# ALERGIJE NA HRANU

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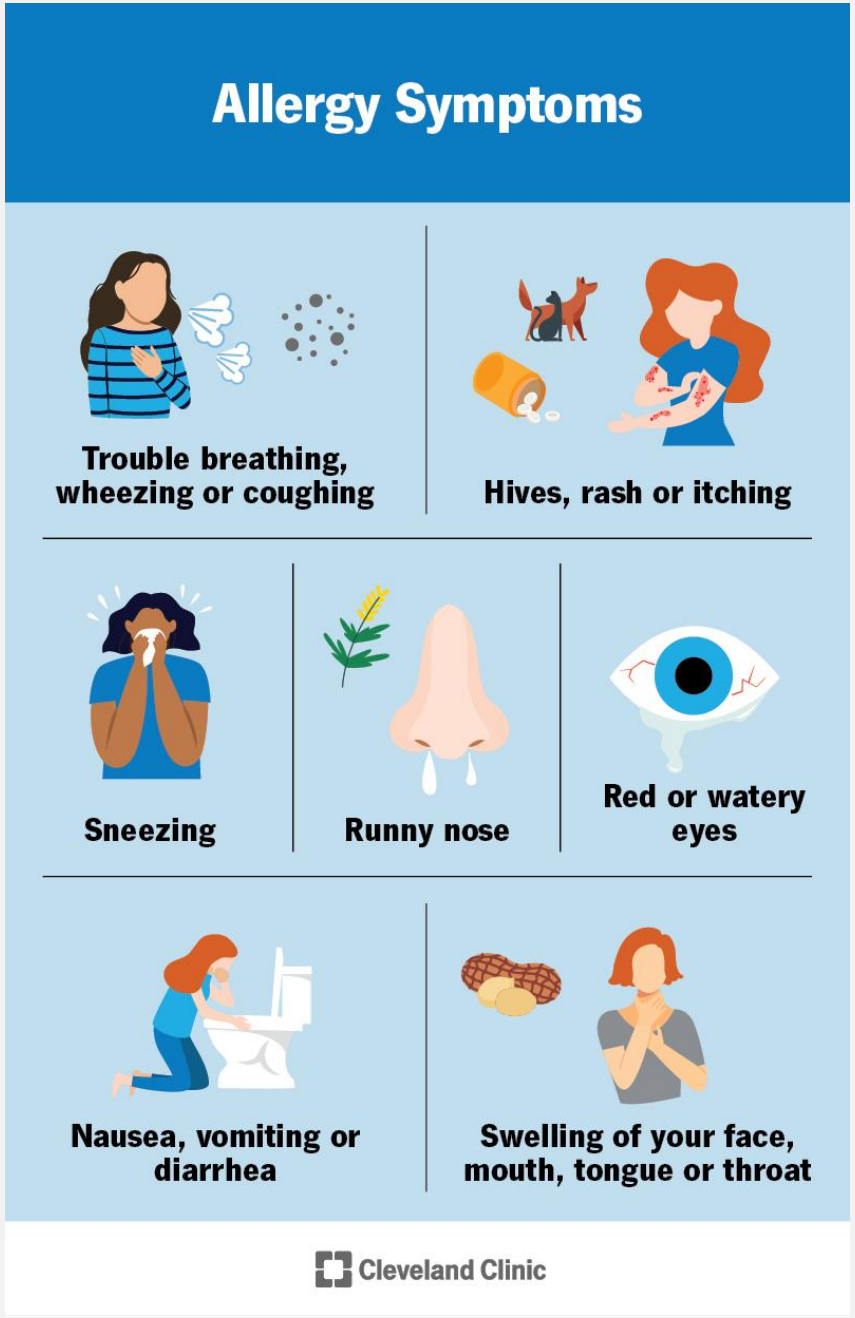
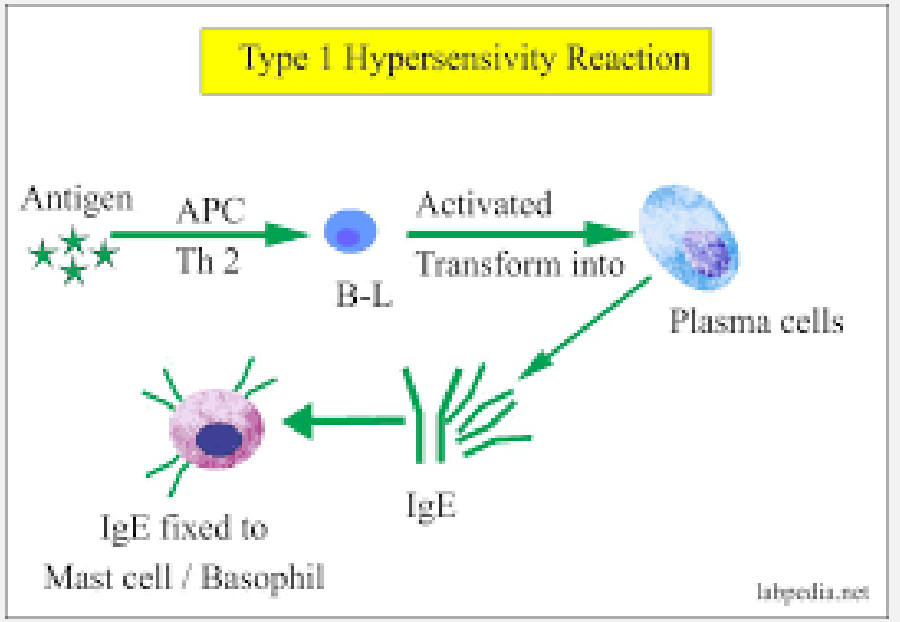
# ALERGIJA

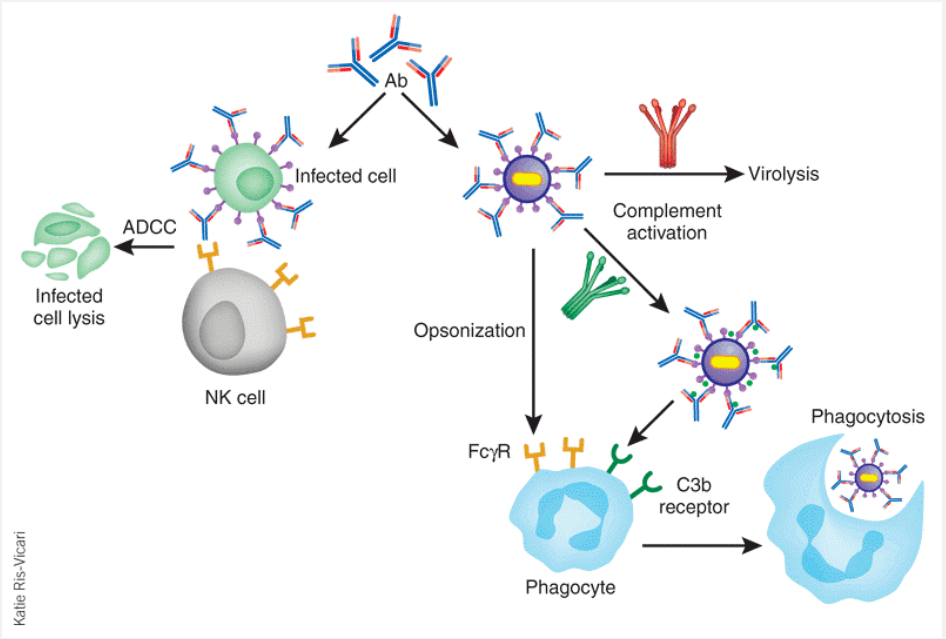
- Alergija – intenzivna reakcija imunosnog sustava na bezopasni antigen
- Antigen koji uzrokuje alergiju = alergen
- Razlog razvoja alergijskih reakcija – nepoznat
- Pretpostavka: okolični čimbenici (nečist zrak, aditivi u hrani, antibiotici u stočarstvu…) + genetski predispozirana osoba



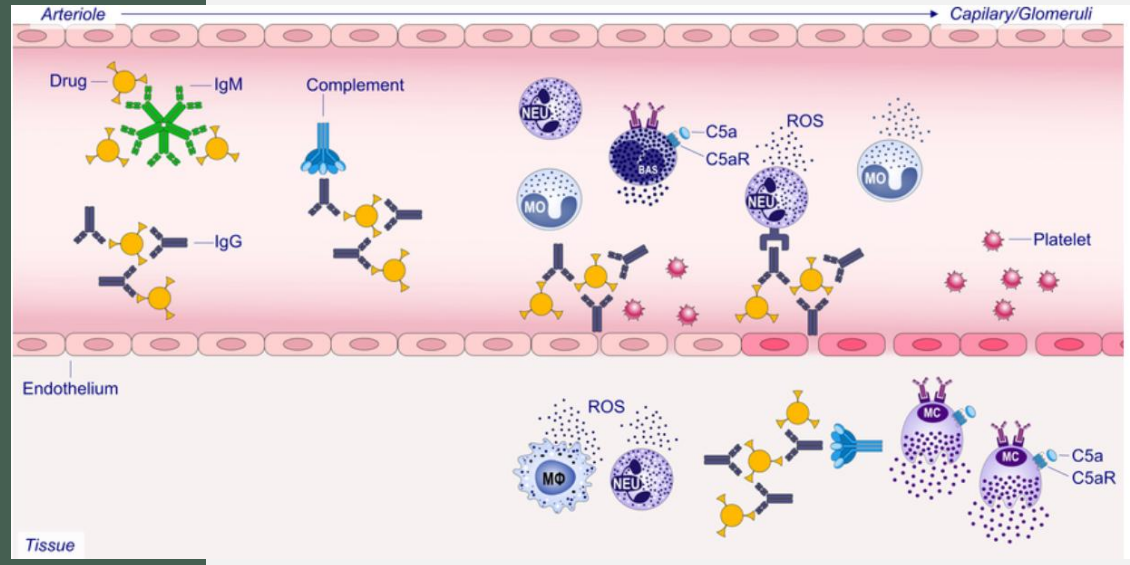
# REAKCIJE PREOSJETLJIVOSTI

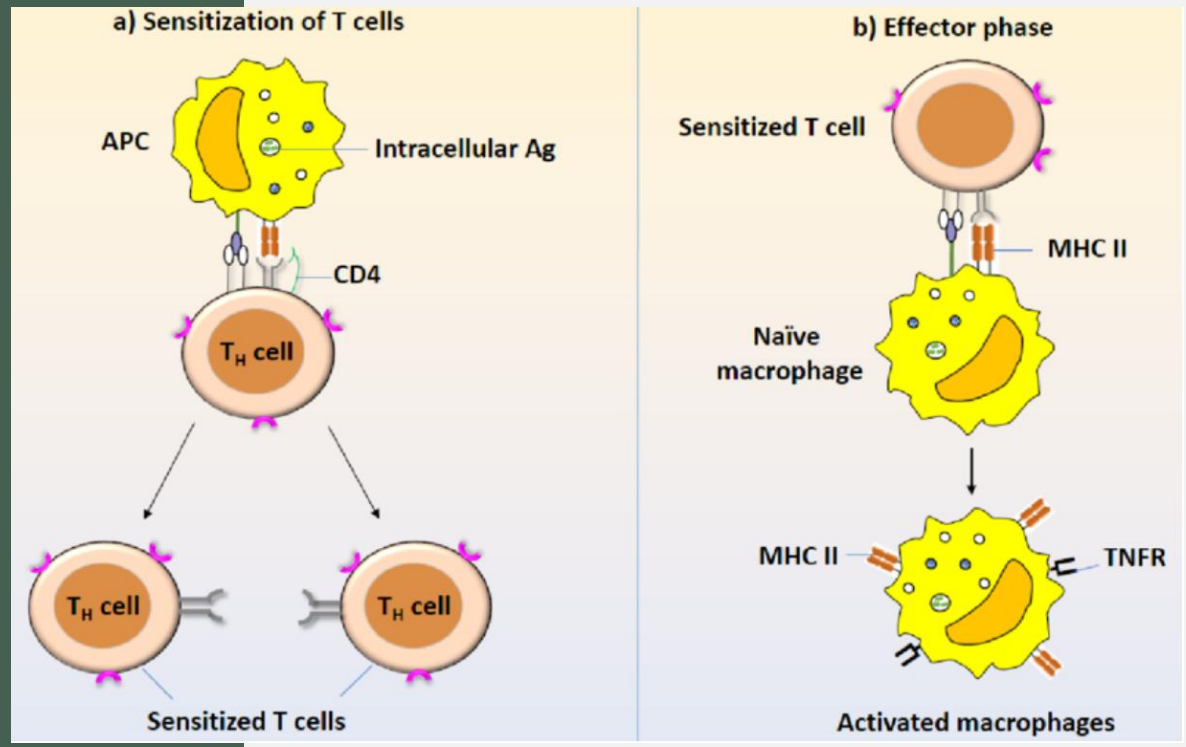
- Tradicionalno podijeljenje u četiri kategorije:
- Tip I – Anafilaktička preosjetljivost
  - Senzibilizacija na specifični alergen
  - Antitijela IgE, mastociti i bazofili
  - Npr. alergijska astma, alergijski rinitis, alergije na hranu
- Tip II – Citotoksična preosjetljivost ovisna o protutijelima
  - Vezanje antitijela IgM ili IgG na stanice – kompleks antitijelo-stanica
  - Aktivacija sustava komplementa i fagocita
  - Npr. hemolitička bolest novorođenčeta



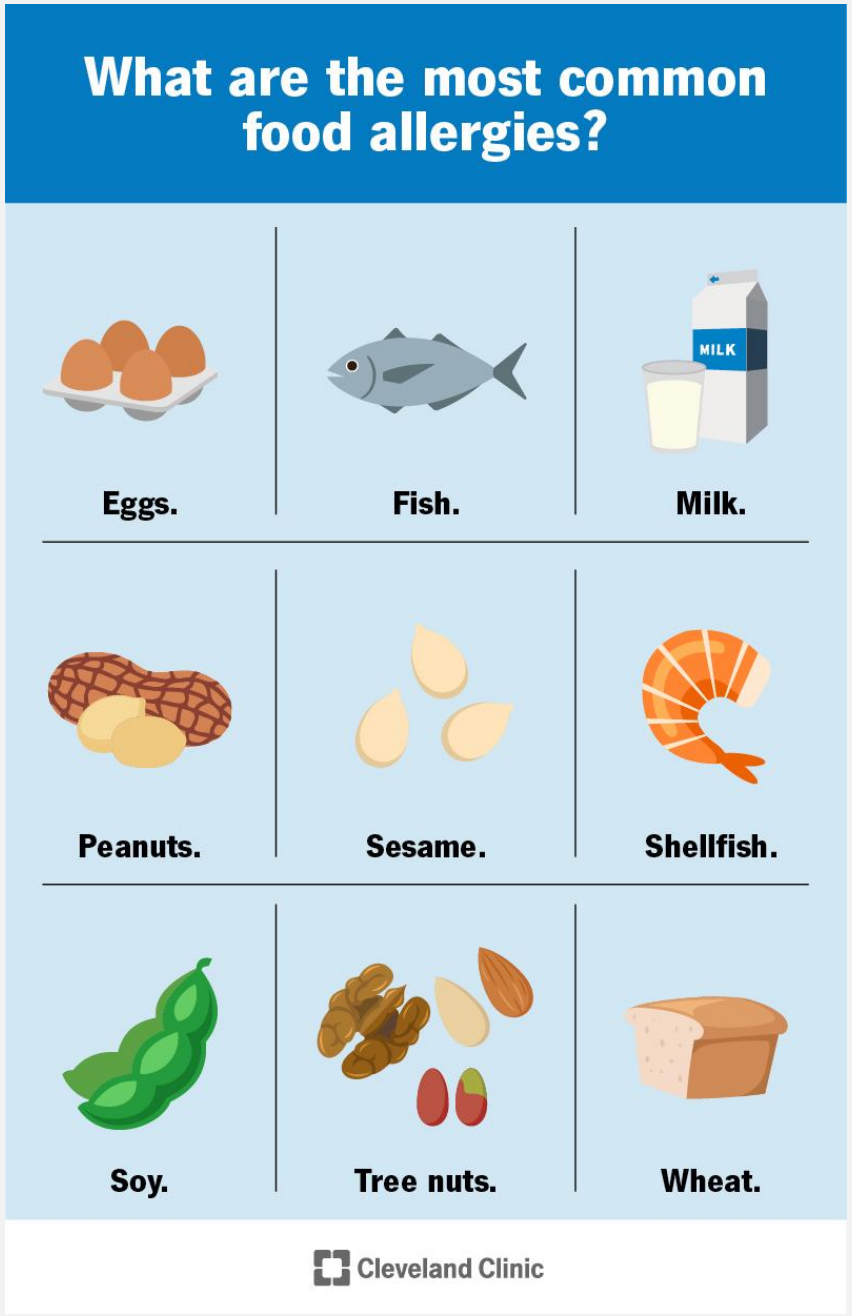
- Tip III – Preosjetljivost uzrokovana imunokompleksima
  - Reakcija antitijela i topljivih antigena – kompleks antitijelo-antigen
  - Receptori CR1 na eritrocitima
    - prepoznavanje kompleksa i odlazak u slezenu
  - Poticanje fagocitoze
  - Npr. reumatoidni artritis
- Tip IV – Preosjetljivost ovisna o stanicama
  - Limfociti T
  - Odgođena reakcija
  - Npr. odbacivanje transplantanta,



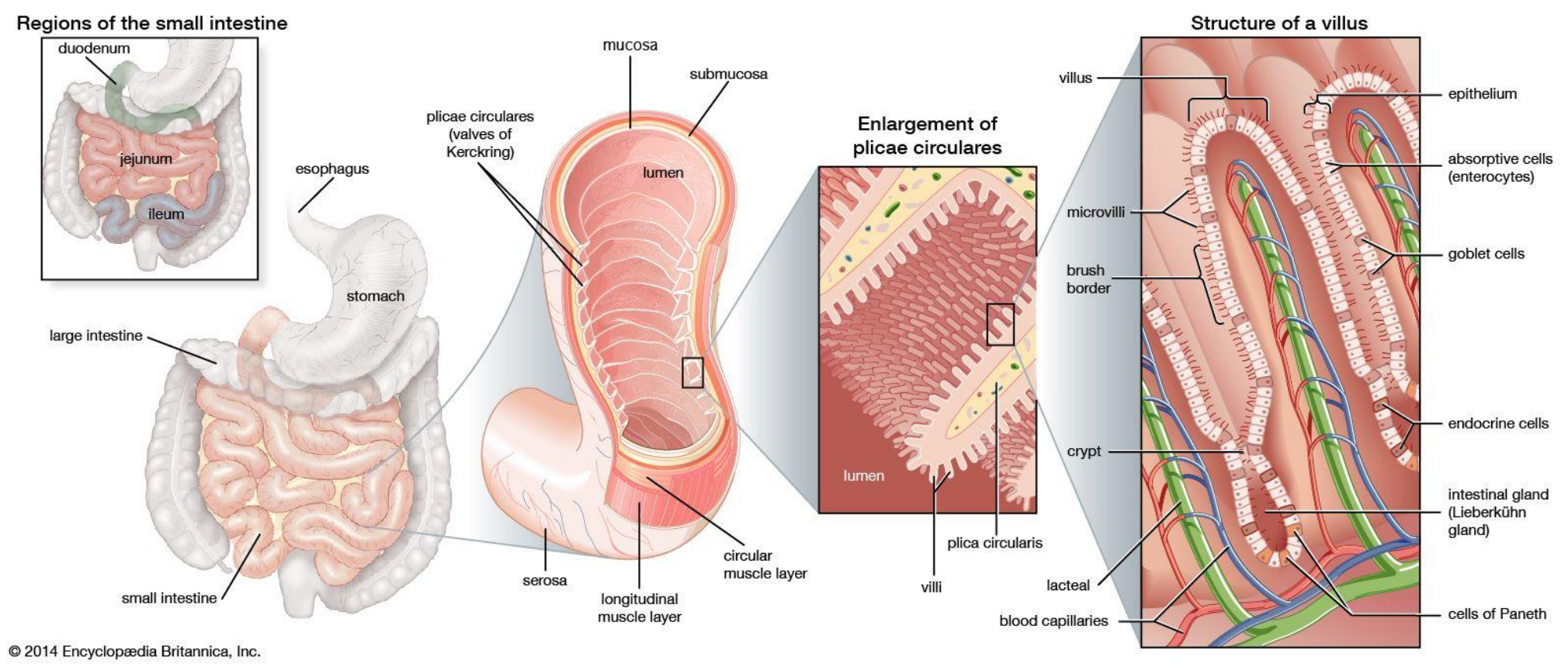



# ALERGENI PORIJEKLOM IZ HRANE

- 8 najčešćih:
  - kravlje mlijeko,
  - pšenica,
  - jaja,
  - soja,
  - kikiriki,
  - orašasti plodovi,
  - školjke i
  - riba

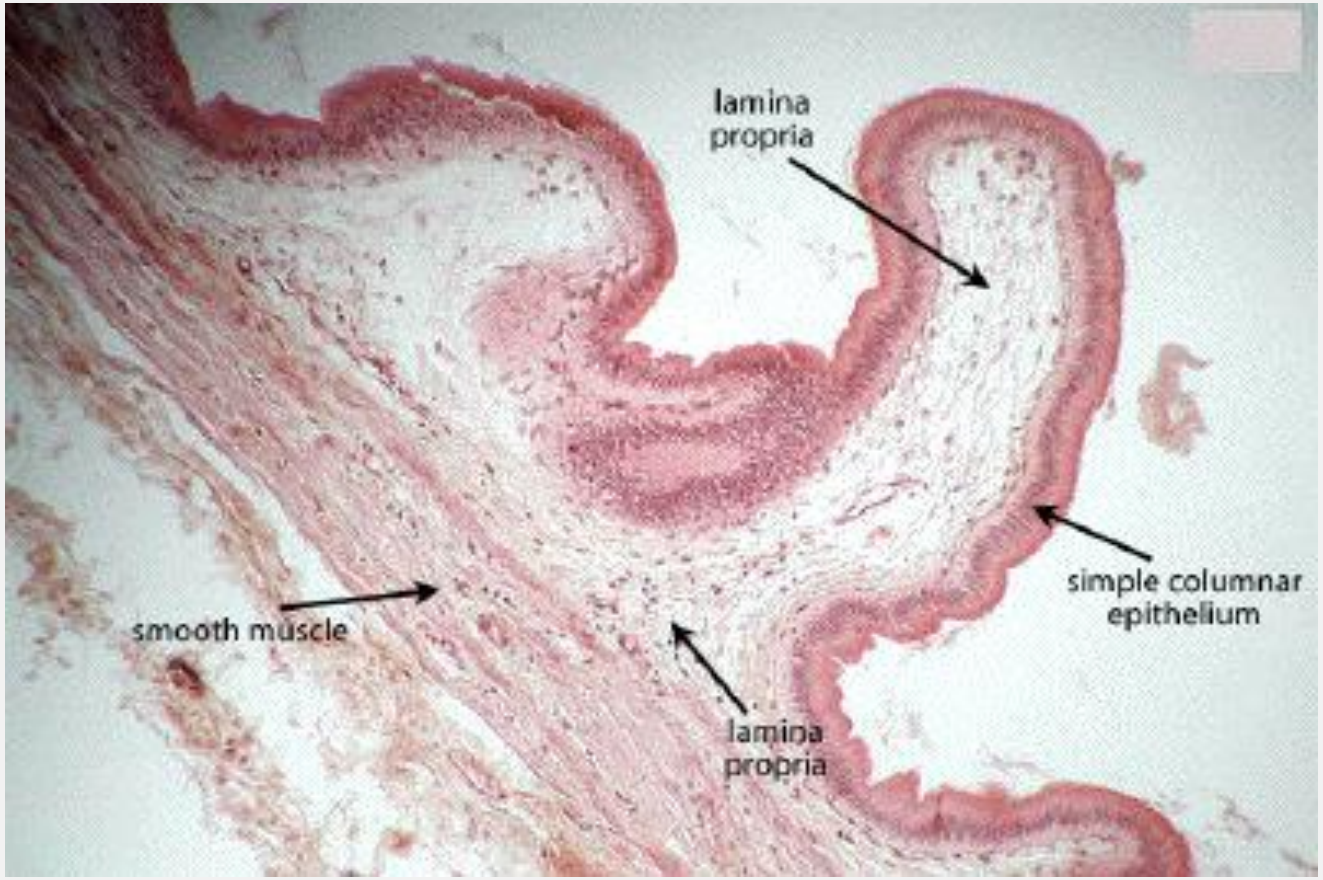


# PROBAVNI SUSTAV



# *LAMINA PROPRIA*

- IgA plazma stanice, γδ limfociti T, dendritične stanice (DC), urođeni limfociti (ILC), RORγt+ limfociti T
- GALT
- TGF-β, IL-10, indolamine-2,3-dioksigenaza DC-a potiču diferencijaciju naivnih limfocita T u Tregs – imunosna tolerancija
- Retinoična kiselina i kratkolančane masne kiseline mikroflore potiču diferencijaciju iTregs u RORγt+ Treg
- Bogata mikroflora = više RORγt+ Treg (20-30%)
- Limfociti B proizvode antitijela IgA i IgG4



# MIKROBIOTA

- Koljena Bacteroidota, Bacillota čine 90% sastava crijevne mikroflore
- Koljena Actinomycetes i Proteobacteria čine 1-5%
- Mikroflora potiče proizvodnju antitijela IgA – smanjena apsorpcija alergena
- *Clostridia* potiče limfocite T na lučenje IL-22 – jačanje epitelne barijere

Table 1: Comparison of changes in intestinal microbiota between food allergic and normal subjects.

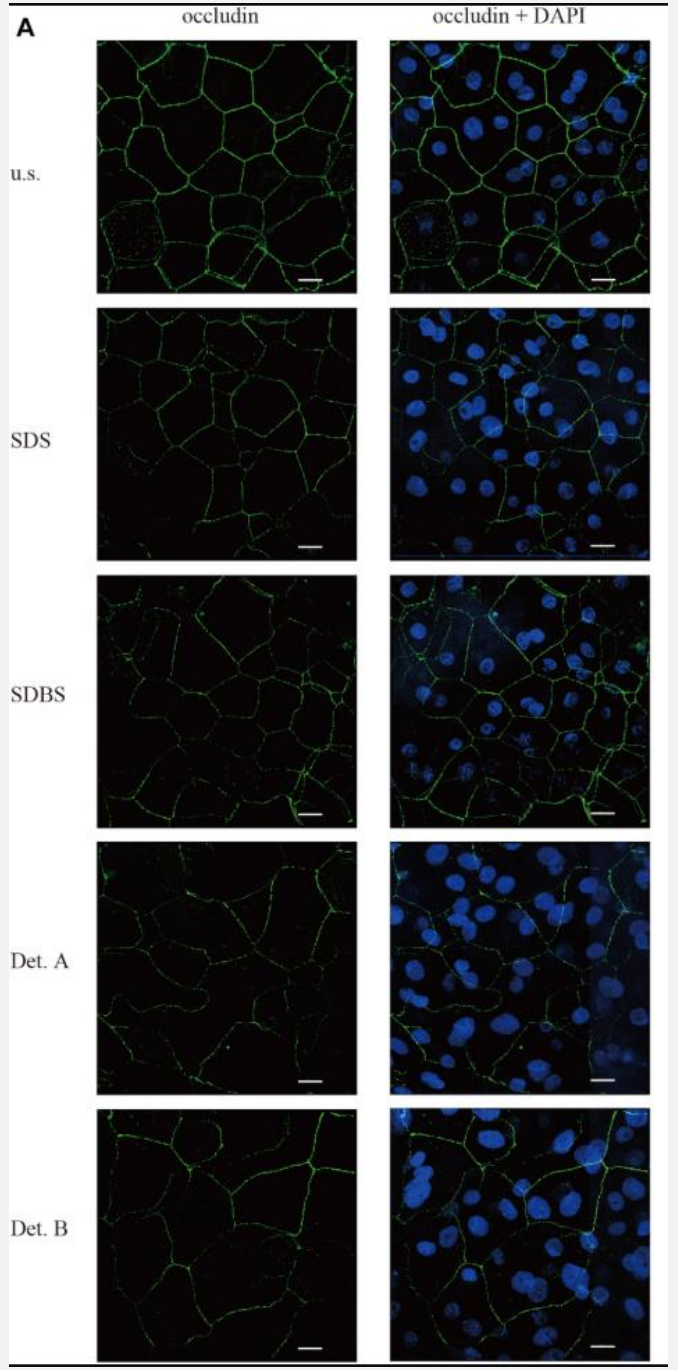
| Source organism | Features of gut microbial community | | Reference |
|---|---|---|---|
| | Decrease | Increase | |
| Human | *Bacteroidetes* (P), *Bacteroides* (G), *Parabacteroides* (G), *Prevotella* (G), *Alistipes* (G), *Streptococcus* (G), *Veillonella* (G), *Bacteroides* (S), *Prevotella* (S), and *Veillonella* (S) | *Firmicutes* (P), *Actinobacteria* (P), *Proteobacteria* (P), *Sphingomonas* (G), *Sutterella* (G), *Bifidobacterium* (G), *Collinsella* (G), *Clostridium sensu stricto* (G), *Clostridium IV* (G), *Enterococcus* (G), *Lactobacillus* (G), *Roseburia* (G), *Faecalibacterium* (G), *Ruminococcus* (G), *Subdoligranulum* (G), *Akkermansia* (G), and *Subdoligranulum* (S) | [19] |
| Human | *Bacteroidetes* (P) | *Firmicutes* (P) | [22] |
| Human | *Bacteroidetes* (P), *Proteobacteria* (P), *Actinobacteria* (P), *Verrucomicrobia* (P), *Bacteroides* (G), *Streptococcus* (G), *Veillonella* (G), *Klebsiella* (G), *Blautia* (G), *Clostridium XI* (G), *Lachnospiracea incertae sedis* (G), and *Megasphaera* (G) | *Firmicutes* (P), *Fusobacteria* (P), *Enterococcus* (G), *Escherichia/Shigella* (G), *Lactobacillus* (G), *Staphylococcus* (G), *Faecalibacterium* (G), *Clostridium XIVa* (G), *Anaerostipes* (G), *Prevotella* (G), *Clostridium XVIII* (G), and *Flavonifractor* (G) | [18] |
| Human | *Leuconostoc* (G) | *Firmicutes* (P), *Verrucomicrobia* (P), *Ruminococcus* (G), *Lactococcus* (G), and *Leuconostoc* (G) | [24] |
| Human | *Bifidobacterial* (G) and *Enterobacteria* (G) | *Lactobacilli* (G) | [13] |
| Human | *Leuconostoc* (G), *Weissella* (G), and *Veillonella* (G) | *Clostridium* (G) | [25] |
| Mouse | *Firmicutes* (F), *Erysipelotrichi* (C), *Erysipelotrichales* (O), and *Erysipelotrichaceae* (F) | *Proteobacteria* (P), *Gammaproteobacteria* (C), *Enterobacteriales* (O), and *Enterobacteriaceae* (F) | [26] |
| Mouse | *Verrucomicrobia* (P) and *Proteobacteria* (P) | *Bacteroidetes* (P) and *Patescibacteria* (P) | [27] |

The increased/decreased microbiota in food allergic group when compared with normal group.

- Preuzeto iz Ning i sur. 2022.

# HIPOTEZA EPITELNE BARIJERE

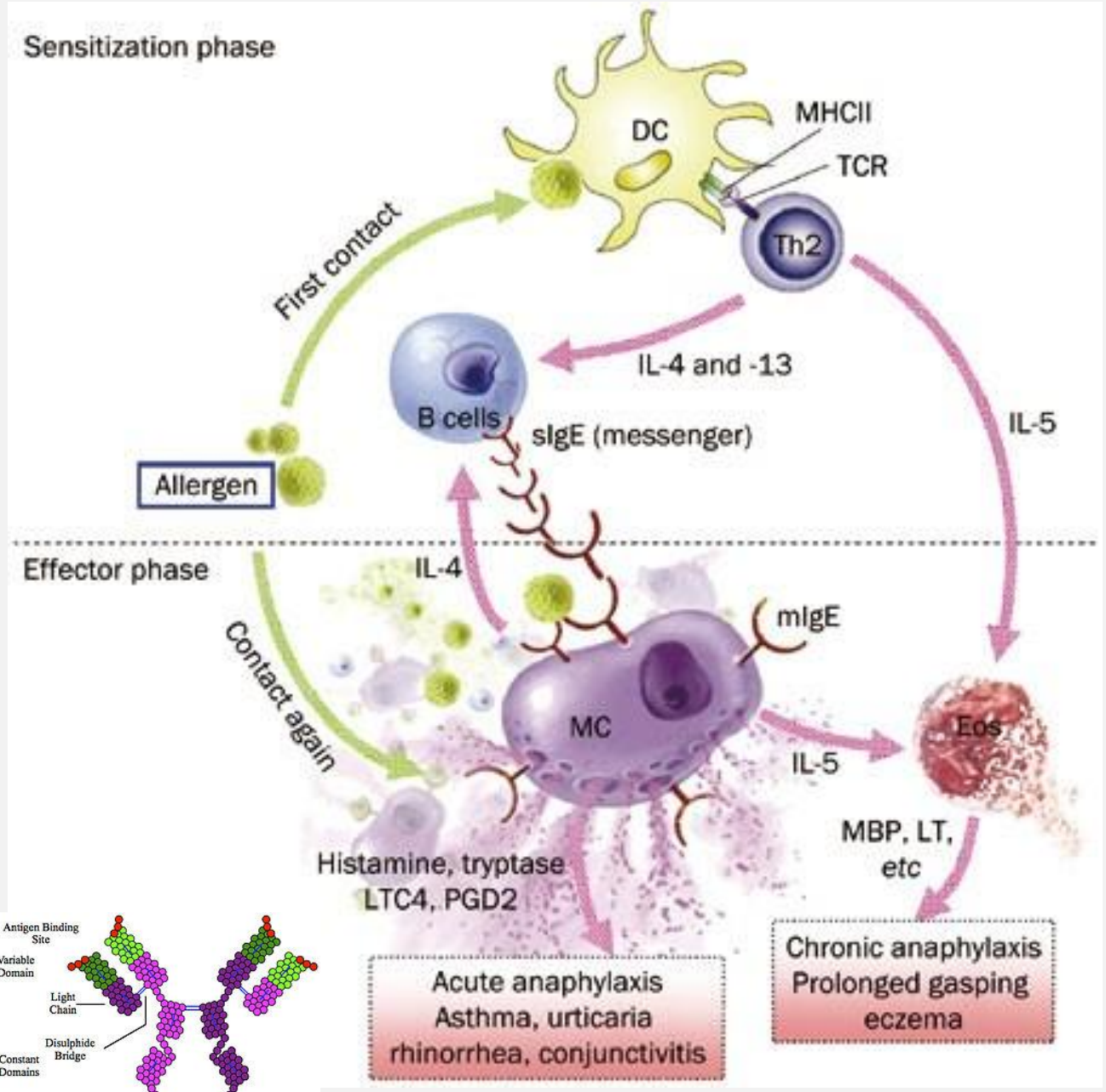
- Eksperiment na kulturi keratinocita čovjeka
- Utjecaj deterdženata na čvrste spojeve (TJ, engl. *tight junctions*)

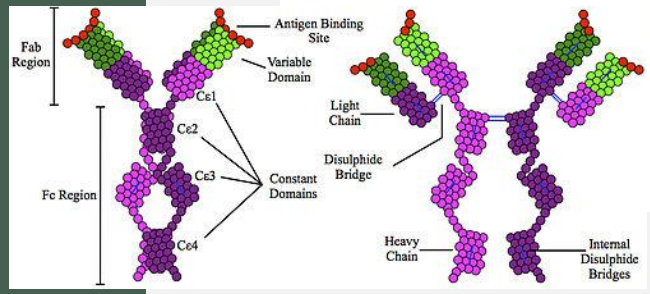


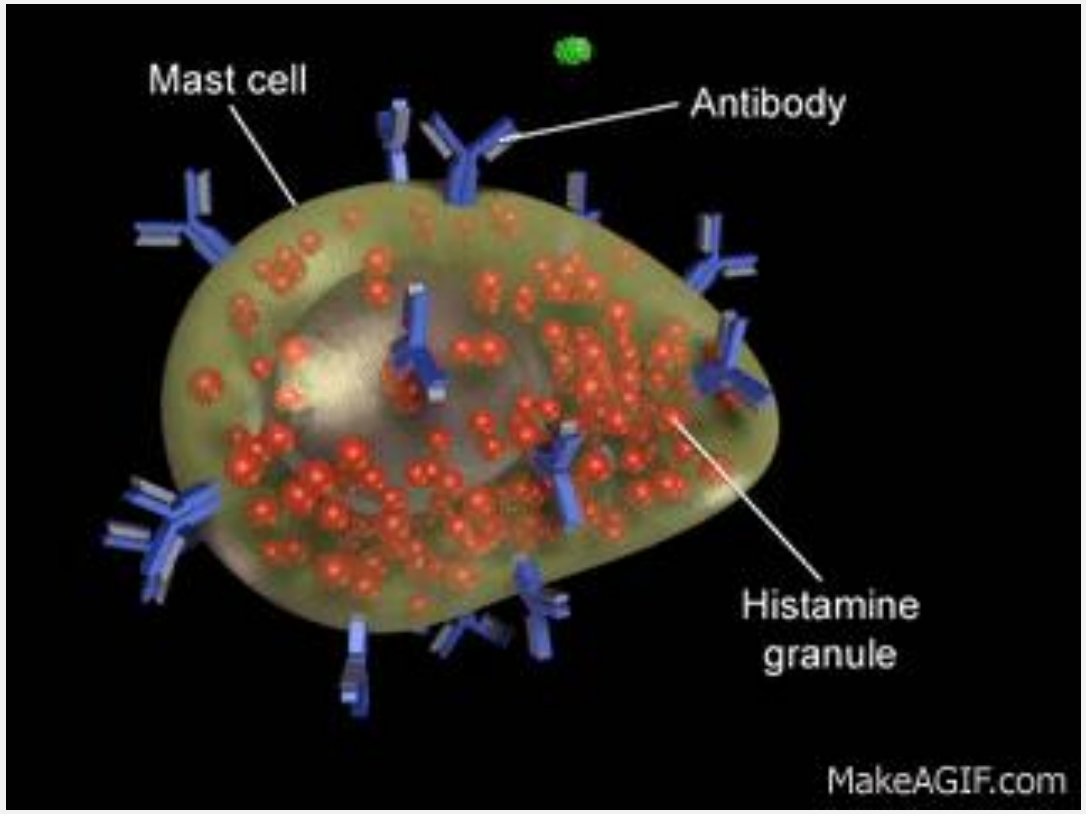

- Preuzeto iz Xian i sur. 2016.

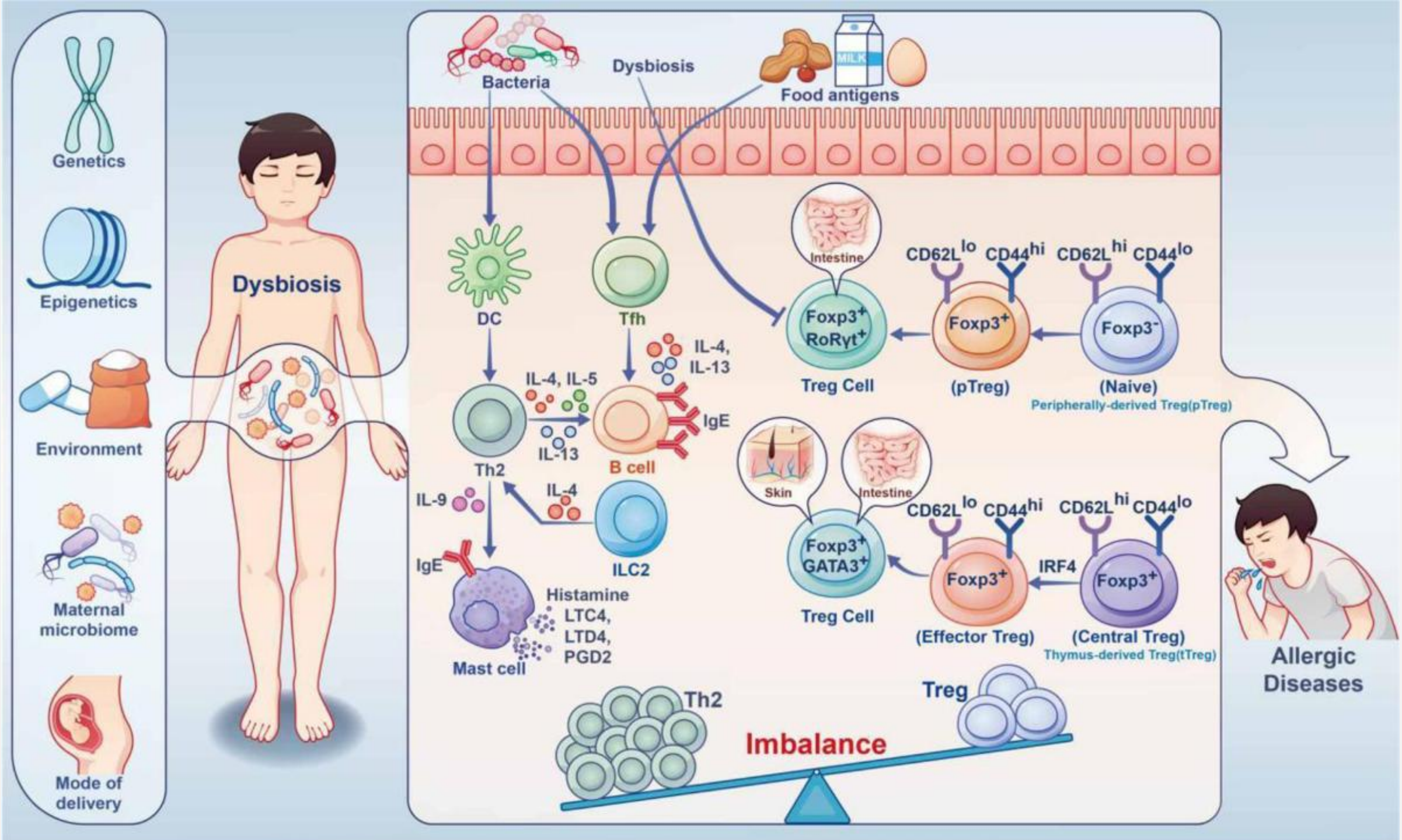
# MEHANIZAM

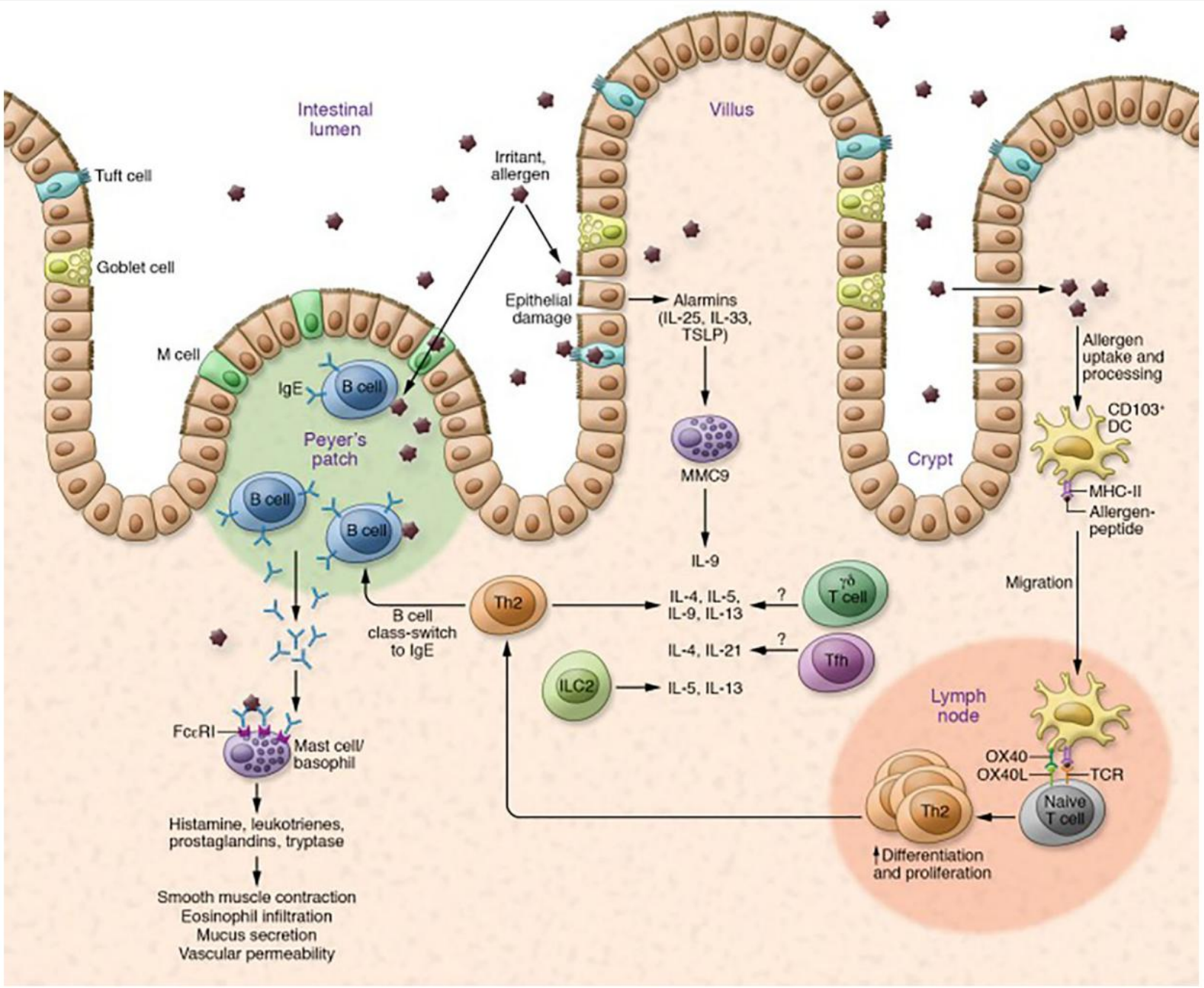
- Prvotno izlaganje alergenu – epitelne stanice luče alarmine (IL-25 i IL-33)
- IL-33 potiče sintezu liganda OX40L DC-a
- Odlazak u limfni čvor – diferencijacija CD4+ naivnih T limfocita u alergen-specifične Th2
- Th2 luče citokine IL-4, IL-5, IL-9 i IL-13
- Prekapčanje razreda limfocita B
- Antitijela IgE vežu na receptore FcεRI mastocita i bazofila
- Senzibilizacija
- Ponovna izloženost alergenu – epitope alergena veže na antitijela IgE
- Degranulacija mastocita i bazofila – histamin i heparin




Mast cell
Antibody
Histamine granule
MakeAGIF.com

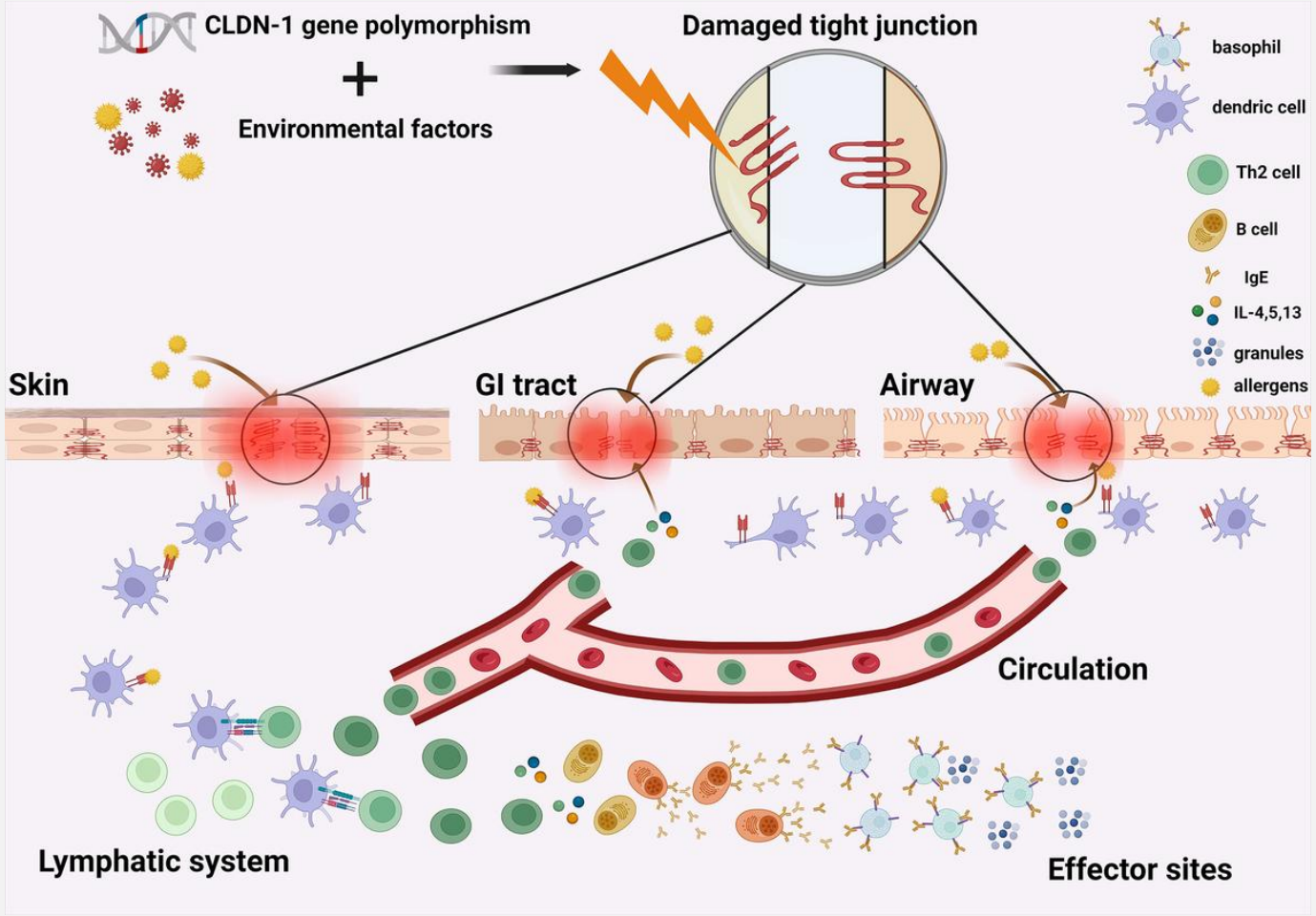

Genetics
Epigenetics
Environment
Maternal microbiome
Mode of delivery
Dysbiosis
Bacteria
Dysbiosis
Food antigens
MILK
DC
Tfh
Intestine
CD62L lo CD44 hi
CD62L hi CD44 lo
Foxp3+ RoRγt+
Foxp3+
Foxp3-
Treg Cell
(pTreg)
(Naive)
Peripherally-derived Treg(pTreg)
IL-4, IL-13
IL-4, IL-5
IL-13
IgE
Th2
B cell
IL-9
IL-4
IgE
ILC2
Mast cell
Histamine
LTC4,
LTD4,
PGD2
Skin
Intestine
Foxp3+ GATA3+
IRF4
Treg Cell
(Effector Treg)
(Central Treg)
Thymus-derived Treg(tTreg)
Th2
Treg
Imbalance
Allergic Diseases




- Preuzeto iz Hund i sur. 2025.

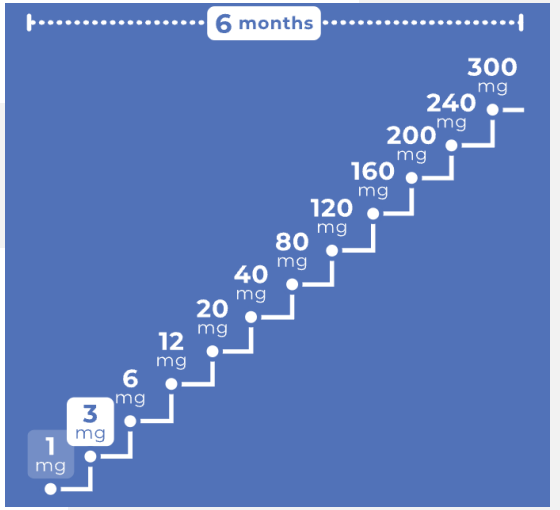
# GENETIKA

- Mutacije u genu *Claudin 1* (*CLDN1*) – osnovni protein za zdrave TJ
- Mutacije u genu *Filaggrin (FLG)* – strukturni protein kože
- Mutacije u genima HLA (engl. *human leukocyte antigen*)
  - Npr. mutacija u *HLA DQB1* i koleracija s alergijom na kikiriki



# LIJEČENJE

- Dijagnostika: OFC (engl. *oral food challenge*) te kožni test
- Imunoterapija specifična za alergen – EPIT (engl. *epicutaneous immunotherapy* ) i SLIT (engl. *sublingual immunotherapy*)
- Palforzia – tablete specifične za alergiju na kikiriki
- Omalizumab – anti IgE antitijela
- Potencijalna primjena cjepiva, nanočestica, inhibitora kinaza
- Epipen – epinefrin (adrenalin)





# HVALA NA PAŽNJI!

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