

ALLERGY, GENETICS

LOSS OF IL33 -/- PROTECTS AGAINST ALLERGY

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A new paper in [Nat Comm](#) shows the power of natural human gene knockouts. Maybe the finding [is not really novel](#) but it finally proves the candidate genes - the most important asthma/allergy paper in the last 2 years!

Outcome	Gene	pLOF variant	Location	EA	RA	AA change	Freq (%)	Beta	SE	P-value	Novel?	MHC locus?
Asthma	FLG	rs61816761	1:152285861	A	G	p.Arg501Ter	1.51	0.21	0.03	1.51×10^{-15}	Yes	No
Asthma	HLA-DQB1	rs28688207	6:32628660	C	T	Splice Acceptor c.773-1A>G	3.14	-0.17	0.02	3.11×10^{-15}	Yes	Yes
Asthma	IL33	rs146597587	9:6255967	C	G	Splice Acceptor c.487-1G>C	0.44	-0.54	0.06	7.79×10^{-17}	No ¹⁵	No

IL33, FLG, HLA-DQB1

Supplementary Table 3. Common ($\geq 5\%$ frequency) loss of function variants significantly associated with traits and disease in UK Biobank.

Outcome	Gene	Variant	Location	EA	RA	Consequence	Frequency (% European)	Beta	SE	P-value	Novel?	MHC Locus?
Asthma	GSDMB	rs11078928	17:38064469	C	T	Splice Acceptor (c.662-2A>G)	46	-0.10	0.007	6.66×10^{-30}	No ¹	No
Asthma	BTN3A2	rs71557335	6:26368279	A	G	Splice Donor (c.-6+1G>A)	13	0.06	0.010	1.67×10^{-8}	Yes	Yes
Asthma	CCHCR1	rs72856718	6:31125257	A	C	p.Glu41Ter	7	-0.13	0.015	2.06×10^{-18}	Yes	Yes

GSDMB, BTN3A2, CCHCR1

This is even a nice addition to the most recent review of [primary atopic disorders](#) although IL33 is only depicted there in Fig 1.