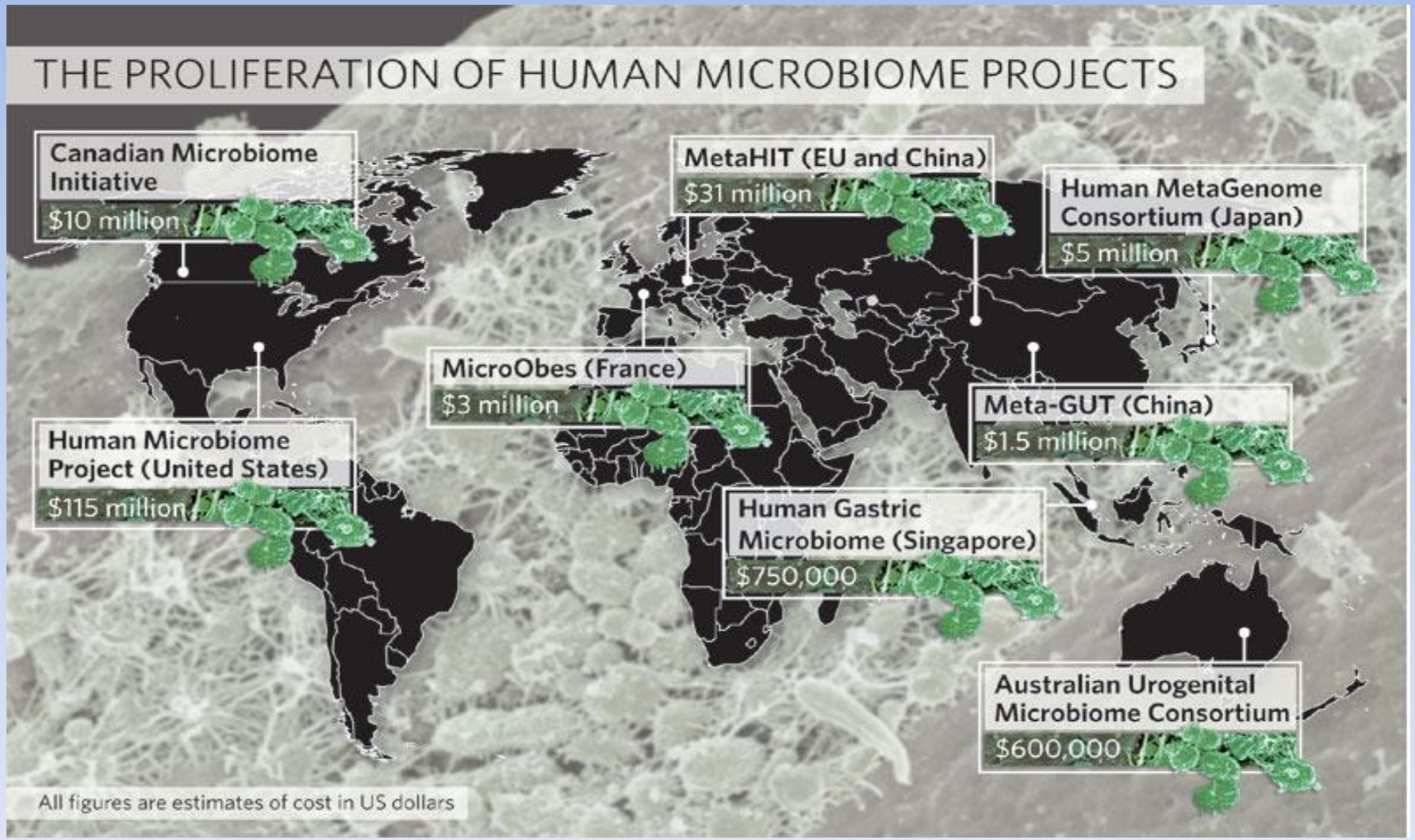
MICROBIOMA E IMMUNITA’

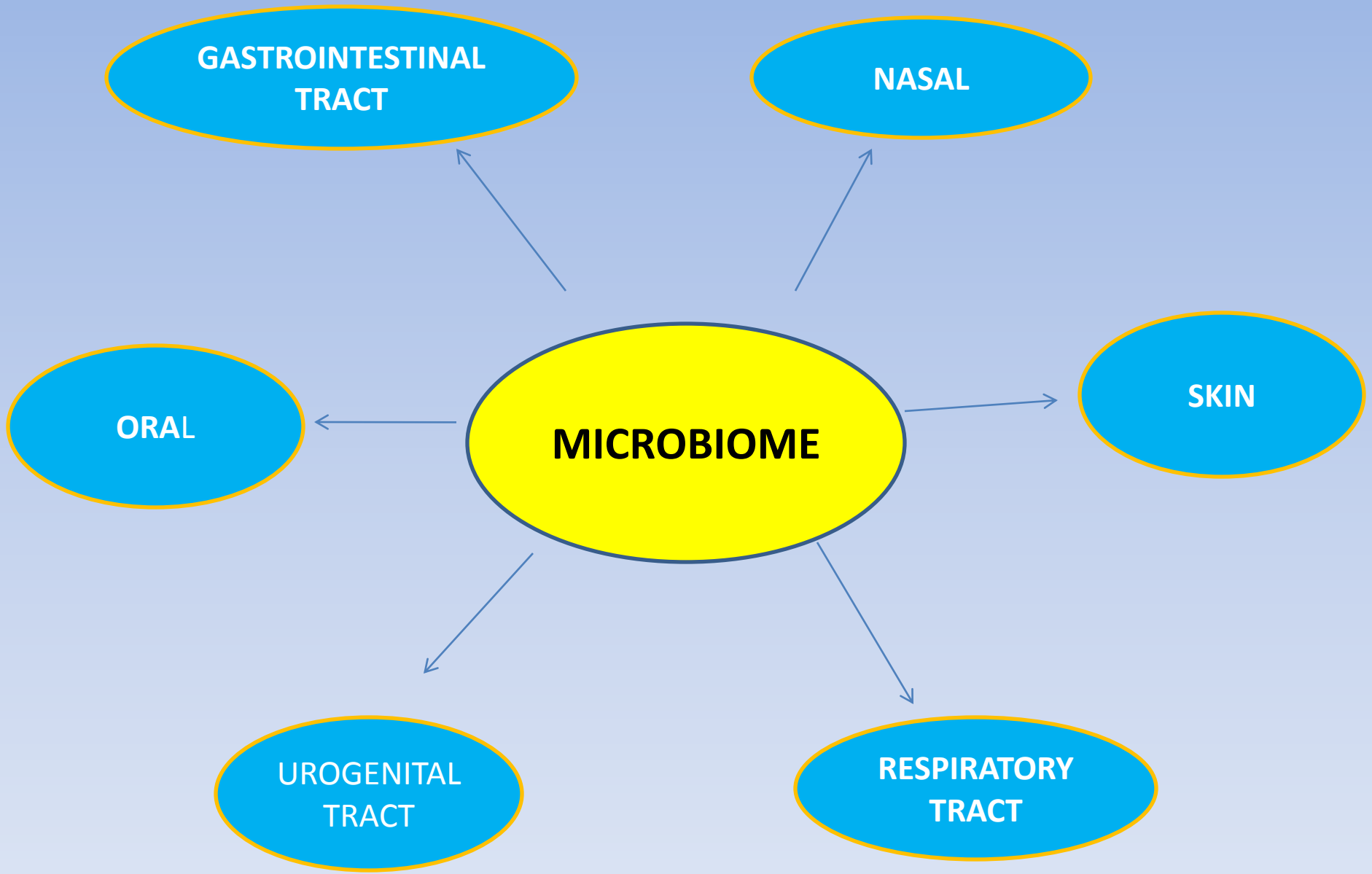
LORENZO EMMI

Human Microbiome Project

The Human Microbiome Project has characterized the microbial communities found at several different sites on the human body.

Human Microbiome Project

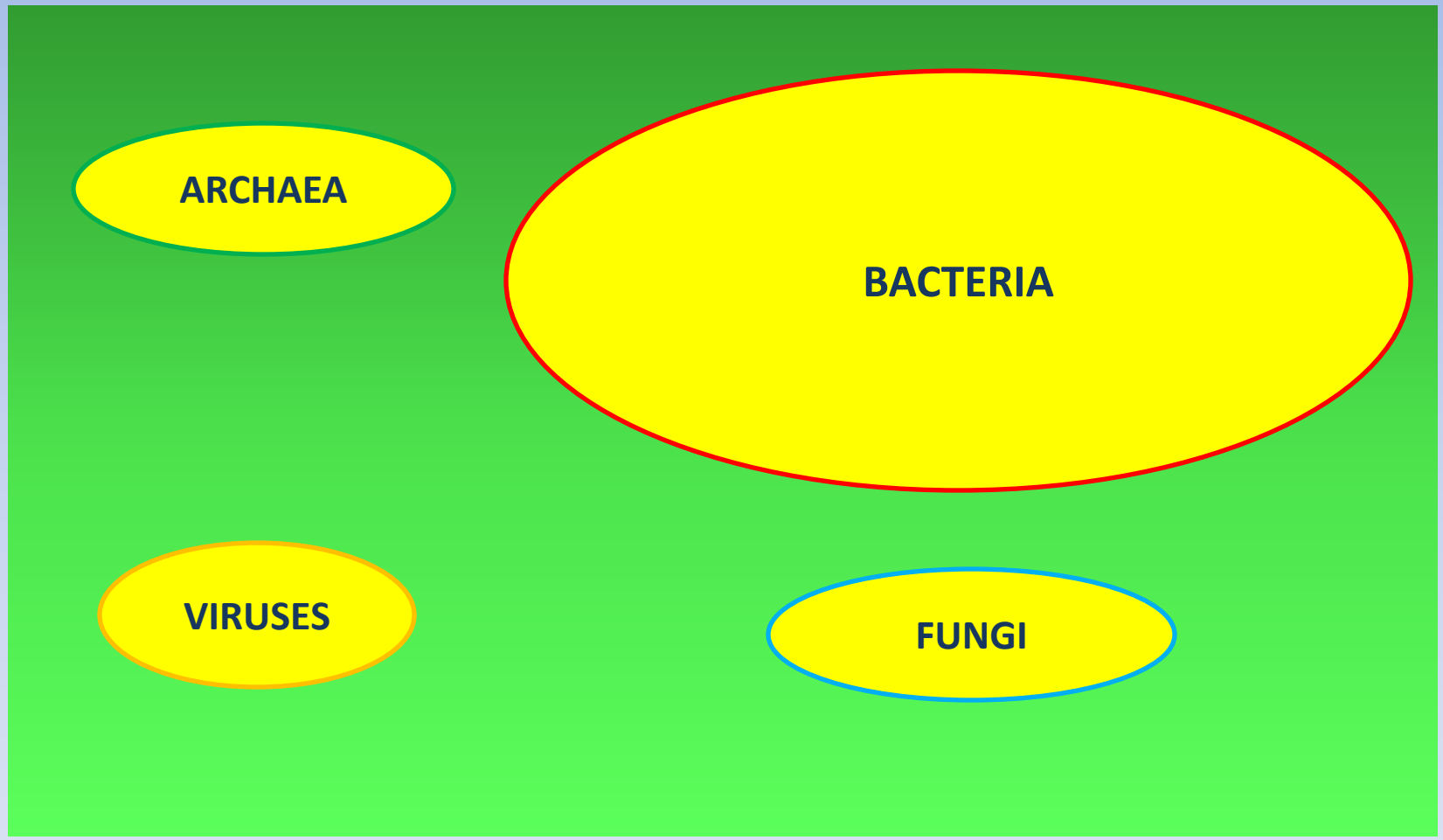



GASTROINTESTINAL TRACT
NASAL
ORAL
MICROBIOME
SKIN
UROGENITAL TRACT
RESPIRATORY TRACT

GUT MICROBIOME

Human gastrointestinal tract is known to host trillions of microbs, the number of which reaches approximately 10^{14} cells in the entire gut of a healthy individual.

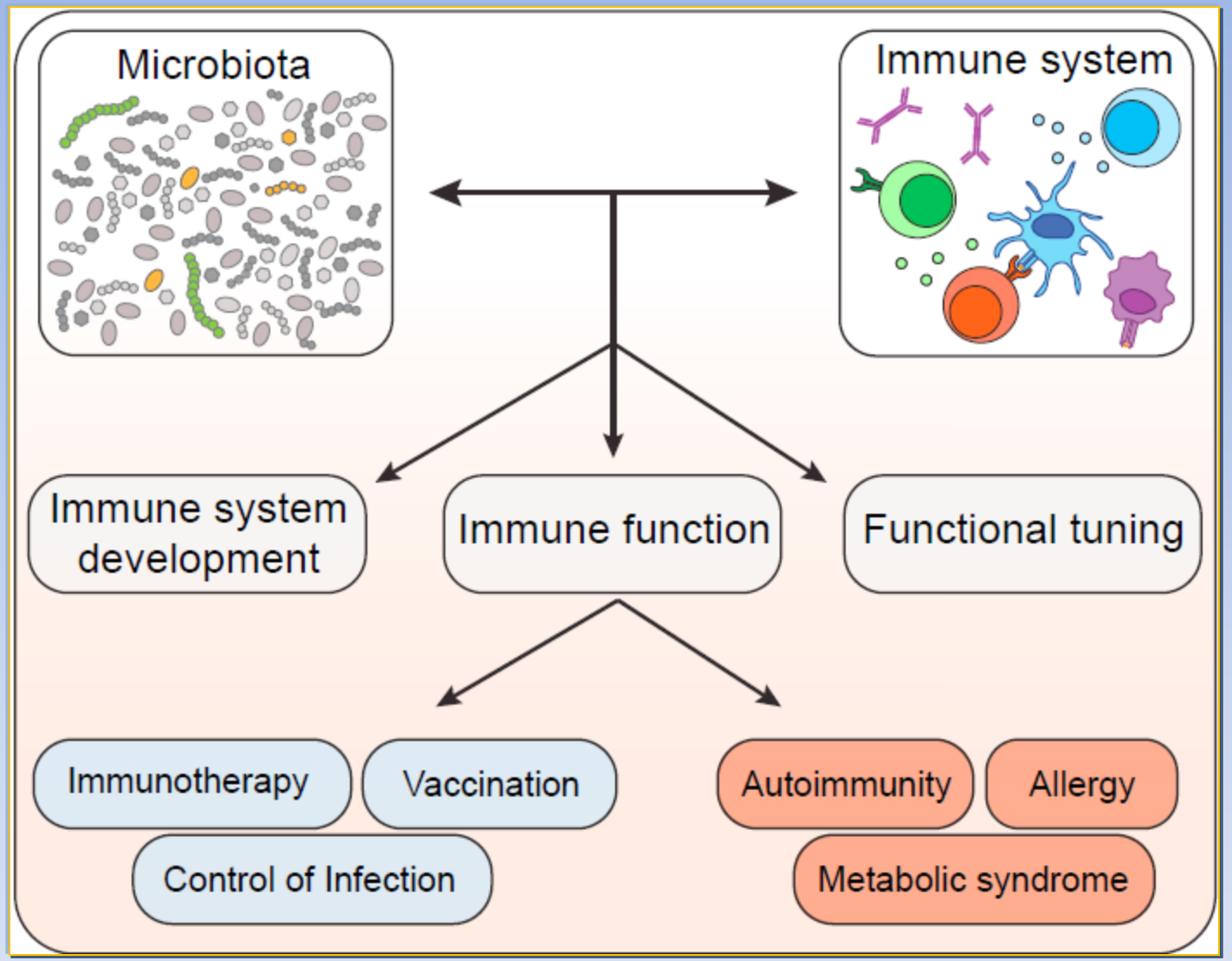
COMPOSITION OF GUT MICROBIOME



Functions of Microbiota-derived metabolites

- Microbiota-derived metabolites can have several functions:
- Anti-inflammatory activity
- Anti-oxidant activity
- Pain relief activity
- Regulation of gut barrier function
- Production of vitamins or energy sources.
- Modulation of immune system
- For example, butyrate, which is produced by bacterial fermentation of dietary fibres, can serve as energy source for colonocytes and can increase satiety.

Microbiome and Immune System



Homeostatic Immunity and the Microbiota, Yasmine Belkaid et al., Immunity Review, 2017

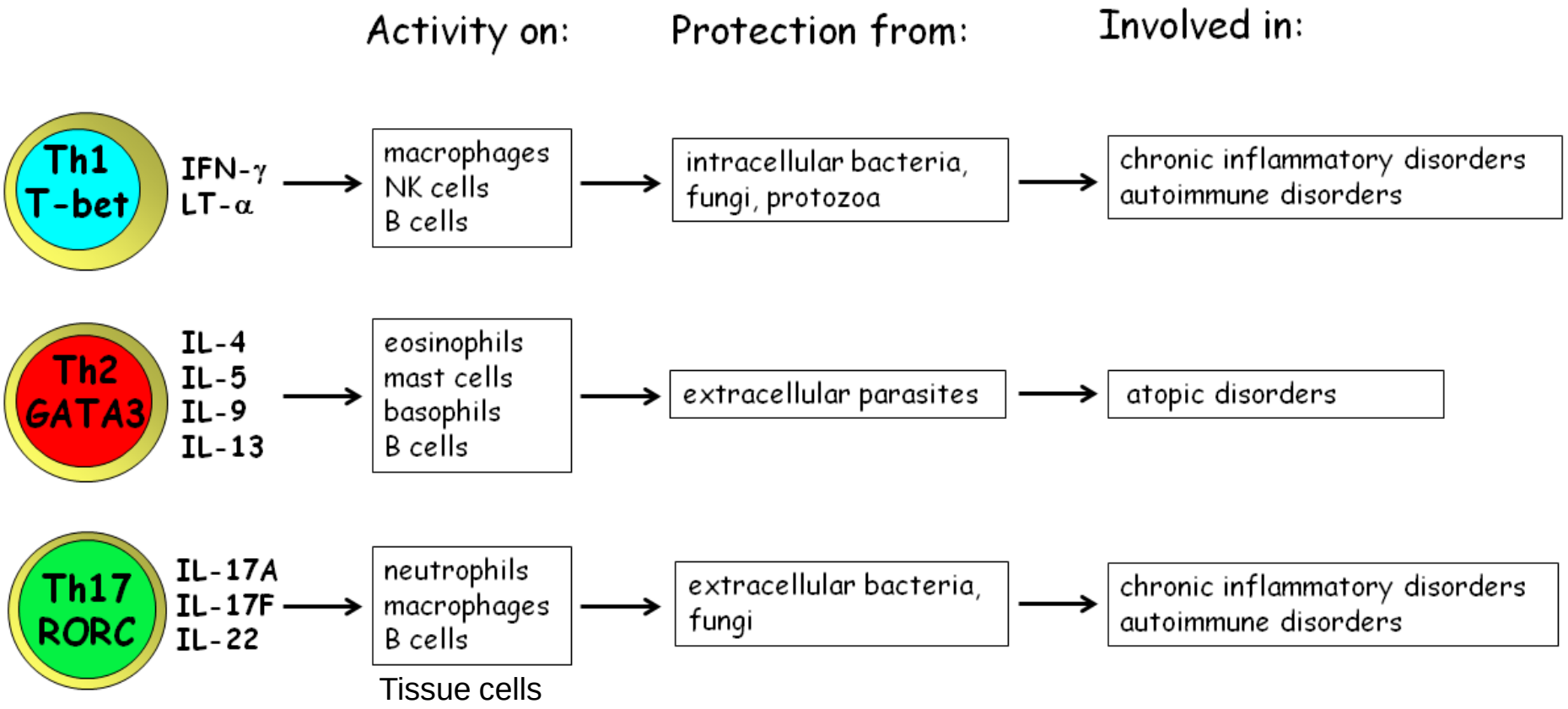
How does the immune system tolerate the microbiome?

Possible mechanisms

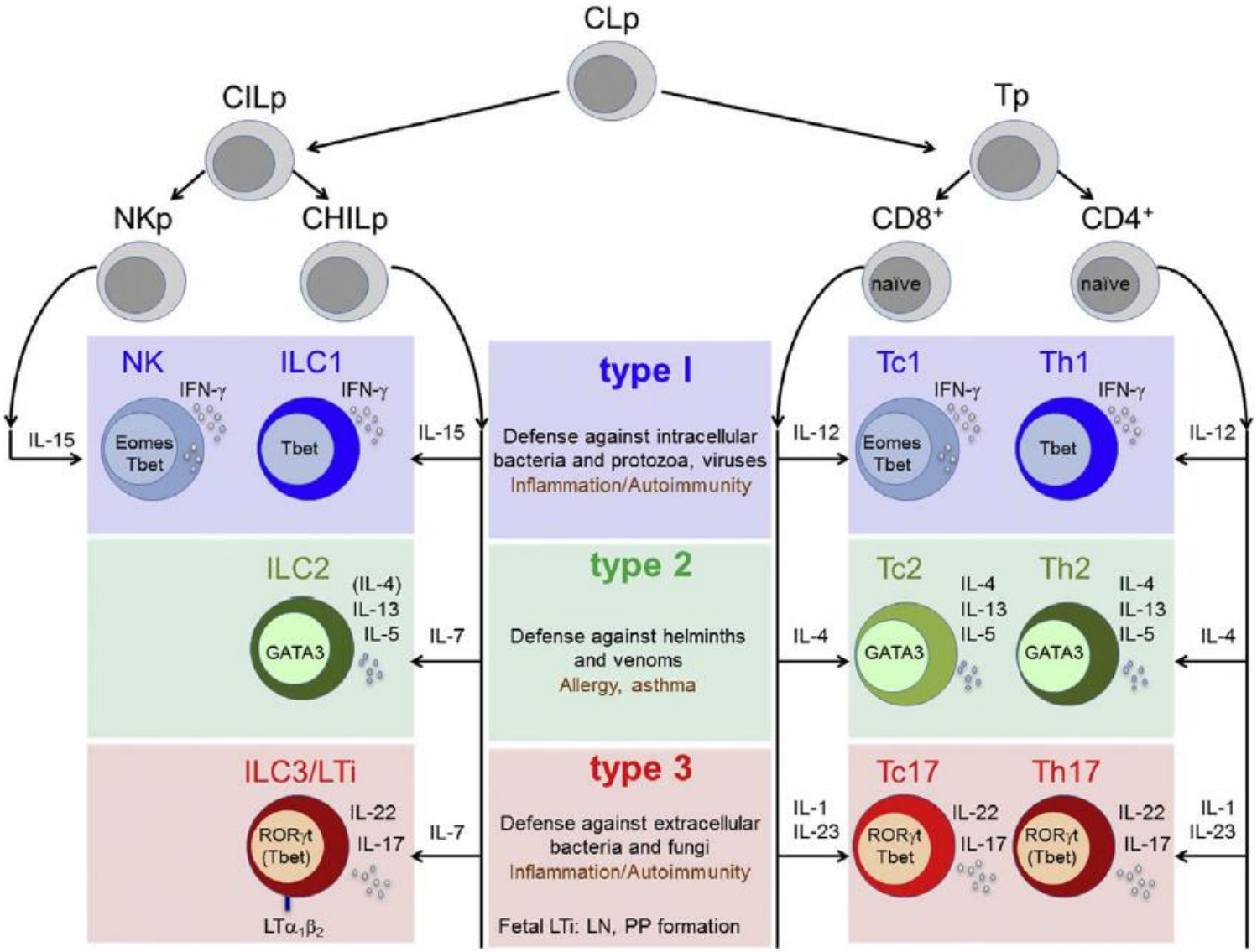
- Co-evolution (contemporary development of IS and Microbiome)
- Tissue adaptation (plasticity of IS, mutualistic symbiosis)
- Particular type of immune response at mucosal level (prevalence of the immunoregulatory response)

Principal protagonists of the immune responses

Principal features of different T helper phenotypes

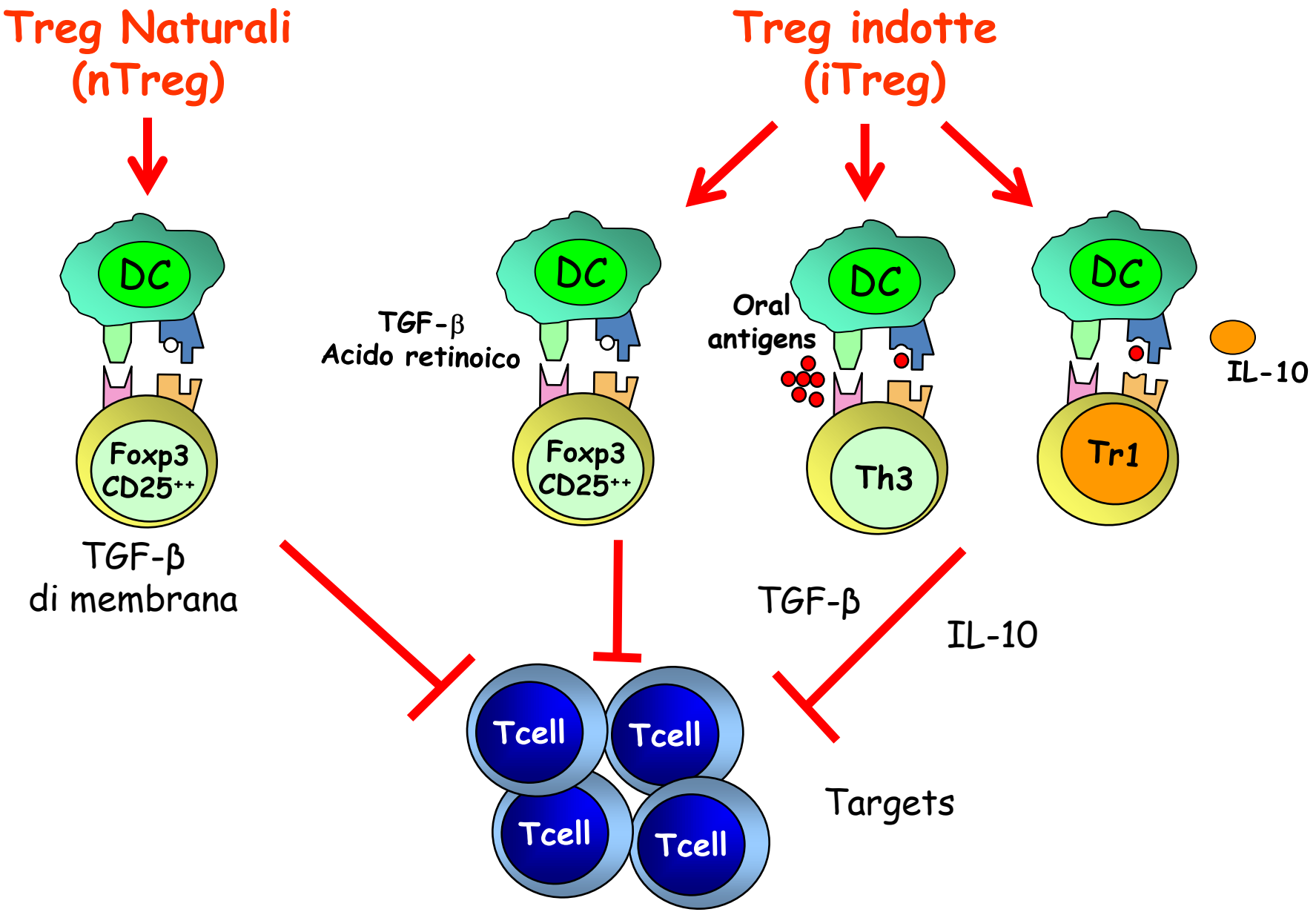


Different populations of innate lymphoid cells (ILC)

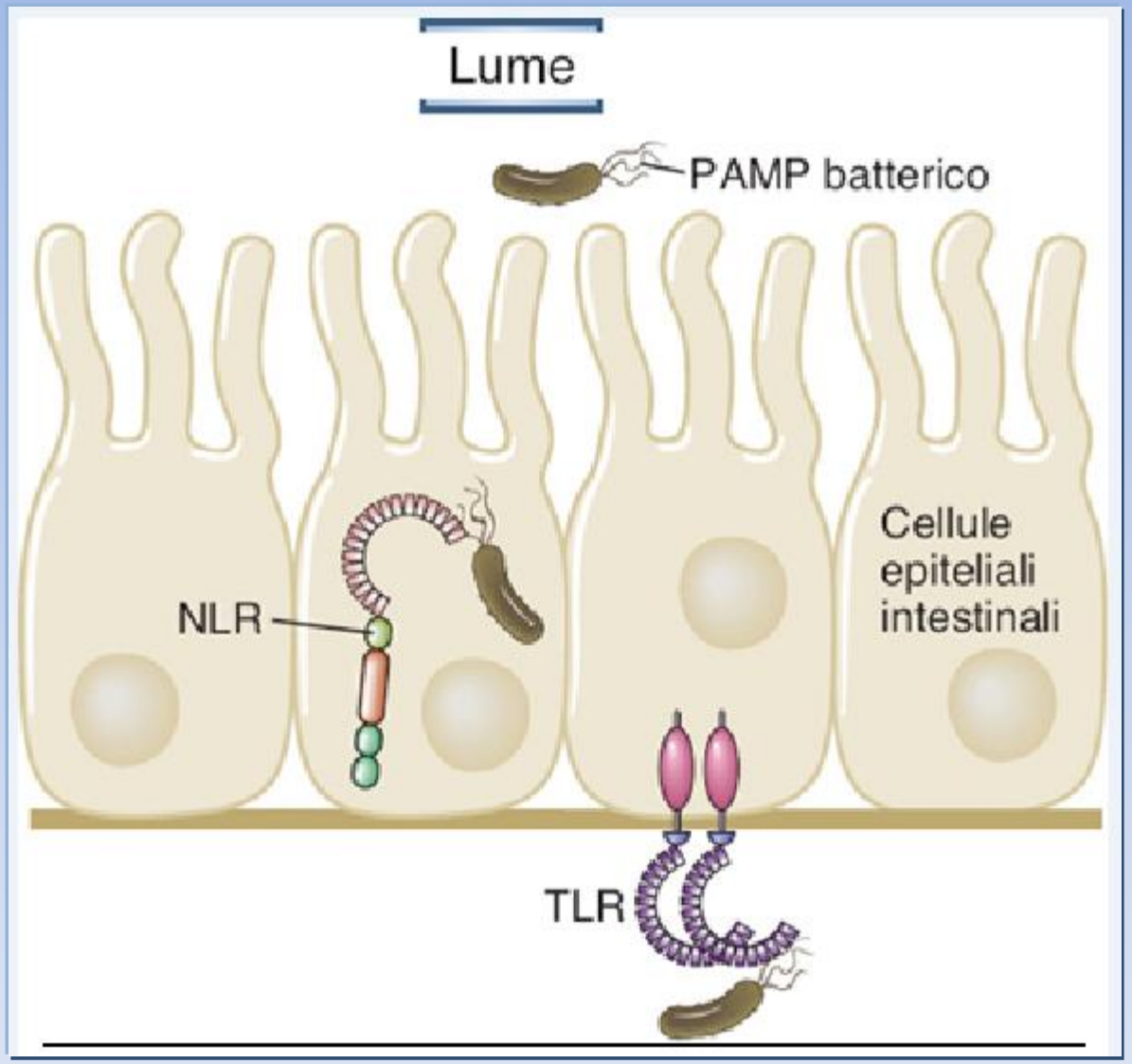


Annunziato et al. JACI 2015

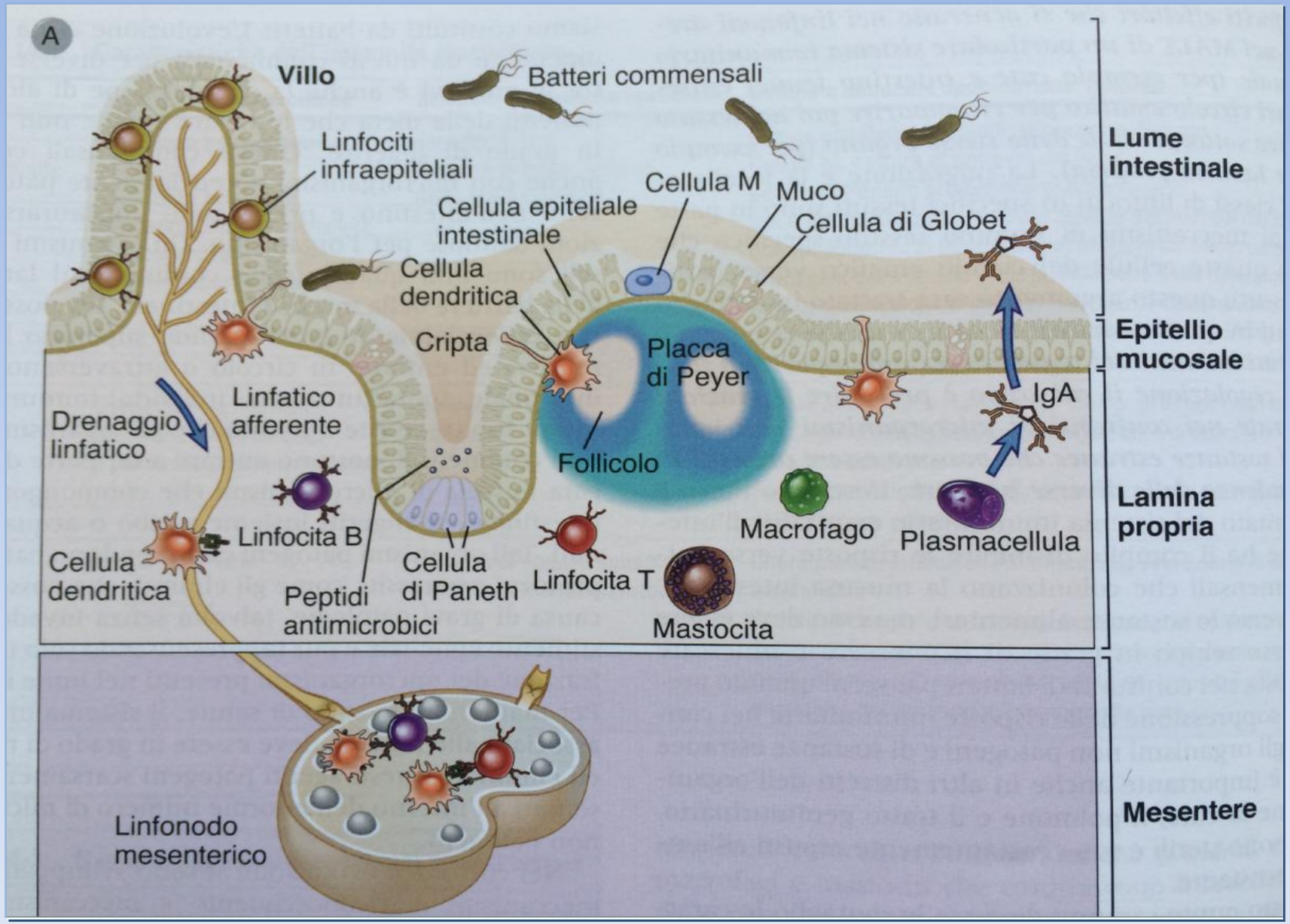
Different types of TReg



Immune responses at intestinal mucosal level



Immunologia Cellulare e molecolare, Abul k. Abbas et al., ottava edizione, 2015.



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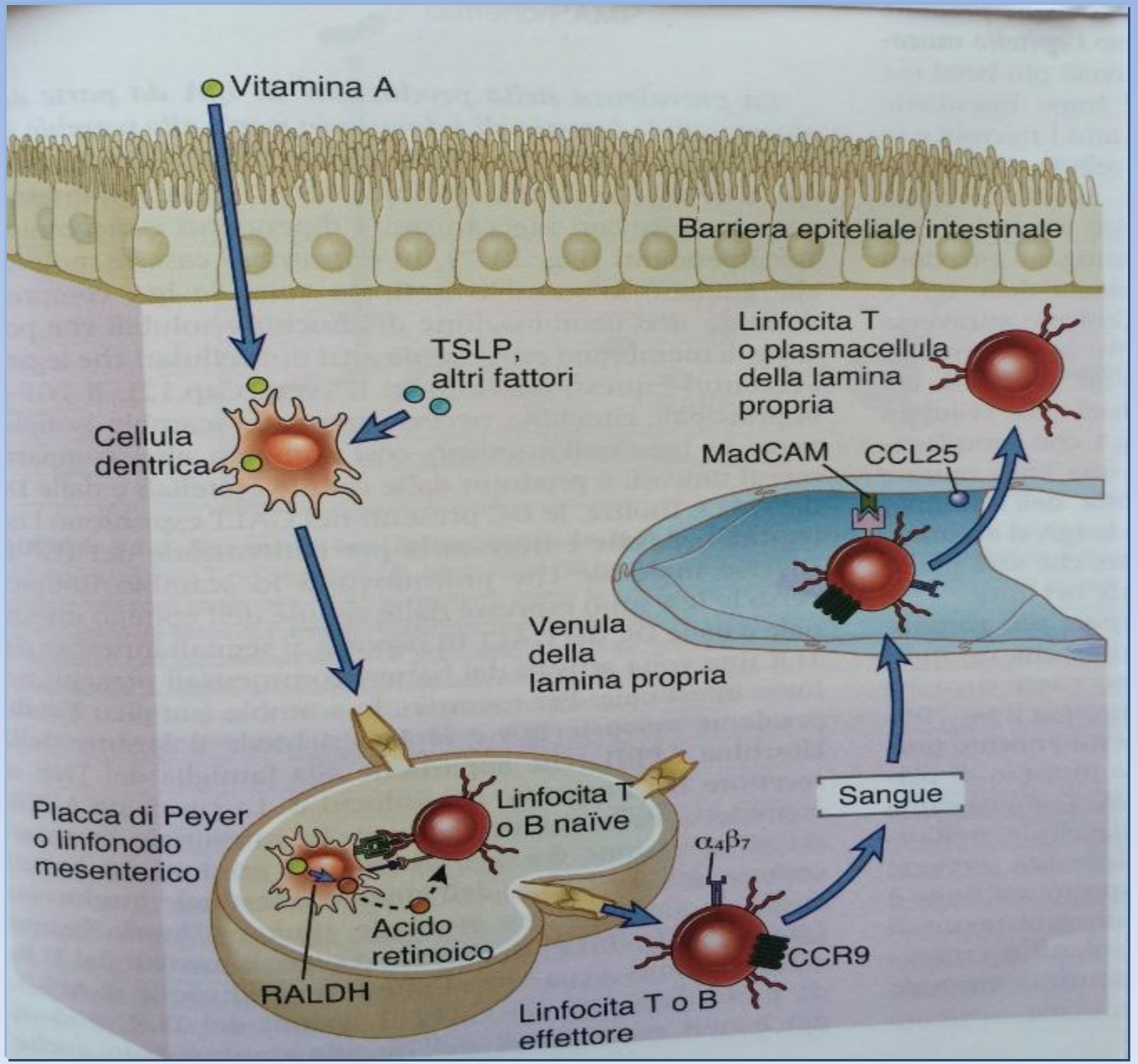
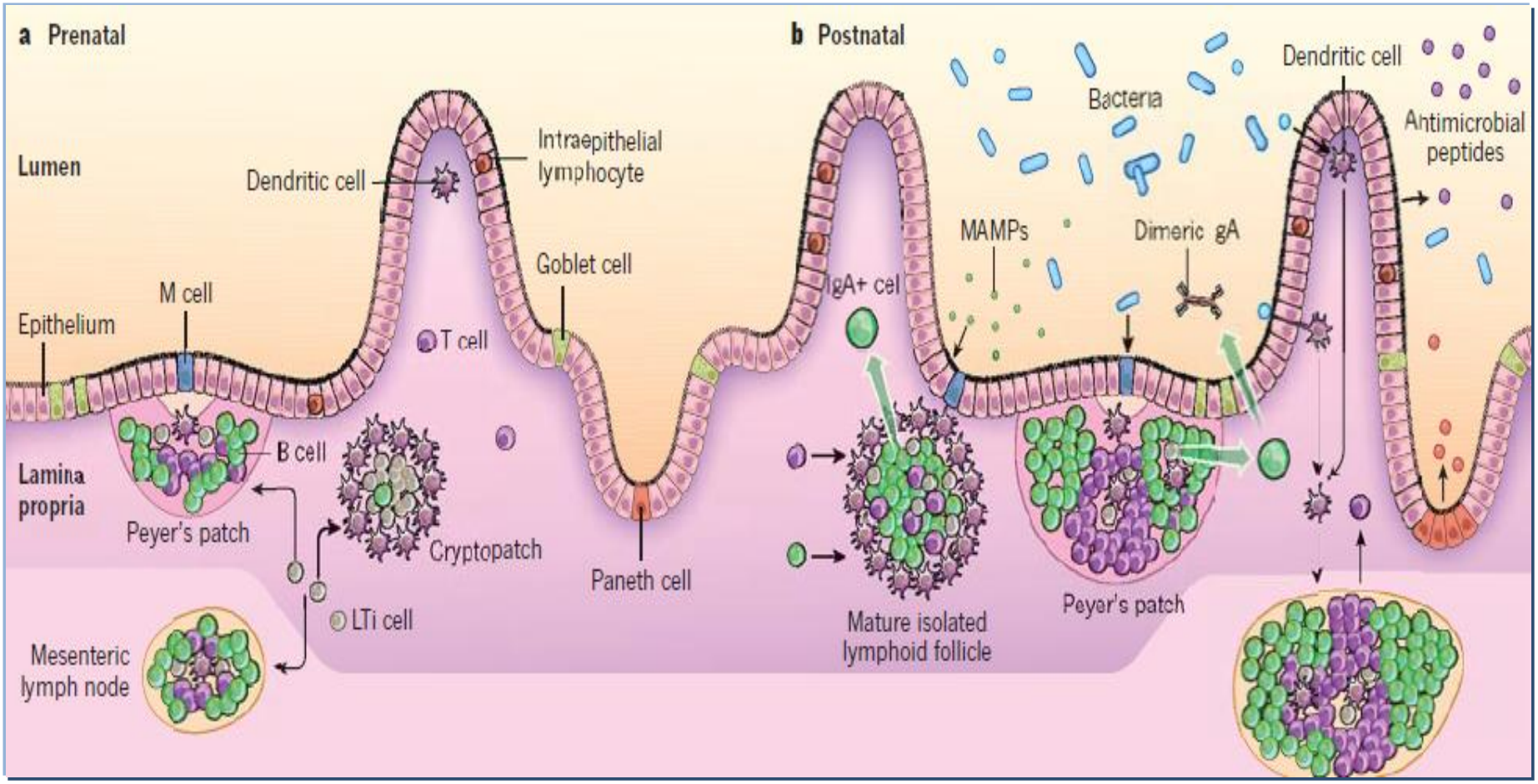


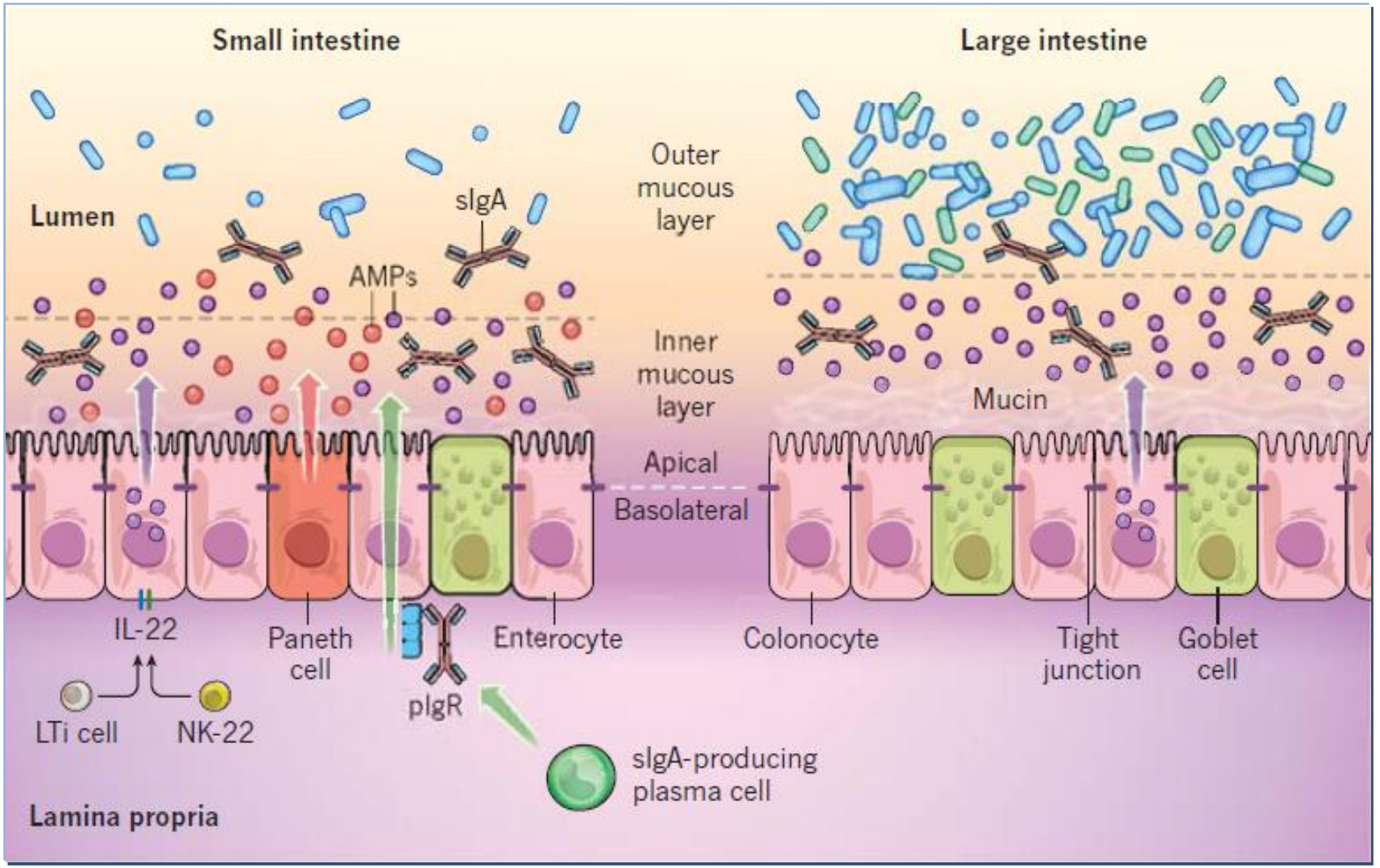
Immunologia Cellulare e molecolare, Abul k. Abbas et al., ottava edizione, 2015.

Reciprocal interactions between microbiome and immune system

- Development, education and mantenaince of immune system
- Homeostasis, shaping and preservation of the function of microbiome



Reciprocal Interactions of the Intestinal Microbiota and Immune System, Craig L. Maynard et al., 2012, Nature Review



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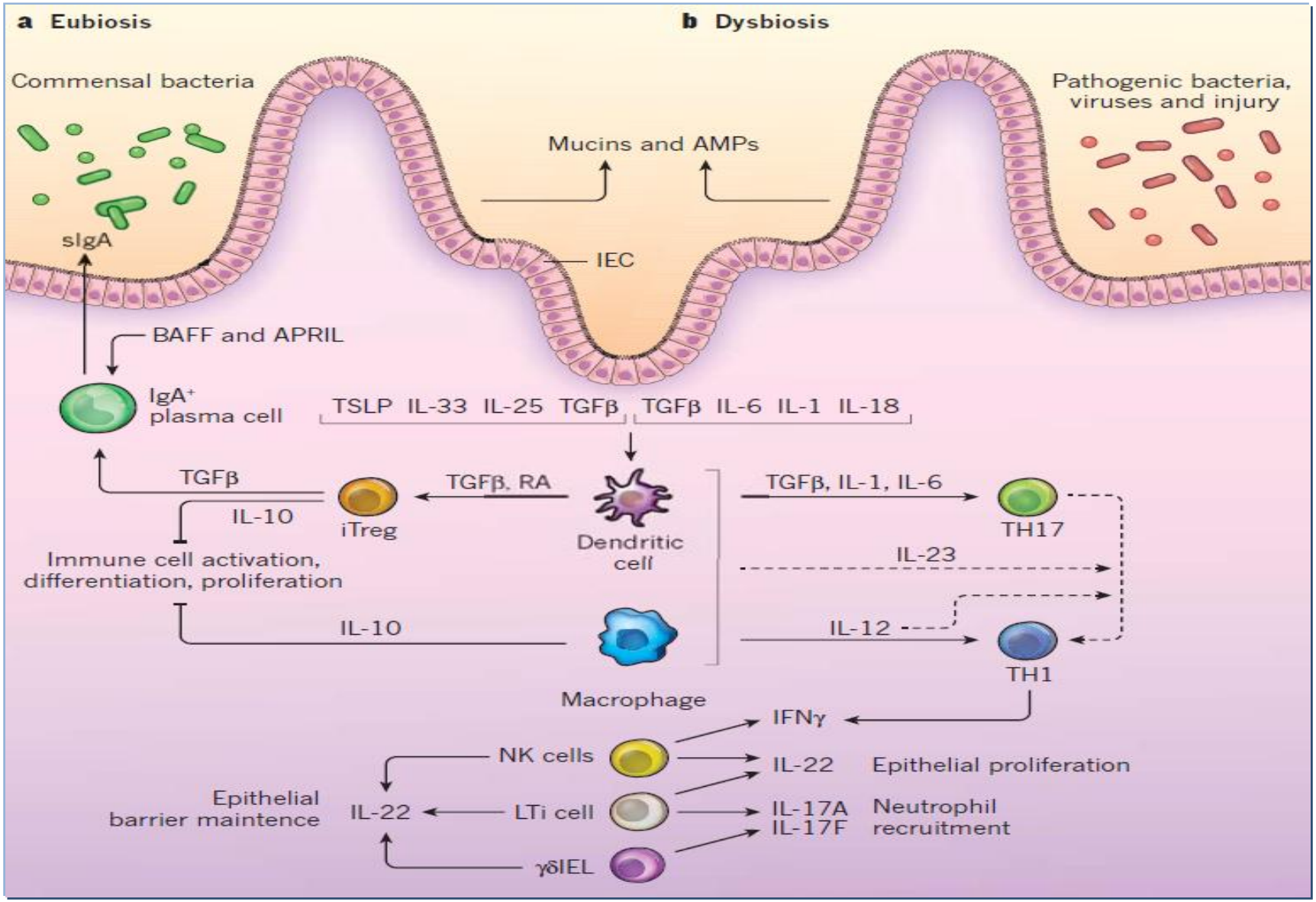

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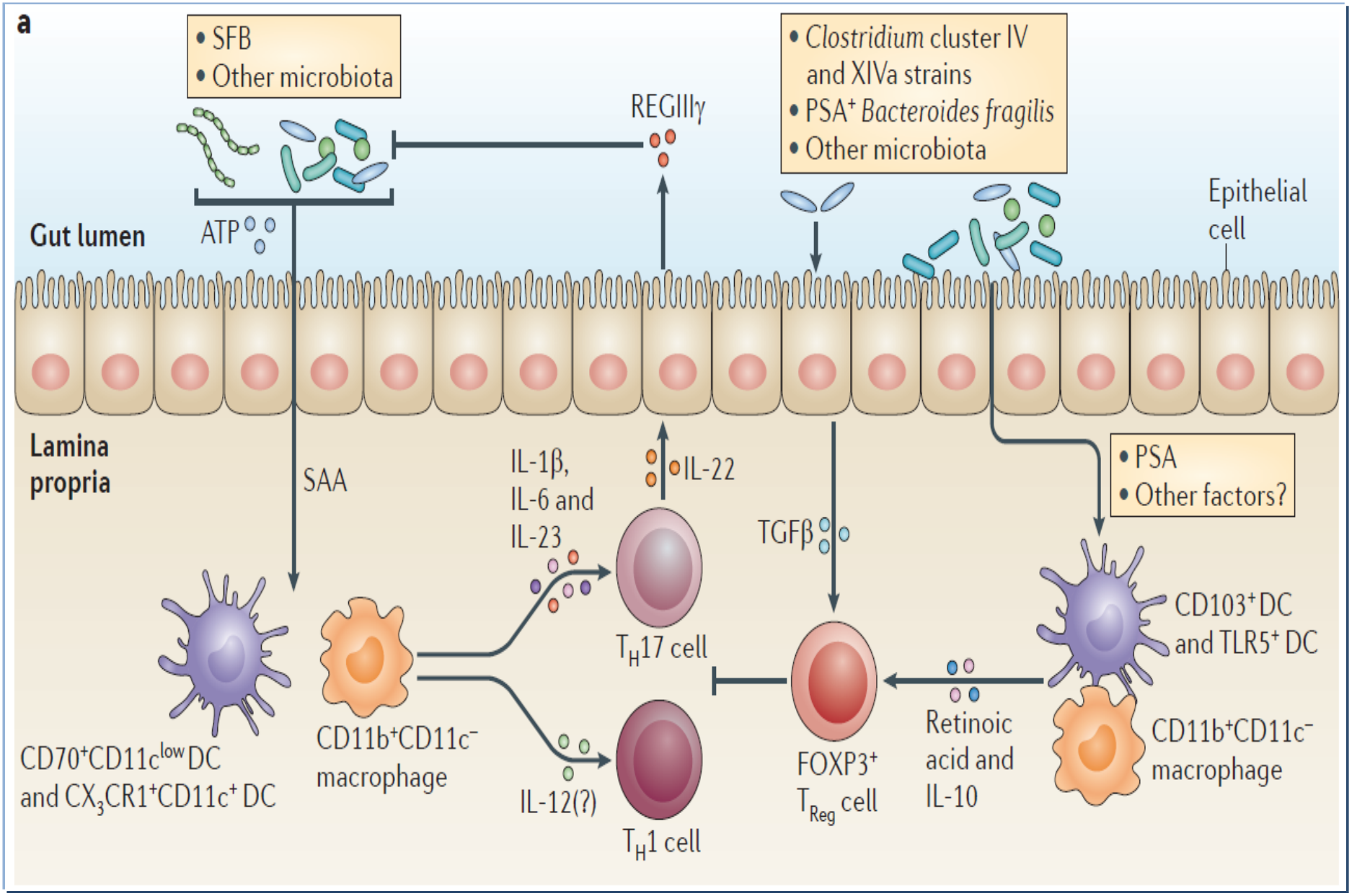

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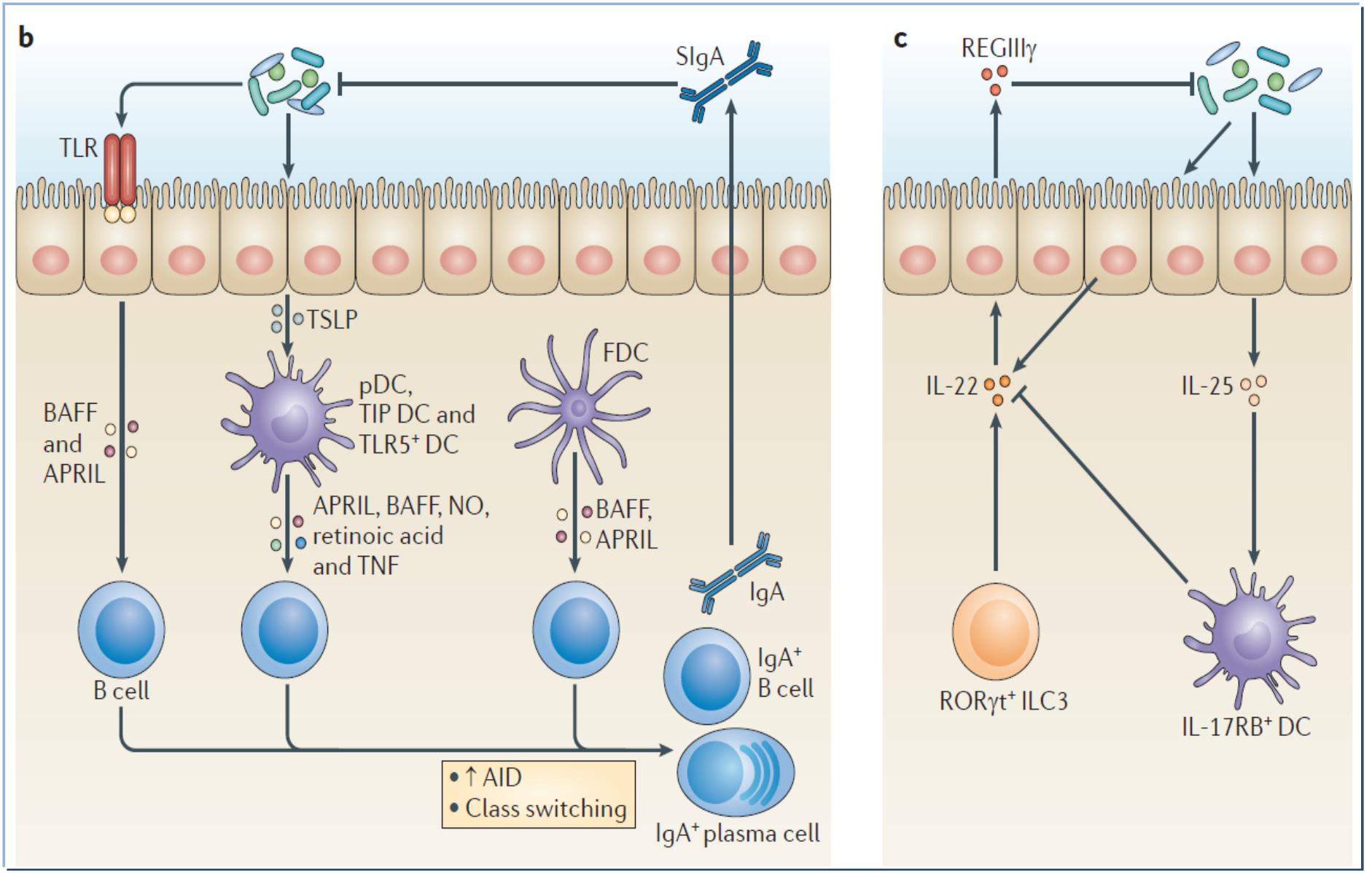
Role of the gut microbiota in immunity and inflammatory disease, *Nobuhiko Kamada et al., 2013, Nature Reviews*



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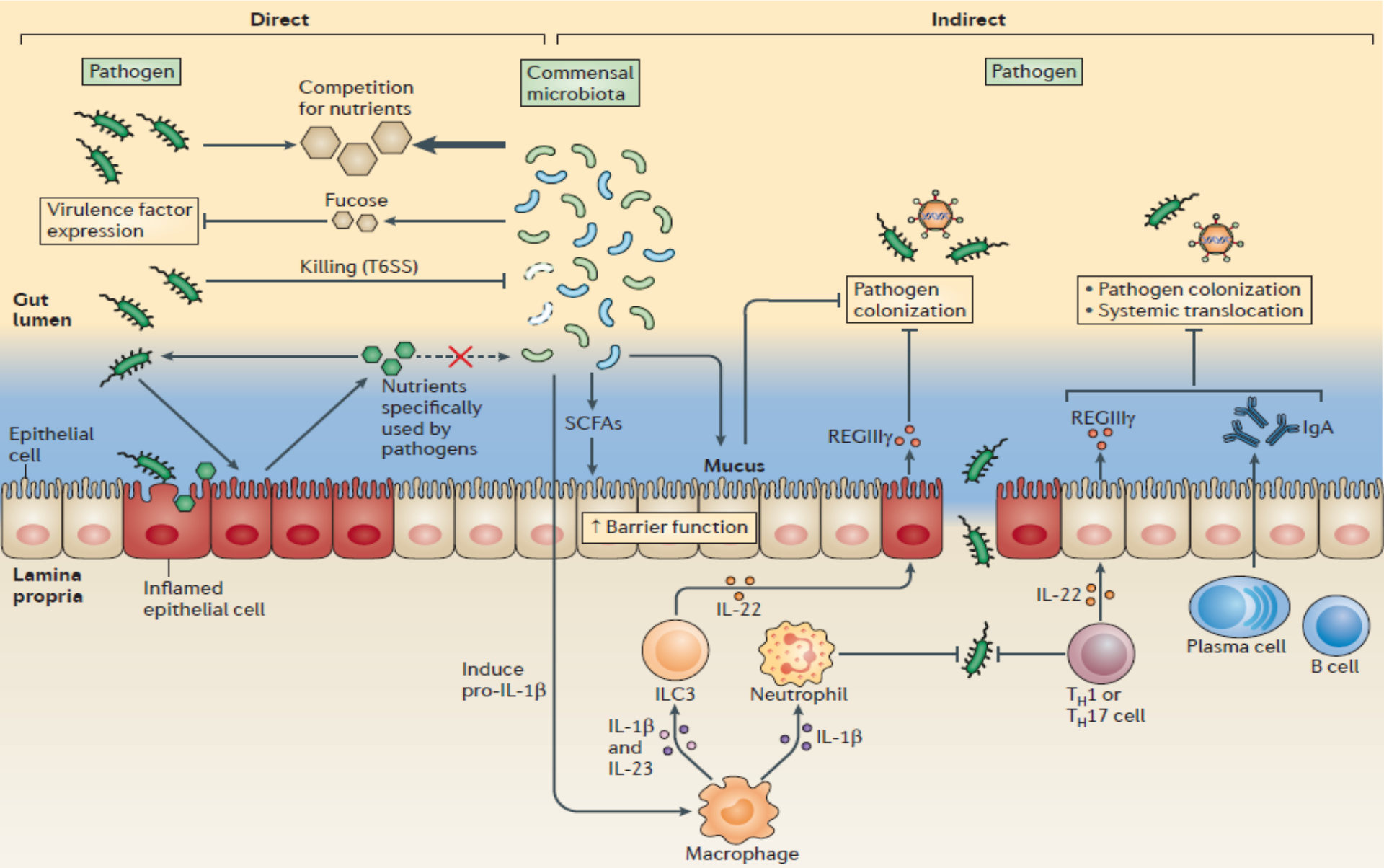
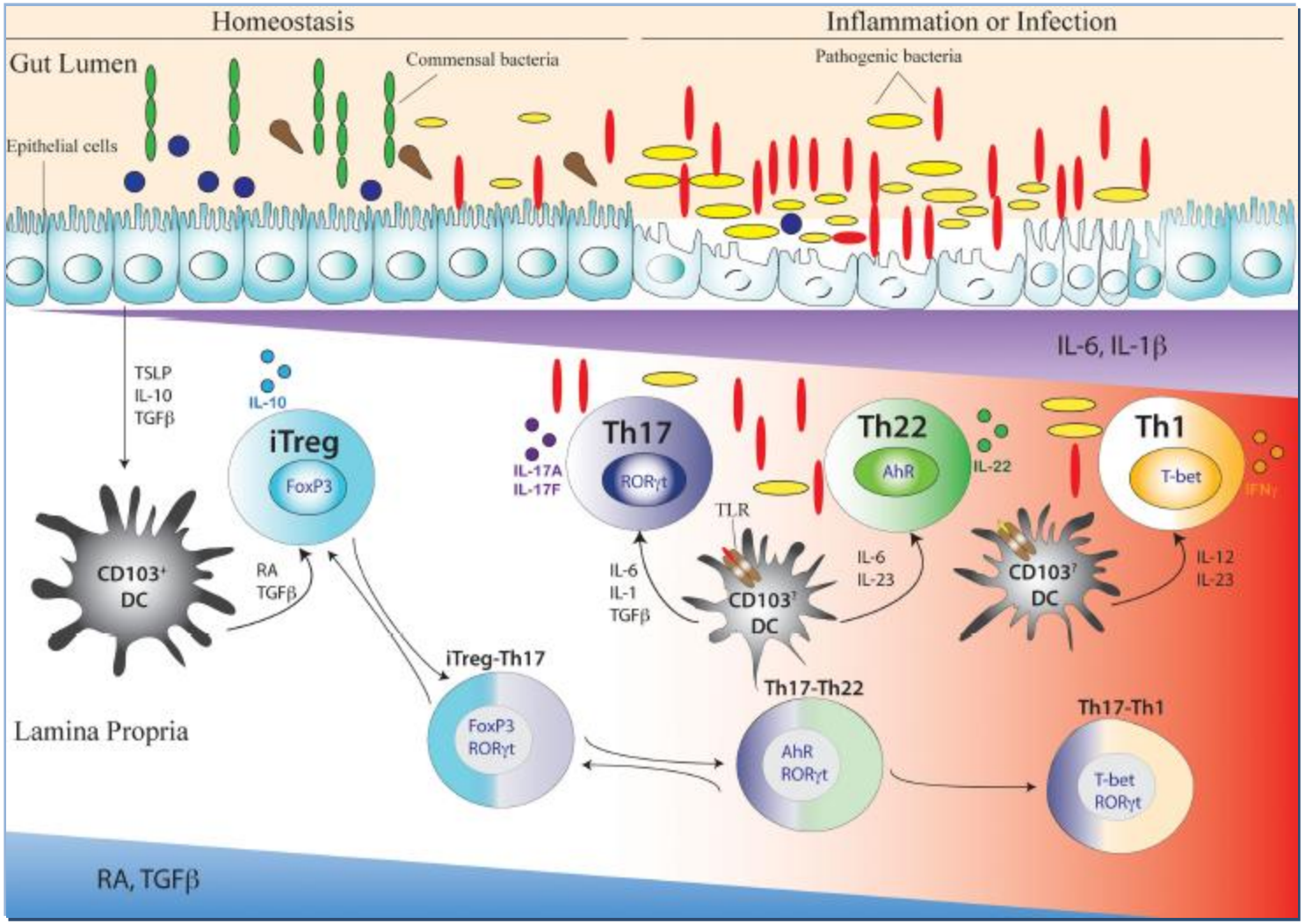


Direct and indirect resistance of the microbiota to colonization by enteric pathogens.

Role of the gut microbiota in immunity and inflammatory disease, *Nobuhiko Kamada et al., 2013, Nature Reviews*



Cellular and Molecular Dynamics of Th17 Differentiation and its Developmental Plasticity in the intestinal immune Response, *Suniti Bhaumik et al.,* Frontiers in Immunology ,2017

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Review

Behçet's syndrome patients exhibit specific microbiome signature

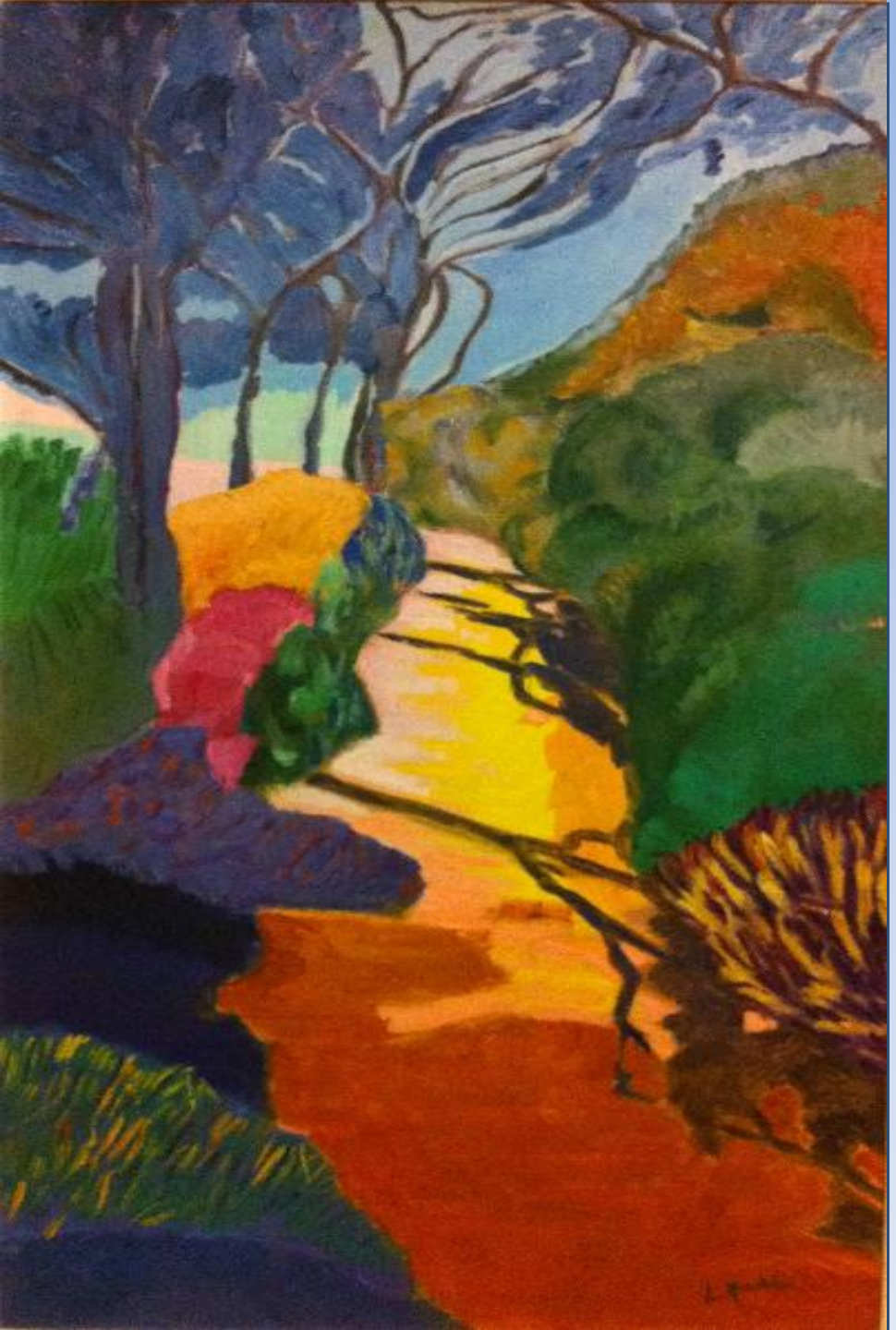
Clarissa Consolandi [a,*,1], Silvia Turroni [b,1], Giacomo Emmi [c,1], Marco Severgnini [a], Jessica Fiori [b], Clelia Peano [a], Elena Biagi [b], Alessia Grassi [c], Simone Rampelli [b], Elena Silvestri [c], Manuela Centanni [b], Fabio Cianchi [e], Roberto Gotti [b], Lorenzo Emmi [d,**], Patrizia Brigidi [b], Nicola Bizzaro [f], Gianluca De Bellis [a], Domenico Prisco [c,d], Marco Candela [b], Mario M. D'Elios [c,d]

AIM OF THE STUDY

The aim of this study was to compare the GM structure and the profiles of SCFA production in BS patients and healthy control relatives eating the same diet and living in the same environment of BS patients. Here, we report that a peculiar dysbiosis of the gut microbial ecosystem is present in patients with BS, corresponding to specific changes in the profiles of SCFA production; in particular a significant decrease of butyrate production in Behçet's patients was demonstrated. Interestingly butyrate is able to induce T regulatory cell (Treg) differentiation via several mechanisms, thus influencing immune regulation probably promoting an abnormal immune system response

TAKE HOME MESSAGES

- BS is a vasculitis with muco-cutaneous, ocular and gastro-intestinal involvement
- BS is associated to a peculiar dysbiosis of the gut microbial ecosystem
- Gut microbiota ecosystem in BS is characterized by a low biodiversity
- Behcet's patients were significantly depleted in the genera Roseburia and Subdoligranulum
- BS patients show a decrease of butyrate production
- The defect of butyrate production leads to reduced T-reg responses and activation of immuno-pathological T-effector responses



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