

## Article

# Association Between *ADAM33* Single-Nucleotide Polymorphisms and Treatment Response to Inhaled Corticosteroids and a Long-Acting Beta-Agonist in Asthma: Supplementary Material

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**Table S1.** Unextended primer (UEP) sequences used for massARRAY analysis along with the extended (E1/E2) alleles and mass in Daltons used for genotyping of *ADAM33* variants in controls and asthma patients.

Sl No.	SNP rs ID	UEP Sequence	Allele (E1/E2)	Mass of UEP/E1/E2
1	rs2280091	GGGCGGCGTTCACCCCA	G/A	5172.4/5419.5/5499.5
2	rs2787094	GTCCACACTCCCCTG	G/C	4448.9/4696.1/4736.1
3	rs3918396	GGCCATGCTCCTCAGC	A/G	5107.3/5378.5/5394.5
4	rs677044	CCAGCCCTCAGGAACCTTCTA	G/A	6021.9/6293.1/6309.1
5	rs2853209	TGGCCTCCCAGTCAAGCG	T/A	5764.7/6036/6091.8

6 rs3918392 GCTCACCTGGAAAGGA A/G 6176/6447.2/6463.2

**Table S2.** Hardy-Weinberg Equilibrium (HWE) test, genotype and Minor Allele Frequency (MAF) of ADAM33 in healthy controls (C) and asthma patients (P).

SNP	Sample Size		Minor allele frequency		Genotype	C	P	OR (95 % CI)	p-value	HWE p-value	
	C	P	C	P						C	P
rs2280091	486	503	G-0.16	G-0.17	AA	344	353	Reference		0.017	0.041
					GA	121	129	1.04(0.78-1.39)	0.795		
					GG	21	21	0.97(0.52-1.81)	0.935		
					A	809	835	Reference			
rs2787094	486	503	C-0.24	C-0.27	G	163	171	1.02(0.80-1.28)	0.891	0.235	0.781
					GG	270	269	Reference			
					GC	191	196	1.03(0.79-1.33)	0.824		
					CC	25	38	1.52(0.89-2.59)	0.119		
rs3918396	486	503	A-0.10	A-0.12	G	731	734	Reference		0.568	0.907
					C	241	272	1.12(0.92-1.37)	0.255		
					GG	387	389	Reference			
					GA	92	107	1.15(0.85-1.58)	0.359		
rs677044	486	503	G-0.23	G-0.23	AA	7	7	0.99(0.34-2.86)	0.992	0.726	0.588
					G	866	885	Reference			
					A	106	121	1.12(0.84-1.47)	0.433		
					AA	345	327	Reference			
rs2853209	486	503	T-0.42	T-0.37	AG	121	155	1.05(0.78-1.42)	0.71	0.017	0.761
					GG	20	21	0.86(0.45-1.64)	0.66		
					A	811	809	Reference			
					G	161	197	0.99(0.78-1.26)	0.978		
rs3918392	486	503	G-0.08	G-0.08	AA	265	247	Reference		0.84	0.562
					TA	147	195	0.98(0.71-1.34)	0.915		
					TT	74	61	0.61(0.40-0.92)	0.018		
					A	677	689	Reference			
rs3918392	486	503	G-0.08	G-0.08	T	295	317	0.80(0.65-0.98)	0.035	0.84	0.562
					AA	432	435	Reference			
					AG	52	64	1.0(0.67-1.50)	0.967		

GG	2	4	1.63(0.29-9.0)	0.57
A	916	934	Reference	
G	56	72	1.05(0.73-1.51)	0.783

**Table S3.** Genotype and allele frequency distribution of *ADAM33* SNPs among controls (C) and patients with Severe (Se), Moderate (Mo) and Mild (Mi) asthma patients.

SNP	Genotype	C	Patients allele count			OR (95 % CI)			p-value		
			Se	Mo	Mi	Se/C	Mo/C	Mi/C	Se/C	Mo/C	Mi/C
<b>rs2280091</b>	AA	344	95	153	105	1(Reference)	1(Reference)	1(Reference)	–	–	–
	GA	121	37	51	41	1.11(0.71-1.71)	0.95(0.64-1.38)	1.11(0.73-1.68)	0.644	0.781	0.622
	GG	21	4	7	10	0.69(0.23-2.05)	0.75(0.31-1.8)	1.56(0.71-3.41)	0.505	0.518	0.266
	A	809	227	357	251	1(Reference)	1(Reference)	1(Reference)	–	–	–
	G	163	45	65	61	0.98(0.68-1.41)	0.90(0.66-1.23)	1.21(0.87-1.67)	0.93	0.526	0.26
<b>rs2787094</b>	GG	270	76	110	83	1(Reference)	1(Reference)	1(Reference)	–	–	–
	GC	191	47	85	64	0.87(0.58-1.31)	1.09(0.78-1.53)	1.09(0.74-1.59)	0.518	0.609	0.65
	CC	25	13	16	9	1.84(0.90-3.78)	1.57(0.81-3.06)	1.17(0.52-2.61)	0.093	0.183	0.7
	G	731	199	305	230	1(Reference)	1(Reference)	1(Reference)	–	–	–
	C	241	73	117	82	1.11(0.82-1.51)	1.16(0.9-1.50)	1.08(0.80-1.44)	0.492	0.25	0.6
<b>rs3918396</b>	GG	387	104	168	117	1(Reference)	1(Reference)	1(Reference)	–	–	–
	AG	92	29	40	38	1.17(0.73-1.87)	1.0(0.66-1.51)	1.37(0.89-2.10)	0.506	0.994	0.156
	AA	7	3	3	1	1.59(0.41-6.27)	0.98(0.25-3.86)	0.47(0.05-3.89)	0.504	0.985	0.485
	G	866	237	376	272	1(Reference)	1(Reference)	1(Reference)	–	–	–
	A	106	35	46	40	1.21(0.80-1.81)	0.99(0.69-1.44)	1.20(0.81-1.77)	0.367	0.997	0.354
<b>rs677044</b>	AA	345	92	140	95	1(Reference)	1(Reference)	1(Reference)	–	–	–
	AG	121	38	63	54	0.85(0.54-1.33)	1.01(0.68-1.48)	1.37(0.89-2.09)	0.479	0.973	0.143
	GG	20	6	8	7	0.81(0.31-2.09)	0.77(0.33-1.82)	1.08(0.44-2.65)	0.67	0.554	0.873
	A	811	222	3433	244	1(Reference)	1(Reference)	1(Reference)	–	–	–
	G	161	50	79	68	1.08(0.44-2.66)	0.95(0.69-1.29)	1.19(0.86-1.66)	0.873	0.73	0.285
<b>rs2853209</b>	AA	265	63	112	72	1(Reference)	1(Reference)	1(Reference)	–	–	–
	TA	147	53	82	60	0.96(0.61-1.53)	0.89(0.60-1.32)	1.17(0.74-1.85)	0.877	0.564	0.508
	TT	74	20	17	24	0.72(0.39-1.32)	0.37(0.20-0.67)	0.93(0.52-1.65)	0.288	0.001	0.799
	A	677	179	306	204	1(Reference)	1(Reference)	1(Reference)	–	–	–
	T	295	93	116	108	0.85(0.63-1.15)	0.65(0.50-0.86)	0.98(0.74-1.32)	0.305	0.002	0.921
<b>rs3918392</b>	AA	432	122	179	134	1(Reference)	1(Reference)	1(Reference)	–	–	–
	AG	52	13	31	20	0.69(0.36-1.32)	1.20(0.74-1.96)	1.06(0.61-1.86)	0.262	0.462	0.833
	GG	2	1	1	2	1.38(0.12-15.38)	1.01(0.09-11.19)	2.76(0.38-19.86)	0.793	0.995	0.313
	A	916	257	389	288	1(Reference)	1(Reference)	1(Reference)	–	–	–

G 56 15 33 24 0.76(0.42-1.37) 1.17(0.74-1.83) 1.18(0.71-1.94) 0.359 0.5 0.523

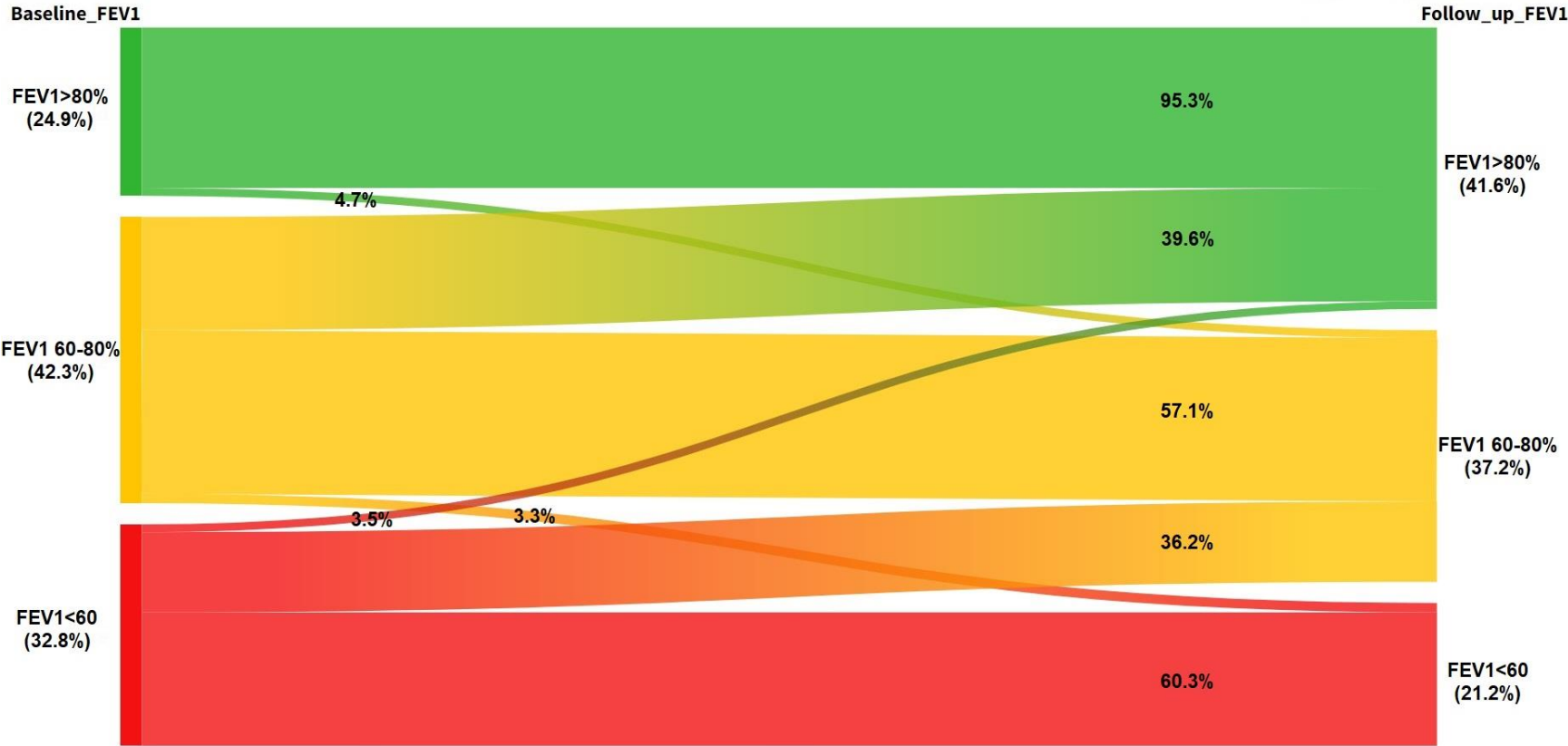
**Table S4.** Haplotype analysis of six SNPs of *ADAM33*.

Locus 1	Locus 2	D'	LOD	r <sup>2</sup>	CI-low	CI-hi	Dist	T-int
rs2787094	rs677044	0.115	1.92	0.011	0.04	0.19	270	90.93
rs2787094	rs2280091	0.944	17.26	0.066	0.82	0.99	1073	-
rs2787094	rs2853209	0.223	2.08	0.012	0.09	0.34	2311	-
rs2787094	rs3918396	0.808	43.53	0.239	0.73	0.87	2604	-
rs2787094	rs3918392	0.763	26.14	0.147	0.66	0.84	6058	-
rs677044	rs2280091	0.923	12.14	0.053	0.76	0.98	803	170.85
rs677044	rs2853209	0.366	10.96	0.061	0.27	0.45	2041	-
rs677044	rs3918396	1	8.07	0.04	0.77	1	2334	-
rs677044	rs3918392	0.952	50.67	0.271	0.88	0.99	5788	-
rs2280091	rs2853209	0.919	60.88	0.26	0.86	0.96	1238	215.41
rs2280091	rs3918396	1	7.35	0.027	0.77	1	1531	-
rs2280091	rs3918392	1	5.73	0.019	0.72	1	4985	-
rs2853209	rs3918396	1	23.15	0.088	0.92	1	293	178.95
rs2853209	rs3918392	0.964	14.31	0.056	0.83	1	3747	-
rs3918396	rs3918392	0.882	1.24	0.009	0.22	0.99	3454	98.09

[D prime (D') between two loci, Log of likelihood odds ratio (LOD), Correlation coefficient between two loci (r<sup>2</sup>), 95% confidence interval lower and upper bound on D' (CI-low and CO-hi), Distance between two loci (Dist) and statistic used by HapMap project in haploview software to measure the completeness of information represented by a set of markers in a region (T-int) are represented]

**Table S5.** Details of significantly associated haplotype SNPs of *ADAM33* among controls and asthma patients under study population.

SNPs	Block	Haplotype	Case-Control frequency	Chi Square	Odds ratio	95% Confidence Interval
rs2853209, rs3918396	AG	0.484	0.505, 0.458	3.337	0.50	0.46-0.55
	TG	0.399	0.376, 0.429	4.469	0.38	0.33-0.42
	AA	0.117	0.120, 0.113	0.146	0.12	0.09-0.15



**Figure S1.** Alluvial chart depicting the changes in FEV<sub>1</sub> of asthma patients after three months of treatment. FEV<sub>1</sub>: Forced expiratory volume in one minute.