Gut Microbiome and Immune Dysregulation in Childhood Atopic Dermatitis with Food Allergy

Yanjie Huang[1], Panpan Zhai[1], Mingzhuo Cao[2], Kamal Srivastava[3], Raj Tiwari[4], Jan Geliebter[4], Anna Nowak-wegrzyn[5], Huanhuan Shao[6], Xia Zhang[1], Guihua Song[1], Yehong Yuan[1], Wensheng Zhai[1], Bingxiang Ma[1], Xianqing Ren[1], Ying Ding[1], Chenhong Xue[7], Ge Qian[8], Xiu Min Li[4], and Mingsan Miao[2]

[1]The First Affiliated Hospital of Henan University of Traditional Chinese Medicine
[2]Henan University of Chinese Medicine
[3]General Nutraceutical Technology LLC
[4]New York Medical College
[5]New York University Grossman School of Medicine
[6]Sichuan Normal University
[7]Zhengzhou Children's Hospital
[8]Henan Provincial People's Hospital

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Abstract

Background: This study aims to investigate whether immune dysregulation and gut microbiome alteration are exacerbated in atopic dermatitis (AD) with food allergy (ADFA) and potential treatment strategies. **Methods:** Total 159 children with AD (tAD) were divided into two groups: AD without-food allergy (ADNFA) and with food allergy (ADFA); 100 children without AD were included as control. Eosinophil counts and total serum IgE levels were measured by routine methods, serum food-specific IgE levels by quantitative fluorescence immunoassay, and serum cytokine levels by multi-microsphere flow immunofluorescence. The intestinal microbiota was evaluated in fecal specimens using metagenomic sequencing. A novel ADFA mouse model was generated to evaluate whether probiotic candidates identified from human fecal samples contributed to the improvement in ADFA pathology. **Results**: The levels of eosinophils, IgE, IL-2, TNF-α, IL-4, IL-5, IL-6, IL-10, IL-17, IL-12P70 and IFN-α were elevated in tAD compared to normal controls. Compared with ADNFA, the levels of eosinophils, IgE and IL-5 were persistently increased, while IFN-γ was decreased, the species of *Lactococcus lactis (L. lactis)* was reduced in ADFA. Compared with AD, the ADFA model had more severe skin lesions on the back and significantly higher serum OVA-specific IgE, IL-4 and IL-5. Following oral administration of *L. lactis* (*L. lactis* 1.1936+1.3992), skin lesions in ADFA mice was significantly improved. The levels of OVA-specific IgE, IL-4 and IL-5 decreased in a dose-dependent manner. **Conclusions**: Food allergy aggravates immune dysregulation and gut microbiome dysbiosis in children with AD. *L. lactis* could be a candidate probiotic for the treatment of ADFA.

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Fig 1

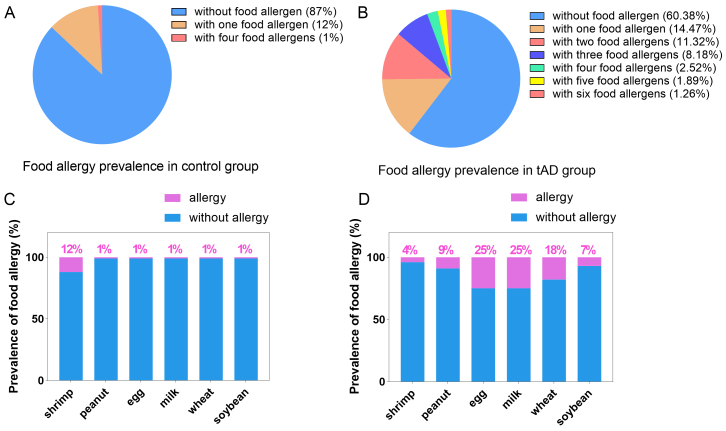


FIG 2

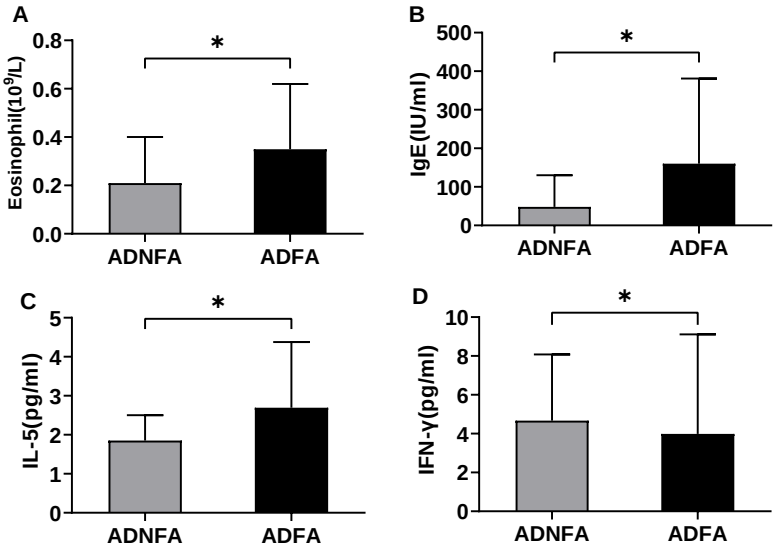


FIG 3

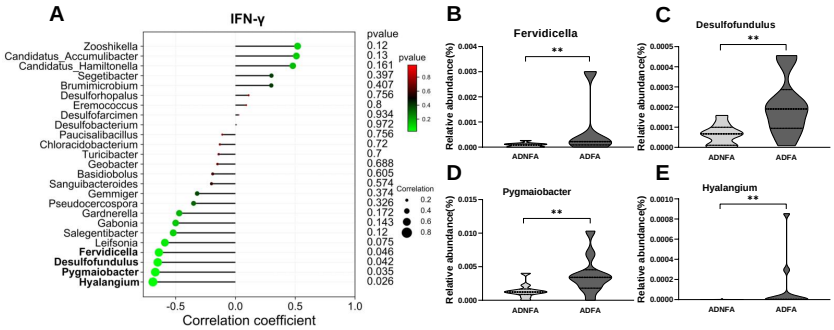


FIG 4

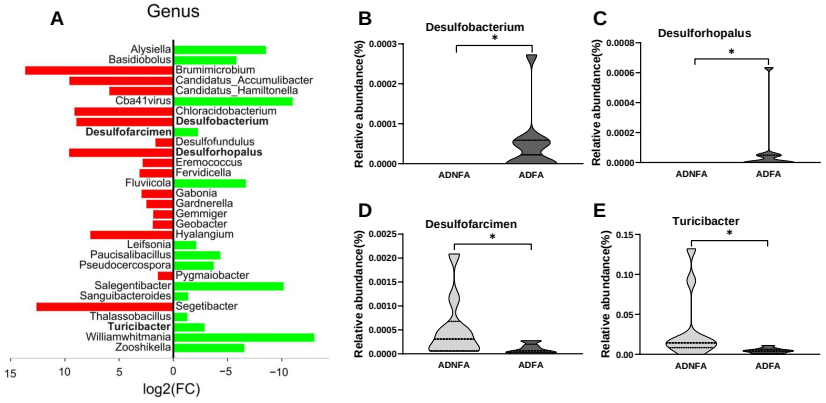


FIG 5

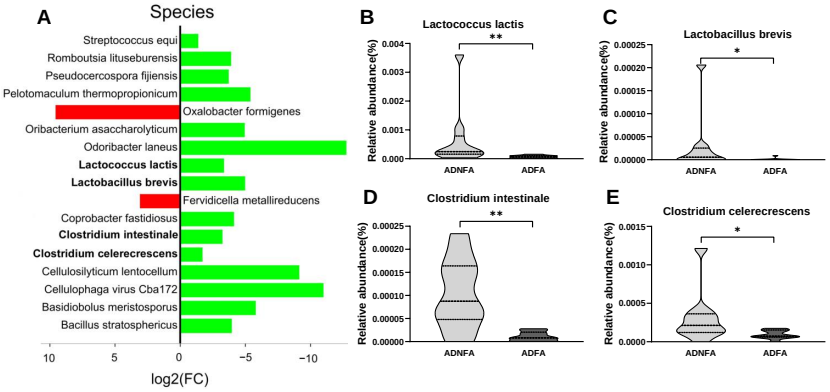
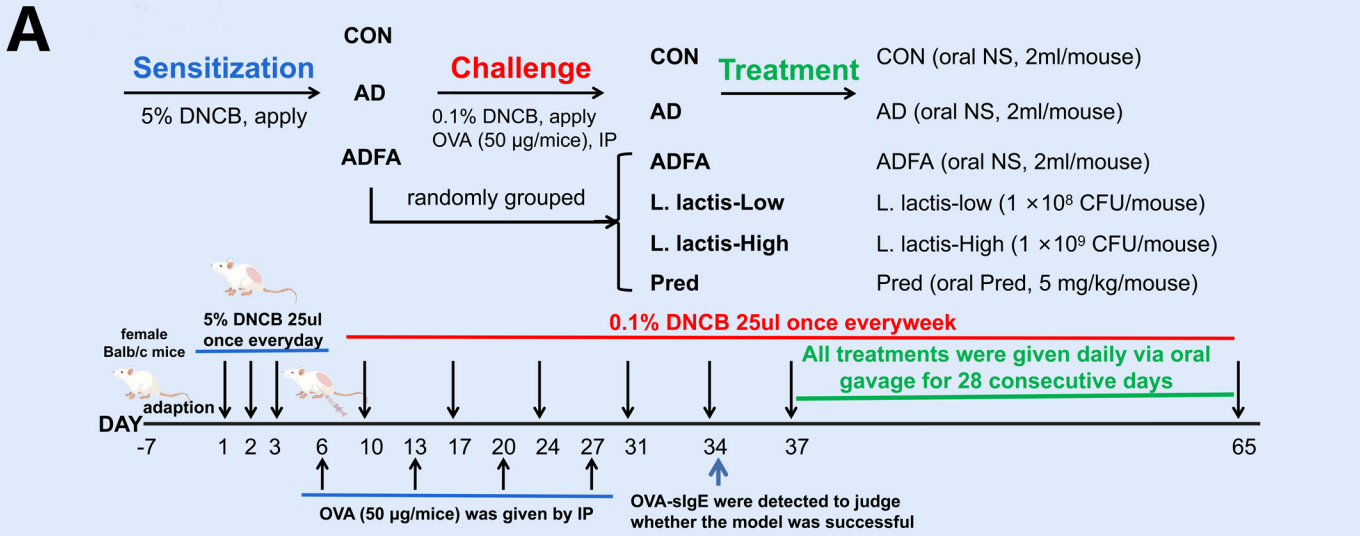
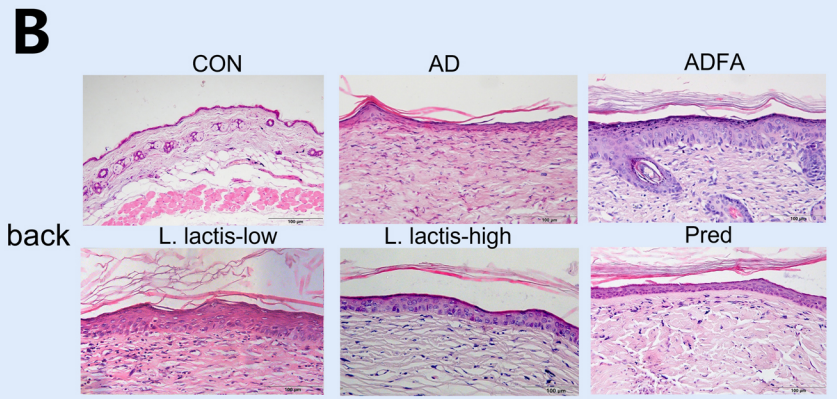
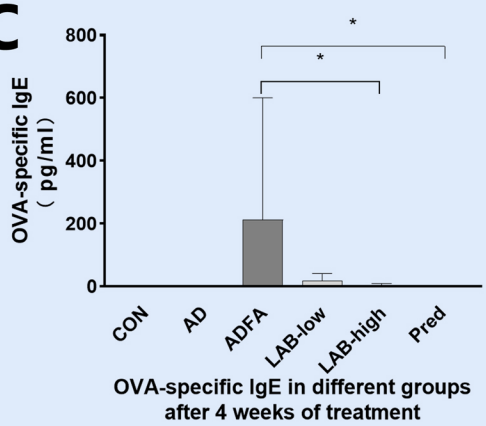
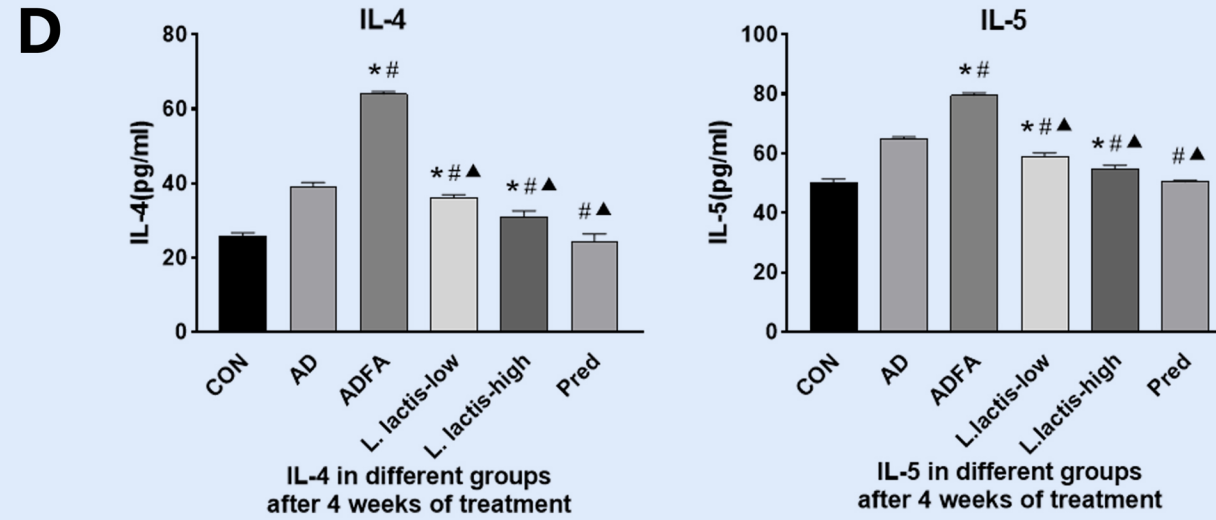


FIG 6


A
Sensitization
5% DNCB, apply
CON
AD
ADFA
Challenge
0.1% DNCB, apply
OVA (50 μg/mice), IP
randomly grouped
CON
AD
ADFA
L. lactis-Low
L. lactis-High
Pred
Treatment
CON (oral NS, 2ml/mouse)
AD (oral NS, 2ml/mouse)
ADFA (oral NS, 2ml/mouse)
L. lactis-low (1 ×10⁸ CFU/mouse)
L. lactis-High (1 ×10⁹ CFU/mouse)
Pred (oral Pred, 5 mg/kg/mouse)
female
Balb/c mice
5% DNCB 25ul
once everyday
0.1% DNCB 25ul once everyweek
All treatments were given daily via oral
gavage for 28 consecutive days
adaption
DAY
-7 1 2 3 6 10 13 17 20 24 27 31 34 37 65
OVA (50 μg/mice) was given by IP
OVA-sIgE were detected to judge
whether the model was successful


B
back
CON
AD
ADFA
L. lactis-low
L. lactis-high
Pred


C
OVA-specific IgE
(pg/ml)
800
600
400
200
0
*
*
CON
AD
ADFA
LAB-low
LAB-high
Pred
OVA-specific IgE in different groups
after 4 weeks of treatment


D
IL-4
IL-4(pg/ml)
80
60
40
20
0
*#
*#▲
*#▲
#▲
CON
AD
ADFA
L. lactis-low
L. lactis-high
Pred
IL-4 in different groups
after 4 weeks of treatment
IL-5
IL-5(pg/ml)
100
80
60
40
20
0
*#
*#▲
*#▲
#▲
CON
AD
ADFA
L.lactis-low
L.lactis-high
Pred
IL-5 in different groups
after 4 weeks of treatment