX
65	65a	GPA	76	M	W	PR3	Active	22	200	1.6	1185.90	2459.09	0.32	11.4	NA	MPD; PLEX
	65b		76				Remission	0	114.7	1.1	1494.68	2642.21	0.43	10.7	9.6	CS; CYIV; RITUX
	65c		77				Remission	0	124.1	1.4	52.12	51.60	0.54	5.9	3.4	None
66	66a	GPA	82	F	W	PR3	Active	19	130	1.4	NA	NA	NA	9.2	8.3	CS; MMF
	66b		82				Remission	0	87.4	1.3	0.20	10.71	0.68	5.2	3.6	CS; RITUX
67	67a	GPA	60	M	W	PR3	*Active	13	79.1	1.4	44.78	108.07	0.39	7.3	NA	CYPO
	67b		60				Remission	0	NA	NA	152.85	593.24	0.4	9.4	8	CS; RITUX
68	68a	MPA	69	M	W	PR3	Active	17	49	1.7	534.11	1705.02	0.44	11.4	9	CS; CYPO
	68b		71				Remission	0	22	2.6	9.03	87.86	1.03	7.5	NA	None
69	69a	GPA	55	M	W	PR3	Active	4	116.9	5.9	14.85	28.68	0.18	15	13.9	CS; RITUX
	69b		58				Remission	0	128.9	5.3	3.39	22.28	0.85	8.4	4.9	None
70	70a	GPA	56	F	W	PR3	*Active	21	99	1.8	1615.41	2695.97	0.28	21.8	19.5	CS
	70b		58				Remission	0	126.8	1.7	108.51	158.83	0.56	7.4	5.2	None
71	71a	MPA	79	M	O	PR3	*Active	16	153.4	5.7	19.85	41.30	0.16	5.7	NA	MPD
	71b		81				Remission	0	100.8	3.8	3.31	14.24	0.38	2.9	2.3	CS; AZA

72	72a	GPA	70	F	W	PR3	*Active	17	145	1.7	27.77	80.64	0.14	14.9	NA	CS; CYIV
	72b		70				Remission	0	99	0.8	240.05	739.77	0.33	12.5	11.4	CS; RITUX
73	73a	GPA	46	M	W	PR3	Remission	0	NA	NA	46.90	106.89	0.3	10.8	9.3	CS; RITUX
74	74a	GPA	61	M	W	PR3	Active	14	42.5	1.5	46.47	321.69	0.68	6.8	4.7	CS
75	75a	GPA	50	F	W	PR3	Active	2	4.1	1.2	9.65	83.23	0.68	6.4	4.7	MMF
76	76a	GPA	32	M	W	PR3	*Active	7	143.4	6.4	54.97	68.96	0.75	NA	NA	None
77	77a	MPA	33	F	W	PR3	Remission	0	95.3	2.1	17.07	114.31	1.76	8.4	NA	None
	77b		34				Remission	0	33.2	1.6	118.40	494.86	0.7	11	7.3	None
78	78a	MPA	24	F	W	PR3	Remission	0	1.2	2.9	NA	NA	NA	NA	NA	CYPO
	78b		30				Remission	0	2.8	1.1	4.84	40.92	0.58	7.3	NA	None
79	79a	GPA	71	M	W	PR3	Remission	0	1.2	2.9	NA	NA	0.91	8.4	5.1	None
	79b		74				Remission	0	2.7	3.1	34.68	162.00	0.71	NA	NA	None
	79c		77				Remission	0	14.6	1.8	16.30	122.37	0.5	NA	NA	None
80	80a	GPA	76	M	B	PR3	Remission	0	NA	NA	135.61	234.91	1	6.3	4.5	None
	80b		77				Remission	0	3.1	1.9	77.39	59.55	0.72	9.1	6.2	None
81	81a	GPA	67	M	W	PR3	Remission	0	36.3	1.7	14.32	77.42	0.87	7.2	NA	None
82	82a	GPA	40	M	O	PR3	Remission	0	200	1.6	16.61	240.41	0.98	10	4.8	None

PR3, proteinase 3; MPO, myeloperoxidase; MPA, microscopic polyangiitis; GPA, granulomatosis with polyangiitis; EGPA, eosinophilic granulomatosis with polyangiitis; Lim, renal limited vasculitis; NA, not available; W, white; B, African-American; U, unknown; H, Hispanic; A, Asian; O, other; BVAS; Birmingham Vasculitis Activity Score; WBC, white blood cells; PMN, polymorphonuclear cells.

Therapy: MMF, mycophenolate mofetil; CyA, cyclosporine A; HD, hemodialysis; AZA, azathioprine; PLEX, plasmapheresis; CS, corticosteroids; CYIV, intravenous cyclophosphamide; CYPO, oral cyclophosphamide; MPD, methylprednisolone; MTX, methotrexate; RITUX, rituximab.

Supplemental Table 2. Complete demographic and clinical data for patient cohort. Eighty-two patients and 184 unique samples collected alongside clinical data and mRNA expression for *PRTN3*, *MPO* and *DNMT1*.

Gene	Primer
PRTN3 (Taqman)	Forward 5'-TGT CAC CGT GGT CAC CTT CTT-3' Reverse 5'-CCC CAG ATC ACG AAG GAG TCT AT-3' Probe FAM-TTG CAC TTT CGT CCC TCG CCG-TAMRA
MPO (Taqman)	Forward 5'-CCA GGA AGC CCG GAA GAT-3' Reverse 5'-CGG AAG GCA TTG GTG AAG A-3' Probe FAM-TGC CCA CGT ACC GTT CCT ACA ATG ACT C-TAMRA
DNMT1 (Taqman)	Thermo Fisher cat. #4331182
PRTN3 (amplicon 5, methylation)	Forward 5'-aggaagagagTTAAAGGGGGAAGAAAATTTTTAGA-3' Reverse 5'-cagtaatacgactcactatagggagaaggctATTACCCAATACCCAAACTAAATCC-3'
PRTN3 (amplicon 20, methylation)	Forward 5'-aggaagagagAAGTGTTGTTGGGTGGGTTTTT-3' Reverse 5'-cagtaatacgactcactatagggagaaggctAACACCTTAATCCACCCCAACTT-3'
PRTN3 (amplicon 22, methylation)	Forward 5'- aggaagagagTTGTGATGGTATTATTTAAGGAATAGATTT-3' Reverse 5'-cagtaatacgactcactatagggagaaggctCCTCCCCTCCCTATATAAAAAAAAC-3'
MPO (amplicon 11, methylation)	Forward 5'- aggaagagagGTTGGGGGTGGTTGTAGGAAT -3' Reverse 5'-cagtaatacgactcactatagggagaaggctCAACTAACCCCATTACATAAACATAAA-3'
MPO (Amplicon 12, methylation)	Forward 5'-aggaagagagAAGTTGATTTGTTAGGAAGTAGGGG-3' Reverse 5'- cagtaatacgactcactatagggagaaggctAACCTCTCTCTATACCTCAAATCCC-3'
LTF (amplicon 3, methylation)	Forward 5'-GGA GTT TTG TTT TGT TTT AGG GTT T-3' Reverse 5'-CTC CTA TTC CTC CCC ATA TAA AAA A-3'
ELANE (amplicon 5, methylation	Forward 5'-TGG TGG GGG ATT TAG AGG TT-3' Reverse 5'-AAC TAC AAA AAC ACC ATA AAA AAC CA-3'

Supplemental Table 3. Primers used for Taqman mRNA expression studies and DNA methylation studies.

Gene_Amplicon	Chromosome	Browser position	
PRTN3_005	19	840498	840945
PRTN3_022	19	847822	848215
PRTN3_020	19	843571	843964
MPO_11	17	56356480	56356874
MPO_12	17	56355180	56355526
LTF_003	3	46506126	46506547
ELA_005	19	852792	852954

Supplemental Table 4. Gene coordinates for each of the seven loci studied.