



Differential gene expression among infants at high-risk for peanut allergy

AL Devonshire, DB Gursel, H Fan,
KA Erickson, JA Pongratic, M
Schipma, AM Singh*, S Berdnikovs*,
R Kumar*

AAAAI Mentor: Dr. Wesley Burks



Peanut allergy in infancy: the LEAP cohort

- 9.1% of infants in the LEAP study screening cohort were excluded due to a peanut skin prick test size >4 mm.
- 2.2% of infants randomized to peanut consumption failed their baseline peanut OFC.

The transcriptome in food allergy

- Differential gene expression has been characterized in clinical egg allergy phenotypes and in peanut-stimulated memory T cells of peanut allergic subjects.
- Peripheral blood gene expression patterns associated with acute peanut allergic reactions have been identified.

Watson, CT et al. *Nature Communications*. 2017; 8: 1943. 1-13.

Kosoy, R et al. *PlosOne*. 2016; 11(10): 1-20.

Brough, HA et al. *J Allergy Clin Immunol*. 2014; 134(6): 1329-1338.e10.

Hypotheses

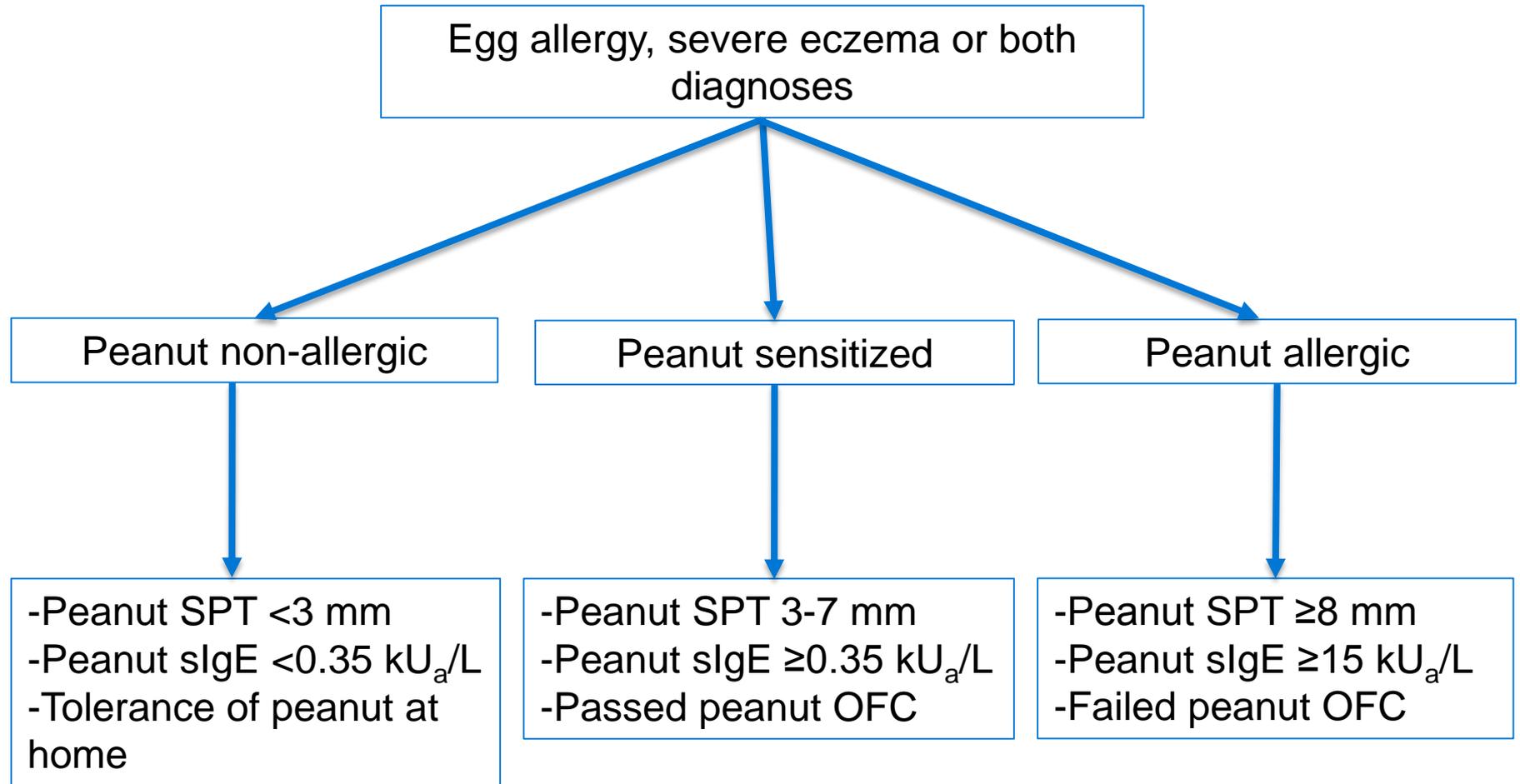
There are differentially expressed genes that will distinguish high-risk infants who are peanut allergic, peanut sensitized and peanut non-allergic.

This differential gene expression can be used to distinguish those who are clinically allergic.

Methods: Study subjects

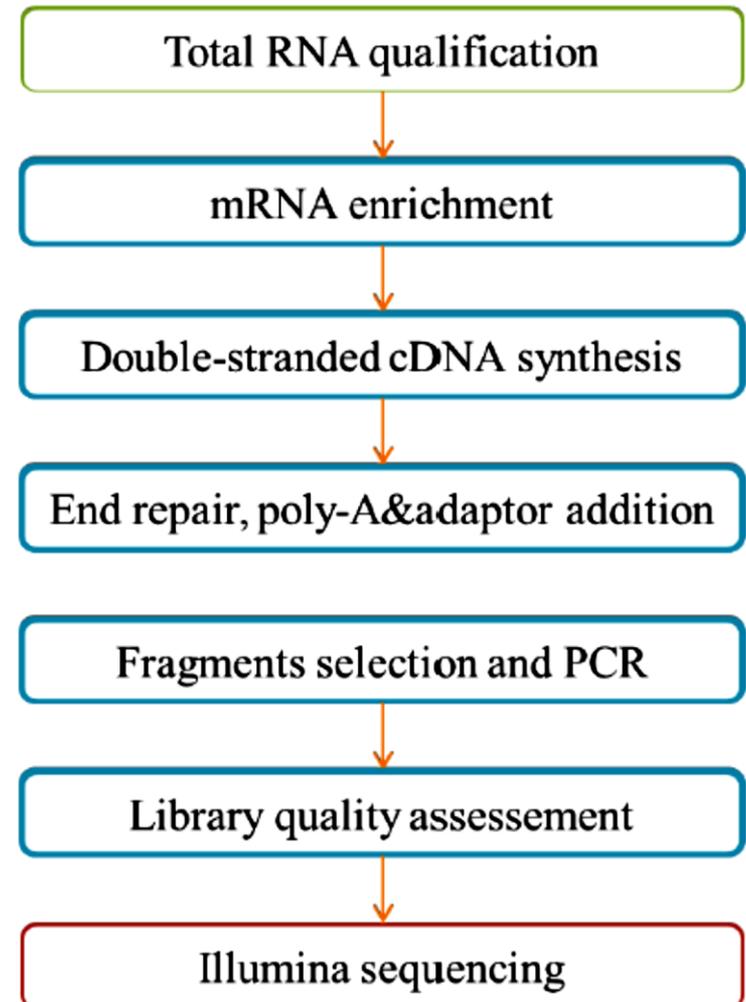
- Infants 4-11 months of age with severe eczema, egg allergy or both diagnoses recruited from an early introduction clinic.
- Peanut skin prick testing was performed (+/- sIgE) and then home peanut introduction, peanut OFC or peanut avoidance were recommended.
- Subjects were categorized as peanut allergic, peanut sensitized or peanut non-allergic.

Methods: Categorization of study subjects



Methods: Transcriptomic analysis of whole blood

- Quality control, library preparation, sequencing and bioinformatics were performed by Novogene, a commercial genomics laboratory



Results: Participant characteristics (N=20)

Age at first visit, median (IQR) months	8 (3.5)
Gender, N (%) male	13 (65)
Age of solid food introduction, median (IQR) months [†]	6 (1)
Duration of exclusive breastfeeding, median (IQR) months [‡]	5.5 (4)
Peanut skin prick test wheal, median (IQR) mm [¥]	4 (4.5)
Peanut specific IgE, median (IQR) kU _a /L [§]	9.46 (16.8)
Peanut allergic, N	8
Peanut sensitized, N	5
Peanut non-allergic, N	7

[†]N=19; [‡]N=18; [¥]N=16; [§]N=13

Results: Differential gene expression, PA vs. PS

Up-regulated in peanut allergic			
Gene	Gene Name	Log₂ fold change	FDR adjusted p-value
LINC00649	Long intergenic non-protein coding RNA 649	0.65	0.01123
CEP192	Centrosomal protein 192	0.58	0.01278
TNFRSF10D (DCR2)	TNF receptor superfamily member 10D	0.52	0.01278
Down-regulated in peanut allergic			
Gene	Gene Name	Log₂ fold change	FDR adjusted p-value
COL18A1	Collagen type XVIII alpha 1 chain	-0.93	0.00299
EVA1B	Eva-1 homolog B	-0.85	0.01123

Results: Differential gene expression, PA vs. PS controlling for age and gender

Up-regulated in peanut allergic			
Gene	Gene Name	Log₂ fold change	FDR adjusted p-value
LCN2	Lipocalin 2	2.73	0.00098
CAMP	Cathelicidin antimicrobial peptide	2.38	0.00440
LTF	Lactotransferrin	3.50	0.03104
ALPL	Alkaline phosphatase, liver/bone/kidney	3.37	0.03104
ORM1	Orosomucoid 1	3.34	0.04371
TREM1	Triggering receptor expressed on myeloid cells 1	1.66	0.04371
CA4	Carbonic anhydrase 4	2.31	0.04371
RBPMS2	RNA binding protein with multiple splicing 2	2.57	0.04371
Down-regulated in peanut allergic			
Gene	Gene Name	Log₂ fold change	FDR adjusted p-value
LOC1005061	Uncharacterized LOC1005061	-6.73	0.00050

Summary

- There is differential gene expression between PA and PS infants and this may change upon controlling for age and gender.
- Some up-regulated genes are involved in innate immunity and may reflect dysregulation of the innate immune response in infants with food allergy and atopic dermatitis.

Limitations

- Small sample size
- Validation and reproducibility
- Specificity for peanut
- Challenge-confirmation of peanut allergy

Acknowledgements

Division of Allergy & Immunology, Ann &
Robert H. Lurie Children's Hospital of Chicago

Dr. Rajesh Kumar
Dr. Jacqueline Pongracic

Robert H. Lurie Comprehensive Cancer
Center of Northwestern University, Pathology
Core Facility

Dr. Demirkan Gursel
Hanli Fan

University of Wisconsin School of Medicine
and Public Health

Dr. Anne Marie Singh

Cincinnati Children's Hospital Medical Center

Dr. Leah Kottyan
Dr. Marc Rothenberg
Dr. Amal Assa'ad

Division of Allergy & Immunology,
Northwestern University

Dr. Sergejs Berdnikovs
Dr. Robert Schleimer
Meagan Yong
Kris Erickson

Biostatistics Collaboration Center,
Feinberg School of Medicine

Dr. Lauren Balmert

Indiana University School of
Medicine

Dr. Joan Cook-Mills

Funding Sources

Northwestern University Allergy and
Immunology Training Grant (NUAIR)
T32
Brinson Foundation

Power Considerations

