ALLERGY, GENETICS

LOSS OF IL33 -/- PROTECTS AGAINST ALLERGY

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A new paper in <u>Nat Comm</u> shows the power of natural human gene knockouts. Maybe the finding <u>is not really novel</u> 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	Α	G	p.Arg501Ter	1.51	0.21	0.03	1.51 × 10 ⁻¹⁵	Yes	No
Asthma	HLA- DQB1	rs28688207	6:32628660	С	Т	Splice Acceptor c.773-1A > G	3.14	-0.17	0.02	3.11× 10 ⁻¹⁵	Yes	Yes
Asthma	IL33	rs146597587	9:6255967	С	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 (≥5% frequency) loss of function variants significantly associated with traits and disease in UK

Daniel Marie											MHC Locus?	
Outcome	Gene	Variant	Location	EA	RA	Consequence	(%, European)	Beta	SE	P-value	Novel?	MHC Locus?
Asthma	GSDMB	rs11078928	17:38064469	С	т	Splice Acceptor (c.662-2A>G)	46	-0.10	0.007	6.66*10 ⁻⁵⁰	No	No
Asthma	BTN3A2	rs71557335	6:26368279	A	G	Splice Donor (c6+1G>A)	13	0.06	0.010	1.67*10*	Yes	Yes
Asthma	CCHCRI	rs72856718	6:31125257	A	С	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 <u>primary atopic disorders</u> although IL33 is only depicted there in Fig 1.

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