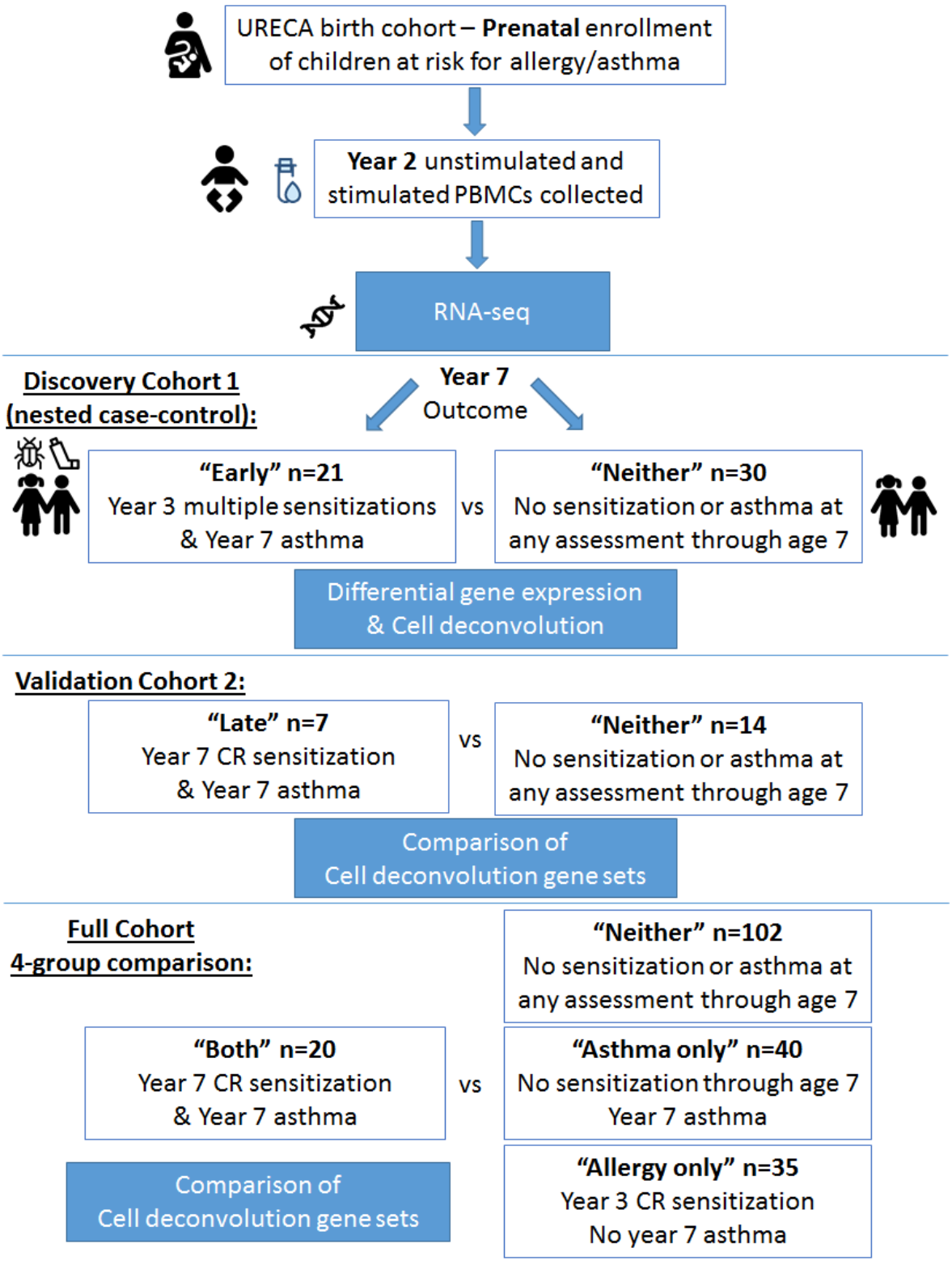
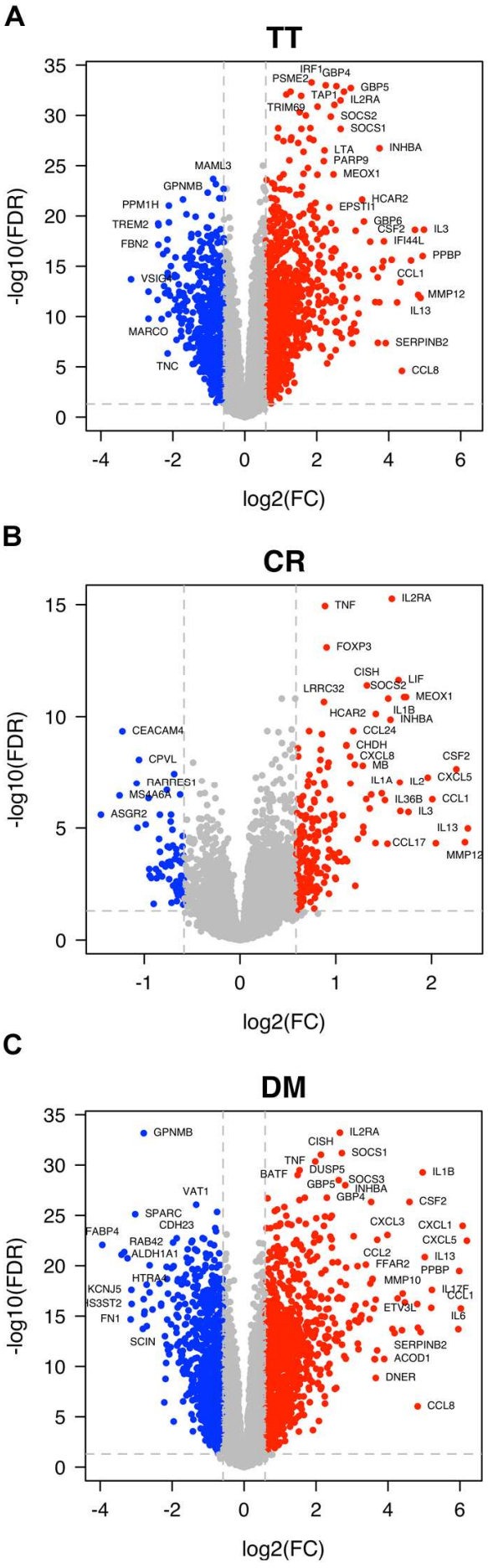
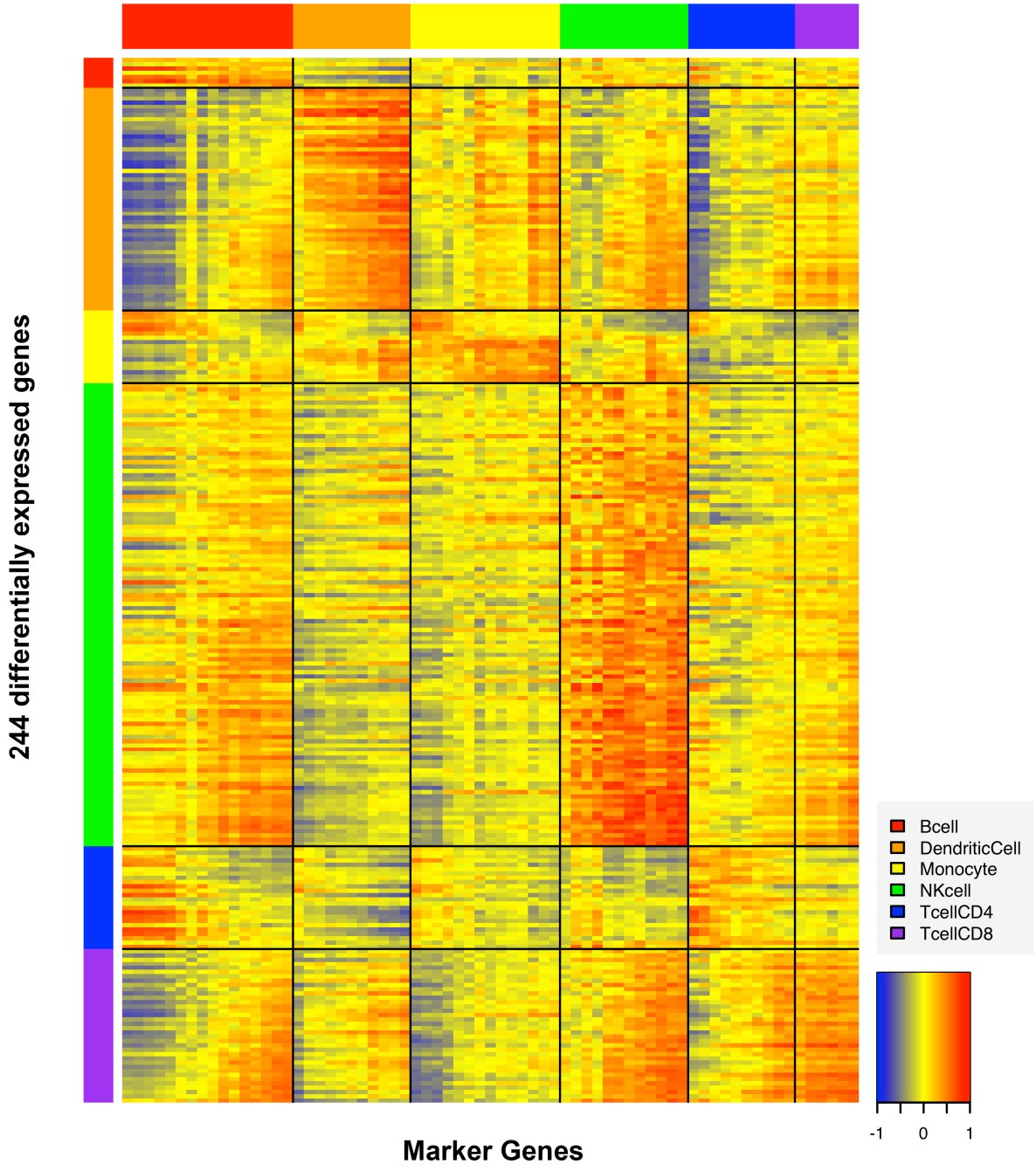
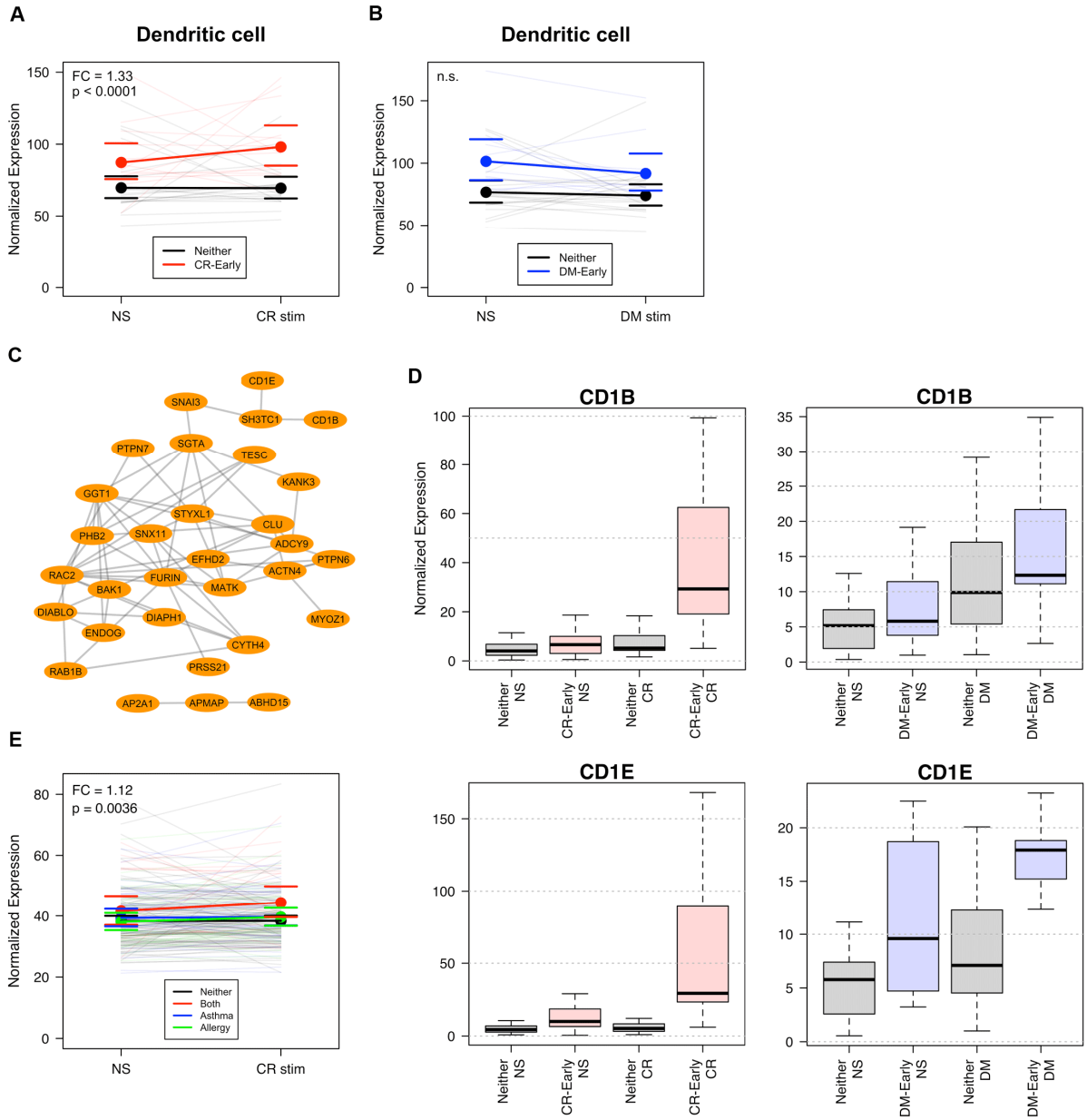

URECA birth cohort – **Prenatal** enrollment of children at risk for allergy/asthma
Year 2 unstimulated and stimulated PBMCs collected
RNA-seq
Discovery Cohort 1 (nested case-control):
Year 7 Outcome
"Early" n=21 Year 3 multiple sensitizations & Year 7 asthma
vs
"Neither" n=30 No sensitization or asthma at any assessment through age 7
Differential gene expression & Cell deconvolution
Validation Cohort 2:
"Late" n=7 Year 7 CR sensitization & Year 7 asthma
vs
"Neither" n=14 No sensitization or asthma at any assessment through age 7
Comparison of Cell deconvolution gene sets
Full Cohort 4-group comparison:
"Neither" n=102 No sensitization or asthma at any assessment through age 7
"Both" n=20 Year 7 CR sensitization & Year 7 asthma
vs
"Asthma only" n=40 No sensitization through age 7 Year 7 asthma
Comparison of Cell deconvolution gene sets
"Allergy only" n=35 Year 3 CR sensitization No year 7 asthma


A
TT
-log10(FDR)
log2(FC)
IRF1
GBP4
PSME2
GBP5
TAP1
IL2RA
TRIM69
SOCS2
SOCS1
LTA
INHBA
PARP9
MEOX1
MAML3
GPNMB
HCAR2
PPM1H
EPSTI1
GBP6
TREM2
CSF2
IL3
FBN2
IFI44L
PPBP
CCL1
VSIG4
MMP12
IL13
MARCO
SERPINB2
TNC
CCL8
B
CR
-log10(FDR)
log2(FC)
TNF
IL2RA
FOXP3
CISH
LIF
SOCS2
LRRC32
MEOX1
IL1B
HCAR2
INHBA
CEACAM4
CCL24
CHDH
CPVL
CXCL8
CSF2
MB
CXCL5
IL1A
IL2
MS4A6A
IL36B
CCL1
ASGR2
IL3
IL13
CCL17
MMP12
C
DM
-log10(FDR)
log2(FC)
GPNMB
CISH
IL2RA
SOCS1
TNF
DUSP5
IL1B
BATF
SOCS3
GBP5
INHBA
VAT1
GBP4
CSF2
SPARC
CXCL3
CXCL1
CDH23
FABP4
CXCL5
RAB42
CCL2
IL13
ALDH1A1
FFAR2
PPBP
HTRA4
MMP10
KCNJ5
IL17F
CCL1
ETV3L
FN1
IL6
SCIN
SERPINB2
ACOD1
DNER
CCL8


244 differentially expressed genes
Marker Genes
Bcell
DendriticCell
Monocyte
NKcell
TcellCD4
TcellCD8
-1
0
1


A
Dendritic cell
FC = 1.33
p < 0.0001
Normalized Expression
Neither
CR-Early
NS
CR stim
B
Dendritic cell
n.s.
Normalized Expression
Neither
DM-Early
NS
DM stim
C
CD1E
SNAI3
SH3TC1
CD1B
PTPN7
SGTA
TESC
KANK3
GGT1
STYXL1
CLU
PHB2
SNX11
ADCY9
EFHD2
PTPN6
RAC2
FURIN
ACTN4
BAK1
MATK
DIABLO
DIAPH1
MYOZ1
ENDOG
CYTH4
RAB1B
PRSS21
AP2A1
APMAP
ABHD15
D
CD1B
Normalized Expression
Neither NS
CR-Early NS
Neither CR
CR-Early CR
CD1B
Neither NS
DM-Early NS
Neither DM
DM-Early DM
E
FC = 1.12
p = 0.0036
Normalized Expression
Neither
Both
Asthma
Allergy
NS
CR stim
CD1E
Neither NS
CR-Early NS
Neither CR
CR-Early CR
CD1E
Neither NS
DM-Early NS
Neither DM
DM-Early DM

Supplementary Materials

Fig. S1. Overview of study design and analysis flow. The schematic outlines the sample collection, sample selection and analyses conducted. URECA participants were enrolled prenatally. At age 2, PBMCs were collected and stimulated with allergen, antigen, and control medium. The current study was conducted after the children reached age 7. For the initial nested case-control cohort (cohort 1), RNA-sequencing was performed on the preserved year-2 PBMC RNA comparing "Early" cases (n=21) who developed ≥2 aeroallergen sensitizations by age 3 and a diagnosis of asthma at age 7 with "Neither" controls (n=30) who had no aeroallergen sensitization or asthma through age 7. Comparison was done by whole transcriptome differential gene expression followed by cell deconvolution of differentially expressed genes. To validate findings, cohort 2 included the remaining URECA participants who had ≥1 aeroallergen sensitization (including CR) by age 7 and a diagnosis of asthma at age 7, defined as "Late" (n=7), and compared to 14 additional "Neither" controls. A targeted analysis using the cell deconvolution assigned gene sets was performed. Finally all URECA participants with PBMC RNA samples collected at age 2 were compared in a 4 group comparison based on CR sensitization (age 3, yes/no) and asthma (age 7, yes/no). A targeted analysis using the cell deconvolution assigned was performed.

Fig. S2. Allergen and antigen stimulations of PBMCs lead to robust gene expression changes. (A) 7682 genes were differentially expressed comparing TT and NS samples in cohort 1. (B) 282 genes were differentially expressed comparing CR and NS samples in cohort 1. (C) 8009 genes were differentially expressed comparing DM and NS samples in cohort 1.(FDR<0.05

and FC≥1.5) (Stimulation linear modeling with fixed effects for site, gender, blood draw year, and stimulation and random effect for individual; n=51).

Fig. S3. Differentially expressed genes correlate with cell specific marker genes. The 244 genes assigned to one of the 6 cell subsets showed high positive correlation with marker genes specific to the respective cell type (Pearson correlations, red = positive correlation, blue = negative correlation, yellow = no correlation).

Fig. S4. Allergen stimulation of PBMCs cause increased DC gene expression. (A) The DC gene set increases significantly with CR stimulation in the CR-Early group compared to Neither. (B) The DC gene set is not significantly different among the CR-Early, DM-Early, or Neither groups with DM stimulation. Number of individuals in each comparison is represented in parentheses; bounds represent 95% confidence intervals (Stimulation linear models with fixed effects for site, gender, blood draw year, home allergen levels, and stimulation; random effect for individual). (C) DC genes represent a connected network of known gene-gene interactions. (D) Boxplot of normalized expression of *CD1B* and *CD1E* showing group differences with allergen stimulation (Pink=CR-Early, Blue=DM-Early, Grey=Neither). (E) The NK cell gene set shows significantly higher baseline expression in all cases (Red; “Both” = Early and Late groups, n=20) compared to Neither (Black, n=102), asthma only (Blue; “Asthma”, n=40), and CR allergy only (Green; “Allergy”, n=35) groups and increases with CR stimulation only in the Both group.

Table S1. Shown are the clinical and demographic characteristics of cohort 1.

Table S2. Shown are the 244 genes differentially expressed between cases and controls after CR and/or DM expression, including the fold change and FDR values and the cell type assignments.

Table S3. Shown are the cell specific marker genes derived from IRIS and used for SPEC cell type assignment.

Table S4. Shown are the clinical and demographic characteristics of the full cohort divided according to outcome at age 7. “Neither” are those who developed neither allergic sensitization nor asthma. “Both” are those from the CR-Early and Late groups combined into a single group, hence individuals who developed both CR sensitization and asthma. “Asthma only” are those who developed asthma without any allergic sensitization. “Allergy only” are those who developed CR sensitization without asthma.

ensemblID	hgnc_symb	Cell Type	Direction	CR fold cha	CR false dis	DM fold ch	DM false discovery rate
ENSG0000(	FAM110C	Bcell	Positive	2.689	0.022	2.405	0.110
ENSG0000(	ARMCX2	Bcell	Negative	0.769	0.025	0.858	0.197
ENSG0000(	ZNF860	Bcell	Negative	0.550	0.031	0.553	0.093
ENSG0000(	CH507-9B2	Bcell	Negative	0.457	0.039	0.628	0.306
ENSG0000(	FCRL2	Bcell	Negative	0.634	0.044	0.735	0.175
ENSG0000(	PGM1	Bcell	Positive	1.235	0.200	1.478	0.027
ENSG0000(	HLA-G	Bcell	Positive	1.986	0.138	2.457	0.031
ENSG0000(	TPST2	DendriticCe	Positive	1.327	0.002	1.306	0.024
ENSG0000(	APMAP	DendriticCe	Positive	1.305	0.002	1.317	0.007
ENSG0000(	FURIN	DendriticCe	Positive	1.487	0.004	1.393	0.036
ENSG0000(	CD1E	DendriticCe	Positive	3.855	0.006	1.899	0.232
ENSG0000(	RAP1GAP2	DendriticCe	Positive	1.423	0.008	1.341	0.088
ENSG0000(	SLC27A3	DendriticCe	Positive	1.806	0.013	1.304	0.255
ENSG0000(	PRSS21	DendriticCe	Positive	2.268	0.013	1.775	0.208
ENSG0000(	ADGRE5	DendriticCe	Positive	1.328	0.014	1.228	0.130
ENSG0000(	GPR153	DendriticCe	Positive	1.719	0.016	1.609	0.026
ENSG0000(	EFHD2	DendriticCe	Positive	1.396	0.020	1.304	0.110
ENSG0000(	CLU	DendriticCe	Positive	1.917	0.020	1.979	0.068
ENSG0000(	SPN	DendriticCe	Positive	1.284	0.021	1.255	0.067
ENSG0000(	RAB1B	DendriticCe	Positive	1.251	0.021	1.224	0.128
ENSG0000(	VPS16	DendriticCe	Positive	1.194	0.021	1.130	0.190
ENSG0000(	ADCY9	DendriticCe	Positive	1.301	0.027	1.254	0.081
ENSG0000(	LILRA6	DendriticCe	Negative	0.561	0.030	0.582	0.053
ENSG0000(	SGTA	DendriticCe	Positive	1.302	0.030	1.241	0.152
ENSG0000(	PTPN7	DendriticCe	Positive	1.309	0.032	1.316	0.030
ENSG0000(	BAK1	DendriticCe	Positive	1.319	0.033	1.307	0.067
ENSG0000(	GGT1	DendriticCe	Positive	1.394	0.035	1.179	0.324
ENSG0000(	SNX11	DendriticCe	Positive	1.228	0.035	1.245	0.054
ENSG0000(	AP2A1	DendriticCe	Positive	1.216	0.035	1.166	0.180
ENSG0000(	MATK	DendriticCe	Positive	1.597	0.035	1.353	0.232
ENSG0000(	TMEM184E	DendriticCe	Positive	1.221	0.036	1.123	0.299
ENSG0000(	CD1B	DendriticCe	Positive	3.270	0.036	1.427	0.478
ENSG0000(	RAC2	DendriticCe	Positive	1.251	0.037	1.202	0.112
ENSG0000(	CYTH4	DendriticCe	Positive	1.252	0.037	1.104	0.438
ENSG0000(	STYXL1	DendriticCe	Positive	1.318	0.037	1.220	0.145
ENSG0000(	SLC25A25	DendriticCe	Positive	1.281	0.040	1.228	0.138
ENSG0000(	TRIM8	DendriticCe	Positive	1.211	0.040	1.164	0.173
ENSG0000(	MAPKAPK2	DendriticCe	Positive	1.217	0.040	1.179	0.170
ENSG0000(	SH3TC1	DendriticCe	Positive	1.362	0.040	1.250	0.228
ENSG0000(	PTPN6	DendriticCe	Positive	1.270	0.042	1.207	0.152
ENSG0000(	ABHD15	DendriticCe	Positive	1.250	0.042	1.189	0.141
ENSG0000(	CHMP1A	DendriticCe	Positive	1.230	0.042	1.216	0.126
ENSG0000(	DIABLO	DendriticCe	Positive	1.283	0.045	1.266	0.067
ENSG0000(	ENDOG	DendriticCe	Positive	1.445	0.045	1.338	0.216
ENSG0000(	SNAI3	DendriticCe	Positive	1.471	0.045	1.447	0.086
ENSG0000(	DIAPH1	DendriticCe	Positive	1.186	0.045	1.163	0.118
ENSG0000(	TMEM109	DendriticCe	Positive	1.237	0.045	1.217	0.121
ENSG0000(	TESC	DendriticCe	Positive	1.708	0.049	1.719	0.080
ENSG0000(	ACTN4	DendriticCe	Positive	1.236	0.049	1.194	0.127

ENSG0000(	PHB2	DendriticC	Positive	1.210	0.050	1.223	0.074
ENSG0000(	CASS4	DendriticC	Positive	1.515	0.050	1.117	0.600
ENSG0000(	KANK3	DendriticC	Positive	1.420	0.171	1.782	0.013
ENSG0000(	MYOZ1	DendriticC	Positive	2.078	0.086	2.641	0.027
ENSG0000(	SLC35D2	DendriticC	Positive	1.172	0.181	1.338	0.027
ENSG0000(	DHRSX	DendriticC	Positive	1.210	0.161	1.325	0.038
ENSG0000(	SPIRE2	DendriticC	Positive	1.546	0.069	1.695	0.046
ENSG0000(	BORCS6	DendriticC	Positive	1.254	0.081	1.332	0.047
ENSG0000(	SDSL	DendriticC	Positive	1.378	0.193	1.617	0.048
ENSG0000(	KDM2B	DendriticC	Positive	1.102	0.255	1.196	0.048
ENSG0000(	CHST2	Monocyte	Positive	1.402	0.010	1.249	0.232
ENSG0000(	TNFRSF1B	Monocyte	Positive	1.392	0.014	1.196	0.248
ENSG0000(	AOC1	Monocyte	Positive	2.427	0.021	2.286	0.068
ENSG0000(	NEK4	Monocyte	Negative	0.770	0.021	0.811	0.126
ENSG0000(	CEBPD	Monocyte	Positive	1.547	0.021	1.383	0.197
ENSG0000(	FES	Monocyte	Positive	1.530	0.021	1.451	0.125
ENSG0000(	PADI2	Monocyte	Positive	2.069	0.035	1.761	0.118
ENSG0000(	GPR68	Monocyte	Positive	1.518	0.040	1.259	0.310
ENSG0000(	PREX1	Monocyte	Positive	1.230	0.040	1.200	0.152
ENSG0000(	NUDT13	Monocyte	Negative	0.741	0.040	0.728	0.028
ENSG0000(	RETN	Monocyte	Positive	4.708	0.044	2.062	0.390
ENSG0000(	PCCA	Monocyte	Negative	0.722	0.047	0.831	0.280
ENSG0000(	GAB3	Monocyte	Positive	1.221	0.048	1.156	0.247
ENSG0000(	KCTD3	Monocyte	Negative	0.775	0.157	0.706	0.022
ENSG0000(	SYT11	Monocyte	Positive	1.235	0.100	1.320	0.027
ENSG0000(	HIST1H2AC	Monocyte	Negative	0.879	0.232	0.764	0.042
ENSG0000(	TRPA1	Monocyte	Negative	0.641	0.251	0.353	0.042
ENSG0000(	ADGRG5	NKcell	Positive	2.451	0.000	2.044	0.005
ENSG0000(	NCR1	NKcell	Positive	2.305	0.000	2.117	0.007
ENSG0000(	NKG7	NKcell	Positive	2.477	0.000	2.414	0.005
ENSG0000(	GZMB	NKcell	Positive	2.876	0.000	2.293	0.004
ENSG0000(	PRF1	NKcell	Positive	2.299	0.000	2.194	0.018
ENSG0000(	CCNJL	NKcell	Positive	3.129	0.000	2.469	0.017
ENSG0000(	CST7	NKcell	Positive	1.966	0.001	1.898	0.011
ENSG0000(	MLC1	NKcell	Positive	2.512	0.001	2.305	0.010
ENSG0000(	SH2D1B	NKcell	Positive	2.411	0.001	2.115	0.022
ENSG0000(	PRR5L	NKcell	Positive	1.837	0.001	1.695	0.014
ENSG0000(	EOMES	NKcell	Positive	1.802	0.001	1.673	0.005
ENSG0000(	IL2RB	NKcell	Positive	1.811	0.001	1.698	0.005
ENSG0000(	SH2D2A	NKcell	Positive	1.766	0.001	1.640	0.017
ENSG0000(	ITPRIPL1	NKcell	Positive	1.533	0.002	1.566	0.001
ENSG0000(	ADAM8	NKcell	Positive	1.489	0.002	1.329	0.122
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ENSG0000(	MMP12	NKcell	Positive	8.751	0.008	0.622	0.431
ENSG0000(	TIGIT	NKcell	Positive	1.597	0.009	1.573	0.017
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ENSG0000(	DLG5	NKcell	Positive	2.007	0.010	1.761	0.068
ENSG0000(	KLRF1	NKcell	Positive	2.205	0.010	1.893	0.098
ENSG0000(	KLRC1	NKcell	Positive	2.382	0.010	1.654	0.163
ENSG0000(	GZMA	NKcell	Positive	1.856	0.010	1.776	0.058
ENSG0000(	HIC1	NKcell	Positive	1.824	0.011	1.569	0.112
ENSG0000(	ADGRG1	NKcell	Positive	2.024	0.011	1.972	0.037
ENSG0000(	CLDND2	NKcell	Positive	1.845	0.014	1.787	0.048
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ENSG0000(	GADD45B	NKcell	Positive	1.321	0.015	1.169	0.233
ENSG0000(	TAPBP	NKcell	Positive	1.291	0.015	1.214	0.152
ENSG0000(	IL13	NKcell	Positive	8.060	0.015	4.036	0.005
ENSG0000(	CYB561	NKcell	Positive	1.404	0.015	1.409	0.045
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ENSG0000(	SEC24C	NKcell	Positive	1.159	0.021	1.134	0.162
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ENSG0000(	LGALS9B	NKcell	Positive	3.019	0.027	2.463	0.138
ENSG0000(	KRT1	NKcell	Positive	3.151	0.027	3.194	0.029
ENSG0000(	ELF4	NKcell	Positive	1.247	0.028	1.198	0.157
ENSG0000(	SALL4	NKcell	Positive	2.195	0.030	1.892	0.158
ENSG0000(	BCL3	NKcell	Positive	1.415	0.030	1.161	0.430
ENSG0000(	KIR3DL2	NKcell	Positive	2.355	0.030	2.588	0.020
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ENSG0000(	XCL2	NKcell	Positive	1.984	0.035	1.656	0.110

ENSG0000(	LINGO2	NKcell	Positive	2.379	0.035	2.354	0.090
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ENSG0000(	CTSW	NKcell	Positive	1.794	0.037	1.752	0.031
ENSG0000(	JAKMIP1	NKcell	Positive	1.902	0.038	1.769	0.120
ENSG0000(	B3GNT7	NKcell	Positive	1.609	0.039	1.360	0.215
ENSG0000(	SEMA5A	NKcell	Positive	2.637	0.039	3.291	0.035
ENSG0000(	HEATR9	NKcell	Positive	1.579	0.039	1.402	0.266
ENSG0000(	KIR3DL1	NKcell	Positive	2.124	0.039	2.379	0.016
ENSG0000(	CCL17	NKcell	Positive	6.290	0.040	3.201	0.081
ENSG0000(	C9orf172	NKcell	Positive	1.480	0.040	1.317	0.238
ENSG0000(	FAT4	NKcell	Positive	2.642	0.041	2.708	0.051
ENSG0000(	NBEAL2	NKcell	Positive	1.242	0.042	1.167	0.243
ENSG0000(	ENPP1	NKcell	Positive	2.989	0.044	2.543	0.012
ENSG0000(	PCDH1	NKcell	Positive	1.945	0.044	1.983	0.098
ENSG0000(	APOL4	NKcell	Positive	2.474	0.045	1.662	0.214
ENSG0000(	FUT7	NKcell	Positive	1.571	0.045	1.772	0.031
ENSG0000(	IFITM2	NKcell	Positive	1.335	0.045	1.209	0.308
ENSG0000(	JAG2	NKcell	Positive	1.689	0.045	1.552	0.221
ENSG0000(	TBKBP1	NKcell	Positive	1.423	0.045	1.185	0.428
ENSG0000(	EML2	NKcell	Positive	1.170	0.045	1.103	0.291
ENSG0000(	SBNO2	NKcell	Positive	1.325	0.048	1.196	0.284
ENSG0000(	TNFRSF4	NKcell	Positive	1.527	0.048	1.448	0.109
ENSG0000(	OGFR	NKcell	Positive	1.230	0.049	1.143	0.315
ENSG0000(	IL9	NKcell	Positive	2.073	0.356	9.018	0.005
ENSG0000(	KIR2DL3	NKcell	Positive	1.840	0.100	2.528	0.013
ENSG0000(	TMPRSS3	NKcell	Positive	1.552	0.201	2.232	0.013
ENSG0000(	MEOX1	NKcell	Positive	1.907	0.146	2.409	0.017
ENSG0000(	WNT11	NKcell	Positive	2.219	0.120	2.937	0.026
ENSG0000(	B3GAT1	NKcell	Positive	1.885	0.092	2.281	0.027
ENSG0000(	HOXC4	NKcell	Positive	1.878	0.108	1.892	0.027
ENSG0000(	C11orf84	NKcell	Positive	1.117	0.313	1.304	0.030
ENSG0000(	SLC2A1	NKcell	Positive	1.217	0.230	1.433	0.036
ENSG0000(	HN1	NKcell	Positive	1.204	0.064	1.244	0.036
ENSG0000(	CNTNAP2	TcellCD4	Negative	0.269	0.008	0.361	0.098
ENSG0000(	NBPF19	TcellCD4	Negative	0.703	0.014	0.680	0.007
ENSG0000(	RAD52	TcellCD4	Negative	0.781	0.015	0.737	0.013
ENSG0000(	COA1	TcellCD4	Negative	0.796	0.019	0.783	0.079
ENSG0000(	PBX3	TcellCD4	Negative	0.779	0.020	0.855	0.221
ENSG0000(	KLRB1	TcellCD4	Positive	1.802	0.021	1.744	0.068
ENSG0000(	ENTPD4	TcellCD4	Negative	0.799	0.021	0.799	0.049
ENSG0000(	WDR19	TcellCD4	Negative	0.682	0.021	0.759	0.142
ENSG0000(	MRPS25	TcellCD4	Negative	0.841	0.024	0.847	0.122
ENSG0000(	PPM1L	TcellCD4	Negative	0.693	0.030	0.837	0.253
ENSG0000(	PHOSPHO2	TcellCD4	Negative	0.632	0.030	0.832	0.467
ENSG0000(	GNAL	TcellCD4	Positive	1.385	0.031	1.309	0.152
ENSG0000(	MBP	TcellCD4	Positive	1.166	0.032	1.142	0.084
ENSG0000(	C11orf85	TcellCD4	Negative	0.319	0.034	0.386	0.062
ENSG0000(	NPIPB2	TcellCD4	Negative	0.315	0.036	0.320	0.053

ENSG0000(	NBPF9	TcellCD4	Negative	0.718	0.041	0.743	0.027
ENSG0000(	ADAMTSL5	TcellCD4	Positive	1.896	0.042	1.911	0.051
ENSG0000(	RBM45	TcellCD4	Negative	0.745	0.044	0.855	0.340
ENSG0000(	USP44	TcellCD4	Negative	0.622	0.045	0.673	0.152
ENSG0000(	AGBL3	TcellCD4	Negative	0.673	0.049	0.698	0.131
ENSG0000(	DSC1	TcellCD4	Negative	0.318	0.050	0.360	0.165
ENSG0000(	PIGL	TcellCD4	Negative	0.790	0.073	0.704	0.005
ENSG0000(	NEB	TcellCD4	Negative	0.598	0.051	0.605	0.042
ENSG0000(	RASSF6	TcellCD4	Negative	0.754	0.343	0.480	0.048
ENSG0000(	OSBPL5	TcellCD8	Positive	1.644	0.004	1.526	0.041
ENSG0000(	APC2	TcellCD8	Positive	1.461	0.009	1.162	0.398
ENSG0000(	TSEN54	TcellCD8	Positive	1.338	0.010	1.314	0.027
ENSG0000(	DGKQ	TcellCD8	Positive	1.377	0.014	1.274	0.126
ENSG0000(	ABCA2	TcellCD8	Positive	1.352	0.021	1.261	0.152
ENSG0000(	ARHGEF19	TcellCD8	Positive	1.416	0.021	1.345	0.142
ENSG0000(	IER2	TcellCD8	Positive	1.242	0.022	1.232	0.052
ENSG0000(	ARID5A	TcellCD8	Positive	1.281	0.025	1.237	0.145
ENSG0000(	ITGAL	TcellCD8	Positive	1.221	0.026	1.187	0.126
ENSG0000(	FRMD8	TcellCD8	Positive	1.224	0.026	1.167	0.174
ENSG0000(	NPDC1	TcellCD8	Positive	1.580	0.030	1.369	0.182
ENSG0000(	BOK	TcellCD8	Positive	1.960	0.035	2.271	0.011
ENSG0000(	CD7	TcellCD8	Positive	1.531	0.035	1.471	0.086
ENSG0000(	TBC1D13	TcellCD8	Positive	1.211	0.036	1.130	0.279
ENSG0000(	ZFPM1	TcellCD8	Positive	1.376	0.036	1.279	0.162
ENSG0000(	MTA2	TcellCD8	Positive	1.157	0.037	1.149	0.152
ENSG0000(	ZFR2	TcellCD8	Positive	2.384	0.039	1.635	0.245
ENSG0000(	GUK1	TcellCD8	Positive	1.229	0.039	1.250	0.067
ENSG0000(	IL2RG	TcellCD8	Positive	1.205	0.042	1.203	0.127
ENSG0000(	LZTS1	TcellCD8	Positive	3.031	0.043	1.621	0.301
ENSG0000(	CDKN2D	TcellCD8	Positive	1.316	0.043	1.239	0.180
ENSG0000(	SLC9A3R1	TcellCD8	Positive	1.283	0.044	1.341	0.025
ENSG0000(	DMWD	TcellCD8	Positive	1.323	0.045	1.239	0.224
ENSG0000(	DNM2	TcellCD8	Positive	1.185	0.047	1.114	0.303
ENSG0000(	BAP1	TcellCD8	Positive	1.170	0.049	1.131	0.218
ENSG0000(	PLEKHF1	TcellCD8	Positive	1.333	0.161	1.663	0.014
ENSG0000(	IMP3	TcellCD8	Positive	1.121	0.260	1.268	0.024
ENSG0000(	ASMTL	TcellCD8	Positive	1.229	0.080	1.322	0.025
ENSG0000(	GNAO1	TcellCD8	Positive	1.526	0.124	2.173	0.027
ENSG0000(	RNASEH2A	TcellCD8	Positive	1.191	0.151	1.325	0.029
ENSG0000(	MPP2	TcellCD8	Positive	1.744	0.145	1.978	0.030
ENSG0000(	ACTL10	TcellCD8	Positive	1.425	0.080	1.556	0.032
ENSG0000(	IFFO2	TcellCD8	Positive	1.188	0.141	1.305	0.033
ENSG0000(	NCR3	TcellCD8	Positive	1.403	0.092	1.598	0.035
ENSG0000(	RNF187	TcellCD8	Positive	1.182	0.154	1.318	0.035
ENSG0000(	SNTA1	TcellCD8	Positive	1.256	0.179	1.552	0.037

Bcell	TcellCD4	TcellCD8	DendriticCe	Monocyte	NKcell
IL4R	SNPH	FCGBP	GSN	CD14	CHST2
IRF8	PLCL1	CD8A	MDH1	CD93	FCGR3B
CD79A	ANK3	LAG3	CD9	TNFRSF1B	CCL4
POU2AF1	FHIT	GZMK	IDH1	S100A9	APOBEC3G
CD79B	EPHX2	CRTAM	CSTB	CYBB	ADAM8
ADAM28	ICOS	CD8B	TXNRD1	VCAN	IL2RB
BLNK	SCML1	COL6A2	GPX3	FCN1	IL18RAP
MEF2C	EDAR	KLRG1	CTSC	S100A12	GZMB
TCL1A	ANKRD55	CD248	LIPA	LILRB2	KLRD1
P2RX5	TLE2	AGFG2	ADAM9	DUSP6	ATP2B4
SEL1L3	NUF2	RASGRF2	CYP1B1	LILRB3	AUTS2
TCF4	NOG	MAP9	CEBPA	SERPINA1	PRF1
HHEX	EPPK1	ACSL6	ACP5	MEGF9	SLAMF7
TSPAN13	CTLA4	ZNF792	CD1C	SULT1A2	CLIC3
BANK1		JAKMIP1	CD1B	PLBD1	KLRF1
SCD5			PRDX1	C5AR1	GNLY
PAX5			TXN	KLF4	FGFBP2
HVCN1			CD1E	MS4A7	FUT11
MS4A1			A2M	MYADM	C5orf56
FCRL1			GM2A	MPEG1	S1PR5

	n	Overall N=51	Controls N=30	Cases N=21	p-value†
Site: Baltimore	51	19 (37%)	12 (41%)	7 (33%)	
Boston		11 (22%)	7 (23%)	4 (19%)	0.82
New York		9 (18%)	4 (13%)	5 (24%)	
St. Louis		12 (23%)	7 (23%)	5 (24%)	
Mother's education: Less than high school	51	20 (39%)	15 (50%)	5 (24%)	
High school		21 (41%)	10 (33%)	11 (52%)	0.18
More than high school		10 (20%)	5 (17%)	5 (24%)	
Birth season: January – March	51	16 (31%)	9 (30%)	7 (33%)	
April – June		8 (16%)	6 (20%)	2 (10%)	0.81
July – September		15 (29%)	8 (27%)	7 (33%)	
October – December		12 (24%)	7 (23%)	5 (24%)	
Annual income < $15K	51	34 (67%)	19 (63%)	15 (71%)	0.76
Mother is married	51	7 (14%)	3 (10%)	4 (19%)	0.43
Child's race: Black	51	42 (82%)	24 (80%)	18 (86%)	
Hispanic		5 (10%)	3 (10%)	2 (9%)	0.87
Mixed/other		4 (8%)	3 (10%)	1 (5%)	
Child's gestational age (wks.)	51	38.6 ± 1.7	38.6 ± 1.6	38.6 ± 1.7	0.92
Child's birth weight (g)	51	3197 ± 434	3145 ± 421	3271 ± 450	0.32
C-section delivery	51	15 (29%)	9 (30%)	6 (29%)	0.99
Mother breastfed at 3 months	48	9 (19%)	4 (14%)	5 (26%)	0.45
Age of mother at time of birth	51	23.1 ± 4.8	22.6 ± 4.8	23.8 ± 4.9	0.37
Child's gender: male	51	36 (71%)	18 (60%)	18 (86%)	0.09
Mother has had asthma	51	25 (49%)	13 (43%)	12 (57%)	0.49
Exposures in the first year of life					
Mother smoked	51	22 (43%)	15 (50%)	7 (33%)	0.37
Number of smokers in the home	51	1.2 ± 1.2	1.2 ± 1.4	1.1 ± 0.9	0.56
Der f – bedroom (ug/g)	49	0.28 [0.26; 0.35]	0.28 [0.26; 0.34]	0.28 [0.26; 0.45]	0.93
Der f – living room (ug/g)	41	0.27 [0.26; 0.29]	0.27 [0.26; 0.30]	0.27 [0.26; 0.29]	0.80
Der p – bedroom (ug/g)	49	0.46 [0.46; 0.46]	0.46 [0.46; 0.46]	0.46 [0.46; 0.46]	0.33
Der p – living room (ug/g)	40	0.46 [0.46; 0.46]	0.46 [0.46; 0.46]	0.46 [0.46; 0.46]	0.95
Bla g – bedroom (U/g)	47	0.59 [0.20; 12.0]	0.59 [0.20; 14.0]	0.24 [0.20; 4.4]	0.28
Bla g – living room (U/g)	41	0.20 [0.20; 5.7]	0.20 [0.20; 1.2]	1.7 [0.20; 6.2]	0.17
Clinical characteristics in first year of life					
Number of wheezing illnesses	51	0.7 ± 1.1	0.3 ± 0.7	1.2 ± 1.4	0.01
Any doctor visits for wheezing	51	6 (12%)	1 (3%)	5 (24%)	0.07
Any hospitalizations for wheezing	51	0 (0%)	0 (0%)	0 (0%)	n/a
Any wheezing	51	17 (33%)	5 (17%)	12 (57%)	0.01
Number of colds	51	4.4 ± 2.3	4.0 ± 2.3	4.9 ± 2.2	0.17
EASI score	51	1.8 ± 3.3	0.4 ± 0.7	3.7 ± 4.5	<0.01
Runny nose‡	50	18 (36%)	9 (30%)	9 (45%)	0.43
Stuffy nose‡	50	12 (24%)	6 (20%)	6 (30%)	0.51
Frequent sneezing‡	50	12 (24%)	4 (13%)	8 (40%)	0.04

Itchy eyes‡	50	10 (20%)	5 (17%)	5 (25%)	0.49
IgE levels at age 2 (kU/L)					
Total IgE	51	28.7 [10.2; 201]	16.5 [6.2; 31.3]	258 [130; 596]	<0.01
Peanut IgE	51	0.09 [0.09; 0.09]	0.09 [0.09; 0.09]	0.34 [0.09; 6.75]	<0.01
Milk IgE	51	0.09 [0.09; 0.21]	0.09 [0.09; 0.09]	0.23 [0.09; 1.57]	<0.01
Egg IgE	51	0.09 [0.09; 0.24]	0.09 [0.09; 0.09]	0.44 [0.16; 2.03]	<0.01
German Cockroach IgE	51	0.09 [0.09; 0.32]	0.09 [0.09; 0.09]	0.44 [0.09; 2.49]	<0.01
Dermatophageides pteronyssinus IgE	51	0.09 [0.09; 0.17]	0.09 [0.09; 0.09]	0.19 [0.12; 1.33]	<0.01
Dermatophageides farinae IgE	51	0.09 [0.09; 0.14]	0.09 [0.09; 0.09]	0.17 [0.09; 1.14]	<0.01
Cat IgE	51	0.09 [0.09; 0.09]	0.09 [0.09; 0.09]	0.16 [0.09; 0.64]	<0.01
Dog IgE	51	0.09 [0.09; 0.10]	0.09 [0.09; 0.09]	0.18 [0.09; 1.40]	<0.01
Mouse IgE	51	0.09 [0.09; 0.09]	0.09 [0.09; 0.09]	0.09 [0.09; 0.33]	<0.01
Alternaria IgE	51	0.09 [0.09; 0.09]	0.09 [0.09; 0.09]	0.09 [0.09; 0.17]	<0.01
IgE levels at age 7 (kU/L)					
Total IgE	47	77.0 [33.5; 508]	37.0 [16.0; 65.5]	564 [446; 1282]	<0.01
Peanut IgE	47	0.10 [0.09; 0.64]	0.09 [0.09; 0.10]	0.81 [0.15; 25.1]	<0.01
Milk IgE	47	0.12 [0.09; 0.23]	0.09 [0.09; 0.12]	0.26 [0.18; 1.12]	<0.01
Egg IgE	47	0.10 [0.09; 0.26]	0.09 [0.09; 0.10]	0.29 [0.12; 0.91]	<0.01
German Cockroach IgE	47	0.10 [0.09; 2.59]	0.09 [0.09; 0.10]	5.44 [1.69; 41.9]	<0.01
Dermatophageides pteronyssinus IgE	47	0.10 [0.09; 2.47]	0.09 [0.09; 0.10]	3.41 [1.12; 8.36]	<0.01
Dermatophageides farinae IgE	47	0.10 [0.09; 3.05]	0.09 [0.09; 0.10]	4.62 [0.75; 30.1]	<0.01
Cat IgE	46	0.10 [0.09; 0.92]	0.09 [0.09; 0.10]	4.00 [0.50; 20.2]	<0.01
Dog IgE	47	0.10 [0.09; 2.72]	0.09 [0.09; 0.10]	4.57 [0.99; 19.0]	<0.01
Mouse IgE	47	0.09 [0.09; 0.45]	0.09 [0.09; 0.10]	3.06 [0.09; 10.4]	<0.01
Alternaria IgE	47	0.10 [0.09; 0.14]	0.09 [0.09; 0.10]	0.24 [0.10; 2.78]	<0.01
Clinical characteristics at age 7					
Number of wheezing illnesses	51	0.9 ± 1.7	0.0 ± 0.0	2.2 ± 2.1	<0.01
Any doctor visits for wheezing	51	9 (18%)	0 (0%)	9 (43%)	<0.01
Any hospitalizations for wheezing	51	2 (4%)	0 (0%)	2 (10%)	0.16
Any wheezing	51	19 (37%)	0 (0%)	19 (91%)	<0.01
Number of colds	51	2.0 ± 2.4	1.6 ± 1.9	2.5 ± 2.9	0.21
EASI score	46	0.3 ± 1.1	0.0 ± 0.0	0.8 ± 1.7	0.06
Runny nose‡	50	8 (16%)	5 (17%)	3 (15%)	0.99
Stuffy nose‡	50	12 (24%)	6 (20%)	6 (30%)	0.51
Frequent sneezing‡	50	13 (26%)	6 (20%)	7 (35%)	0.39
Itchy eyes‡	50	9 (18%)	3 (10%)	6 (30%)	0.13
Any hay fever	50	10 (20%)	3 (10%)	7 (35%)	0.07

*Values are count (percentage), mean ± standard deviation, or median [IQR].

†P-values are from appropriate test for data – t-test for normally distributed, continuous data, Kruskal-Wallis test for non-normally distributed, continuous data, and either chi-squared or Fisher's exact tests for categorical data.

‡Questions indicate routine occurrence, or greater than 2 days per week over the past year.

	n	Neither N=102	Both= CR Early+Late N=20	Asthma only N=40	Allergy only N=35	p-value†
Site: Baltimore	197	36 (35%)	7 (35%)	6 (15%)	12 (34%)	
Boston		24 (24%)	4 (20%)	13 (33%)	8 (23%)	0.37
New York		7 (7%)	4 (20%)	5 (13%)	3 (9%)	
St. Louis		35 (34%)	5 (25%)	16 (40%)	12 (34%)	
Mother's education: Less than high school	197	39 (38%)	4 (20%)	20 (50%)	15 (43%)	
High school		41 (40%)	11 (55%)	13 (33%)	13 (37%)	0.49
More than high school		22 (22%)	5 (25%)	7 (18%)	7 (20%)	
Birthseason: January – March	197	20 (20%)	5 (25%)	6 (15%)	7 (20%)	
April – June		24 (24%)	2 (10%)	15 (38%)	8 (23%)	0.56
July – September		28 (28%)	7 (35%)	11 (28%)	13 (37%)	
October – December		30 (29%)	6 (30%)	8 (20%)	7 (20%)	
Annual income < $15K	197	63 (62%)	14 (70%)	29 (73%)	30 (86%)	0.06
Mother is married	197	15 (15%)	4 (20%)	3 (8%)	1 (3%)	0.12
Child's race: Black	197	78 (77%)	16 (80%)	33 (83%)	29 (83%)	
Hispanic		15 (15%)	2 (10%)	6 (15%)	3 (9%)	0.82
Mixed/other		9 (9%)	2 (10%)	1 (3%)	3 (9%)	
Child's gestational age (wks.)	197	38.7 ± 1.5	38.5 ± 1.9	38.8 ± 1.5	39.0 ± 1.5	0.67
Child's birth weight (g)	197	3226 ± 419	3314 ± 453	3187 ± 512	3260 ± 540	0.77
C-section delivery	197	27 (27%)	6 (30%)	12 (30%)	9 (26%)	0.96
Mother breastfed at 3 months	185	21 (22%)	5 (26%)	4 (11%)	10 (30%)	0.21
Age of mother at time of birth	197	24.7 ± 6.0	24.1 ± 5.1	24.2 ± 6.2	24.2 ± 5.9	0.95
Child's gender: male	197	49 (48%)	16 (80%)	24 (60%)	21 (60%)	0.05
Mother has had asthma	196	29 (28%)	10 (50%)	24 (62%)	16 (46%)	<0.01
Exposures in the first year of life						
Mother smoked	197	48 (47%)	6 (30%)	17 (43%)	11 (31%)	0.28
Number of smokers in the home	197	1.4 ± 1.3	1.2 ± 0.9	1.4 ± 1.3	1.1 ± 0.9	0.53
Der f – bedroom (ug/g)	196	0.27 [0.26; 0.33]	0.27 [0.26; 0.31]	0.27 [0.26; 0.28]	0.28 [0.27; 0.46]	0.05
Der f – living room (ug/g)	195	0.27 [0.26; 0.31]	0.27 [0.26; 0.29]	0.27 [0.26; 0.29]	0.28 [0.26; 0.36]	0.27
Der p – bedroom (ug/g)	195	0.46 [0.46; 0.46]	0.46 [0.46; 0.46]	0.46 [0.46; 0.46]	0.46 [0.46; 0.46]	0.46
Der p – living room (ug/g)	194	0.46 [0.46; 0.46]	0.46 [0.46; 0.46]	0.46 [0.46; 0.46]	0.46 [0.46; 0.46]	0.59
Bla g – bedroom (U/g)	197	0.20 [0.20; 4.38]	0.85 [0.20; 5.78]	0.20 [0.20; 3.32]	3.60 [0.20; 17.0]	0.02
Bla g – living room (U/g)	197	0.20 [0.20; 3.13]	1.53 [0.20; 5.88]	0.98 [0.20; 7.35]	3.10 [0.20; 13.50]	0.04
Clinical characteristics in first year of life						
Number of wheezing illnesses	197	0.8 ± 1.9	1.2 ± 1.4	2.1 ± 2.4	1.5 ± 2.7	0.01
Any doctor visits for wheezing	197	6 (6%)	3 (15%)	13 (33%)	3 (9%)	<0.01
Any hospitalizations for wheezing	197	0 (0%)	0 (0%)	0 (0%)	0 (0%)	n/a
Any wheezing	197	37 (36%)	12 (60%)	29 (73%)	16 (46%)	<0.01

Number of colds	197	4.2 ± 2.9	5.3 ± 2.1	5.4 ± 2.6	4.3 ± 3.1	0.10
EASI score	197	0.7 ± 1.6	3.6 ± 4.5	1.0 ± 1.9	1.6 ± 3.2	<0.01
Sensitivity to food(s) – milk/egg/peanut	158	18 (21%)	8 (53%)	11 (34%)	11 (41%)	0.03
Clinical characteristics in third year of life						
Number of wheezing illnesses	197	0.4 ± 1.0	1.6 ± 2.4	2.3 ± 2.1	0.7 ± 1.4	<0.01
Any doctor visits for wheezing	197	5 (5%)	8 (40%)	11 (28%)	2 (6%)	<0.01
Any hospitalizations for wheezing	197	0 (0%)	1 (5%)	1 (3%)	0 (0%)	0.16
Any wheezing	197	25 (25%)	11 (55%)	32 (80%)	11 (31%)	<0.01
Number of colds	197	3.5 ± 3.0	4.0 ± 2.9	4.9 ± 3.1	3.2 ± 2.8	0.06
EASI score	180	0.6 ± 2.0	1.4 ± 2.0	0.3 ± 0.9	1.5 ± 6.9	0.40
Sensitivity to food(s) – milk/egg/peanut	175	26 (28%)	7 (44%)	17 (50%)	14 (42%)	0.10

*Values are count (percentage), mean ± standard deviation, or median [IQR].

†P-values are from appropriate test for data – t-test for normally distributed, continuous data, Kruskal-Wallis test for non-normally distributed, continuous data, and either chi-squared or Fisher's exact tests for categorical data.