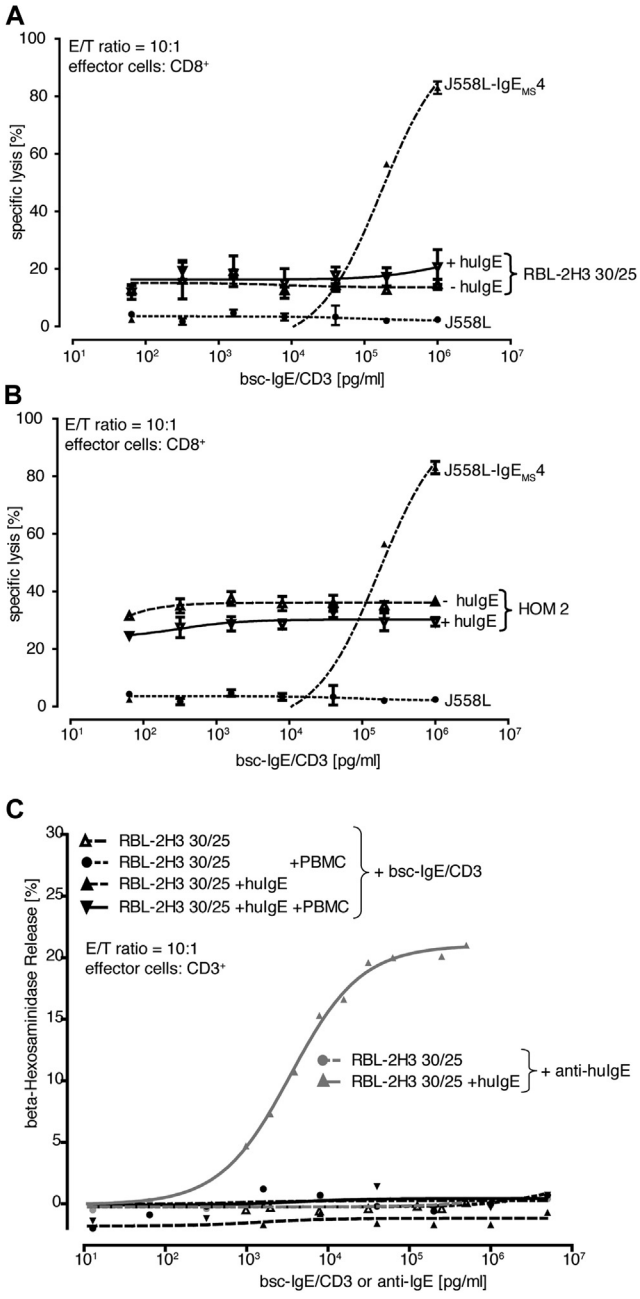

FIG 2. **A** and **B,** Chromium 51 release assays were performed with RBL-2H3 30/25 cells (Fig 2, *A*), which were loaded with soluble human IgE through FcεRI, or HOM2 cells (Fig 2, *B*), which were loaded with human IgE through the low-affinity FcεRII (CD23), to determine possible bystander cytotoxic activity against cells carrying receptor-bound human IgE. **C,** Release of β-hexosaminidase from RBL-2H3 30/25 cells was measured to determine potential degranulation. IgE-loaded RBL-2H3 30/25 cells were coincubated with purified T cells at an effector/target ratio *(E/T ratio)* of 10:1 and different concentrations of the bsc-IgE/CD3 antibody. An anti-human IgE mAb was added to the RBL-2H3 30/25 cells, either loaded or unloaded with soluble human IgE as controls. *Error bars* indicate SEMs.

Thus far, the various experimental data cited above indicate that IgE$^+$ B lymphocytes are indeed the essential source of IgE. With IgE-mediated diseases having reached almost epidemic dimensions and exposure to more common parasites being greatly reduced in industrialized societies, an impaired IgE response might be justified in patients with severe allergic conditions.

In summary, the effective elimination of membrane-bound IgE$^+$ target cells by passively engaged T lymphocytes without inducing significant mast cell degranulation and the remarkable insensitivity to soluble IgE supports this bsc-IgE/CD3 antibody approach as a novel treatment for IgE-mediated diseases.

We thank Lother Vogel for providing both the transfected and untransfected rat RBL mast cell line and Rudolf Wank for providing the HOM2 cell line. We also thank Eugen Kopp for technical assistance. Finally, we thank Beda M. Stadler for providing the anti-IgE hybridoma and for fruitful discussions.

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Supported by grants from Deutsche Forschungsgemeinschaft, Bonn, Germany, SFB 217 and SFB 456, and the Jacqueline Seroussi Foundation, Tel Aviv, Israel. The results of this work were part of a doctoral thesis submitted by Oktay Kirak, MD.
Disclosure of potential conflict of interest: G. Riethmüller has a board membership and stock/stock options from Micromet AG. O. Kirak declares no relevant conflicts of interest.

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Available online March 29, 2015.
http://dx.doi.org/10.1016/j.jaci.2015.02.017

A genome-wide association study reveals 2 new susceptibility loci for atopic dermatitis

To the Editor:

Association studies have identified a total of 23 European and Asian genetic susceptibility loci for atopic dermatitis (AD), although these explain only a small fraction of the estimated total heritability.[1,2]

To identify further risk loci for AD, we analyzed an imputed data set of more than 1.6 million genetic markers from 924 unrelated German tertiary care cases and 5506 population-based control subjects, followed by an additional replication study in a further 1383 AD cases and 1728 control subjects (see the Methods section

TABLE I. SNPs with a *P* value of 5×10^{-7} or less in the combined analysis

					GWAS				Replication				Combined	
					Cases: 870, control subjects: 5293				Cases: 1383, control subjects: 1728				Cases: 2253, control subjects: 7021	
dbSNP ID	Chromosome	Position	A1, A2	Locus	AF_ca	AF_co	P_{GWAS}	OR (95% CI)	AF_ca	AF_co	P_{Repl}	OR (95% OR)	P_{comb}	OR
rs12144049	1	150707534	C, T	*EDC*	0.369	0.279	1.87×10^{-8}	1.47 (1.31-1.64)	0.346	0.286	5.89×10^{-7}	1.33 (1.19-1.48)	1.02×10^{-16}	1.39
rs6720763	2	167700532	C, T	*XIRP2* (intron)	0.221	0.18	5.03×10^{-5}	1.31 (1.15-1.48)	0.211	0.174	2.65×10^{-4}	1.27 (1.12-1.44)	4.37×10^{-8}	1.29
rs3091307	5	132017035	A, G	*RAD50 /IL13/ KIF3A*	0.276	0.228	5.42×10^{-5}	1.3 (1.14-1.47)	0.283	0.247	1.69×10^{-3}	1.2 (1.07-1.35)	4.18×10^{-7}	1.24
rs10738626	9	22363457	C, T	*DMRTA1*	0.443	0.494	1.96×10^{-6}	0.77 (0.69-0.86)	0.474	0.517	7.95×10^{-4}	0.84 (0.76-0.93)	1.45×10^{-8}	0.81
rs1665050	15	57080897	A, G	*RNF111* (intron)	0.299	0.252	7.12×10^{-5}	1.27 (1.13-1.43)	0.296	0.255	3.48×10^{-4}	1.23 (1.1-1.38)	9.65×10^{-8}	1.25

SNPs are ranked by chromosomal position (National Center for Biotechnology Information build 36 [hg18]). ORs and 95% CIs for allele A1 are shown.
A1, Minor allele; *A2*, major allele; *AF_ca/AF_co*, allele frequencies in cases/control subjects; *OR*, odds ratio; $P_{GWAS}/P_{Repl}/P_{comb}$, *P* values in GWAS/replication/combined analysis.

TABLE II. Replication results of 23 established AD loci from GWASs

Locus	Reported gene(s)	Reported SNP(s)	References	Top SNP in region	Position	EA/RA	OR	*P* value
Loci identified through GWASs in European populations								
1q21.3	Tags *FLG* signal	rs3126085	1, 3, 6	rs12144049	152440176	C/T	1.47 (1.31-1.64)	1.87×10^{-8}
4q27	*IL2/IL21*	rs17389644	1	rs17454584	123497697	A/G	0.83 (0.77-0.89)	1.60×10^{-4}
5q31.1	*RAD50/IL13/IL4/KIF3A*	rs1295686, rs2897442, rs848	1, 7, 8	rs3091307	131995843	G/A	1.3 (1.14-1.47)	5.42×10^{-5}
6p21.33	*HLA-C/HLA-B/MICA*	rs9368677, rs2251396	2, 8	rs3021366	31324100	A/C	0.48 (0.33-0.78)	2.36×10^{-5}
6p21.33	*BAT1*	rs2844509	2	rs3130048	31510924	C/T	0.75 (0.68-0.82)	4.88×10^{-5}
6p21.33	*C6orf48*	rs9368699	2	rs9368699	31802541	C/T	0.51 (0.32-0.83)	2.55×10^{-4}
6p21.33	*TNXB/CREBL1*	rs12153855	2	rs12153855	32074804	C/T	0.77 (0.68-0.86)	5.55×10^{-3}
11p12	*PRR5L*	rs12295535	1	rs7945962	36344202	A/G	0.79 (0.74-0.84)	2.16×10^{-5}
11q13.1	*OVOL1*	rs479844	7, 8	rs479844	65551710	T/C	1.20 (1.25-1.14)	5.22×10^{-4}
11q13.5	*C11orf30/LRRC32*	rs7927894, rs11236809, rs7110818	1, 3, 8	rs2155219	76281593	T/G	0.81 (0.76-0.86)	1.74×10^{-4}
16p13.13	*CLEC16A/DEXI*	rs9923856, rs2041733	1, 8	rs2041733	11223454	C/G	1.23 (1.18-1.28)	1.31×10^{-4}
17q21.32-33	*ZNF652*	rs16948048	1	rs7209400	47440466	C/T	0.85 (0.80-0.90)	3.32×10^{-3}
19p13.2	*ACTL9*	rs2164983	7	rs12611036	8789381	A/G	1.12 (1.08-1.18)	5.23×10^{-2}
Loci identified through GWASs in Asian populations								
2q12.1	*IL18R1/IL18RAP/ SLC9A4*	rs13015714, rs759382	1, 8	rs13015714	102945378	T/G	1.23 (1.17-1.29)	6.55×10^{-4}
3p22.3	*GLB1*	rs7613051	8	rs13091893	33065339	G/C	1.13 (1.07-1.19)	3.43×10^{-2}
3q13.2	*CCDC80*	rs12634229	8	rs2129844	112376308	T/C	1.52 (1.37-1.67)	2.93×10^{-3}
5q22.1	*TMEM232/SLC25A46*	rs7701890	6	rs11241070	109858821	G/A	1.17 (1.08-1.26)	6.47×10^{-2}
6p21.32	*GPSM3*	rs176095	8	rs6941112	32158319	A,G	1.31 (1.25-1.37)	1.66×10^{-5}
7p22.2	*CARD11*	rs4722404	8	rs11983024	3081727	C/G	0.82 (0.76-0.88)	1.75×10^{-3}
10q21.2	*ZNF365*	rs10995251	8	rs7919747	64380336	T/C	0.71 (0.62-0.8)	3.28×10^{-4}
11p15.4	*OR10A3/NLRP10*	rs878860	8	rs10769866	7968359	G/C	0.88 (0.82-0.94)	1.89×10^{-2}
20q13.2	*CYP24A1/PFDN4*	rs16999165	8	rs6013912	52807221	C/T	0.80 (0.74-0.86)	8.61×10^{-5}
20q13.33	*TNFRSF6B*	rs909341	1, 6	rs16984240	62328742	T/C	0.79 (0.71-0.87)	6.83×10^{-3}

Previously reported genes and SNPs (dbSNP ID) are sorted by chromosomal position (locus). The top associated SNP from imputed GWAS data for each locus (±250 kb) is displayed.
EA/RA, Effect/reference allele; *OR*, odds ratio.

and Table E1 in this article's Online Repository at www.jacionline.org). Cases used for the screen had also been genotyped on Affymetrix 500K/5.0 platforms (Affymetrix, Santa Clara, Calif) and used for a previous genome-wide association study (GWAS).[3]

Genome-wide single nucleotide polymorphism (SNP) genotyping of patients was performed by an Affymetrix service facility (South San Francisco, Calif) using the Affymetrix Genome-Wide Human SNP Array 6.0 (1000k), according to the manufacturer's protocols. SNP genotype imputation was carried out with MACH version 1.10.16 and HapMap II CEU phased haplotypes release 22 (http://hapmap.ncbi.nlm.nih.gov/downloads/phasing/2007-08_rel22/phased/) as the reference data set to increase marker density. After stringent quality control filtering (see the Methods section in this article's Online