INSTITUT PASTEUR

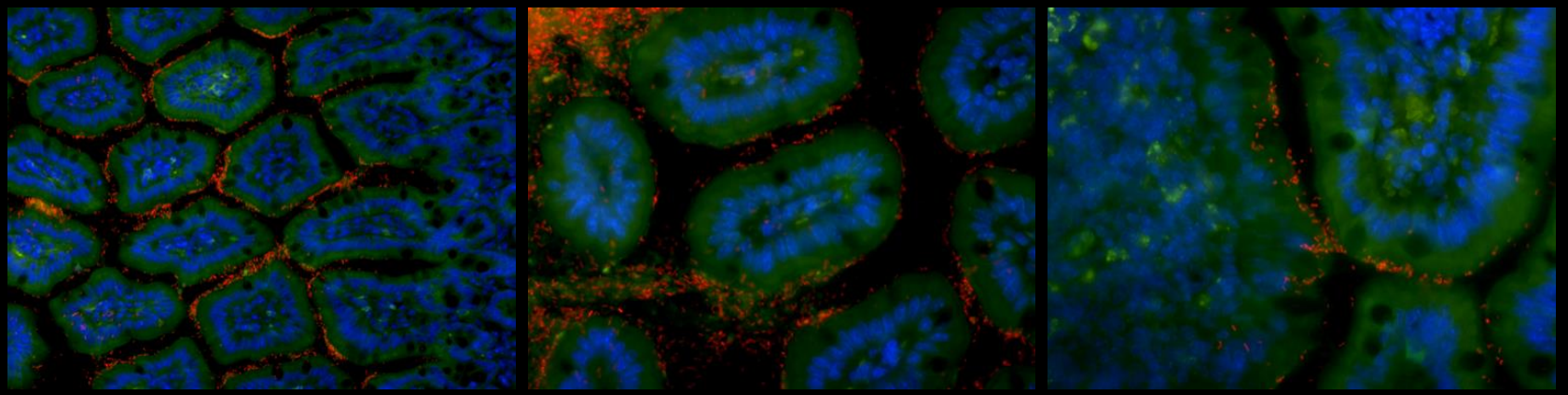
Regulation of inflammation by microbiota

Microenvironment & Immunity Unit
Gérard Eberl

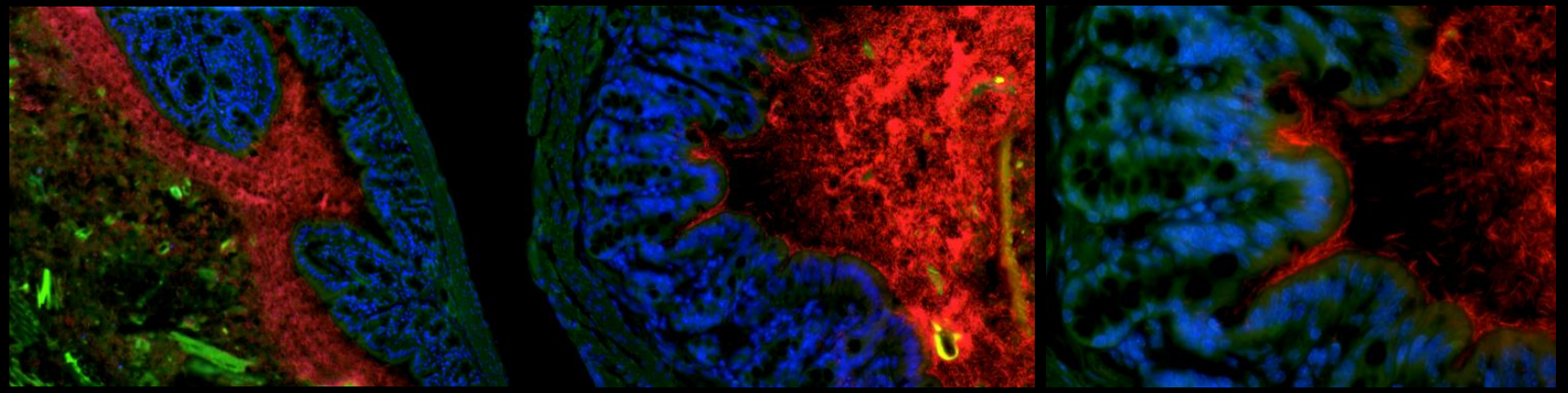
Bacterial symbionts of the adult gut

AutoF Bact 16S DAPI

Ileum

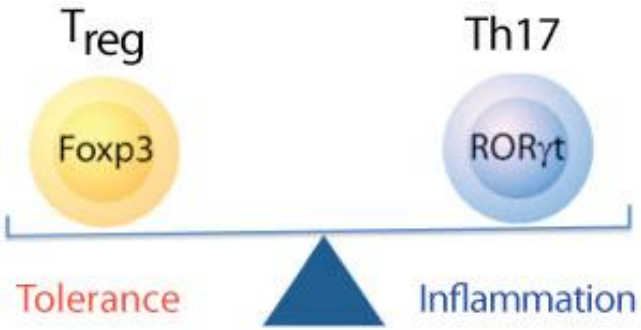


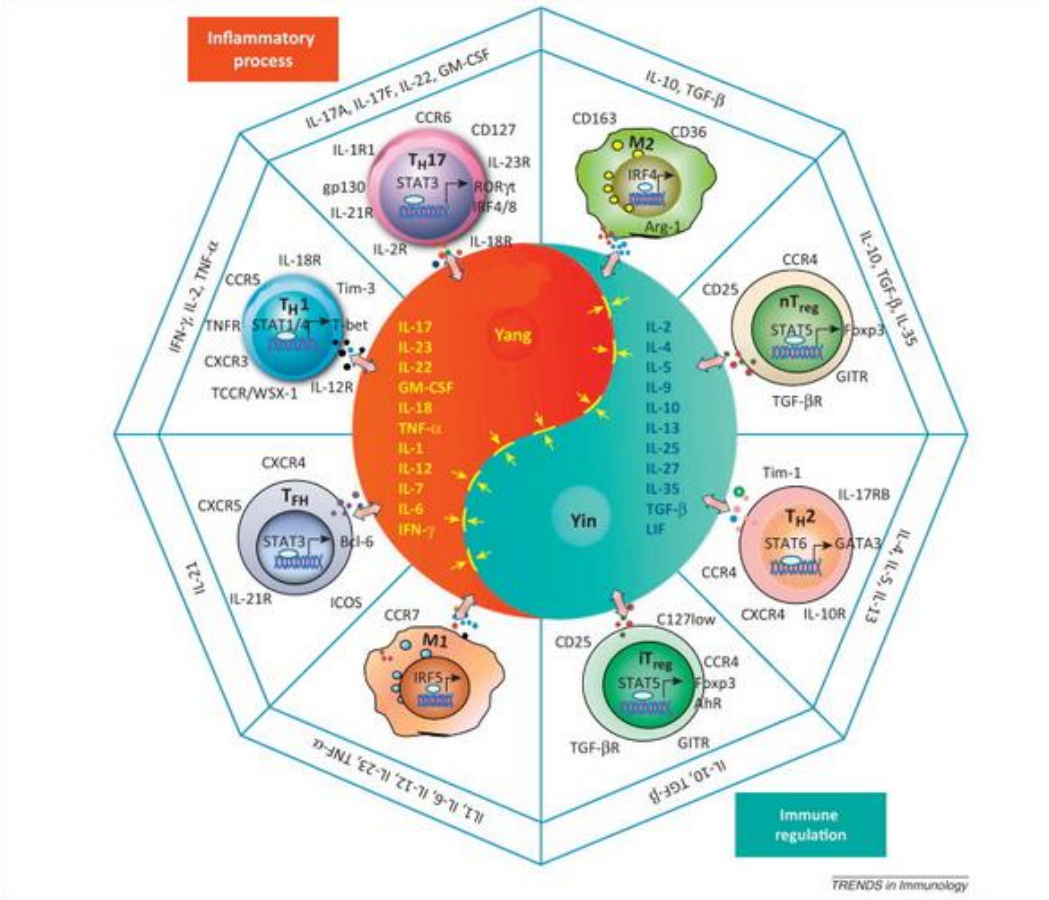
Colon



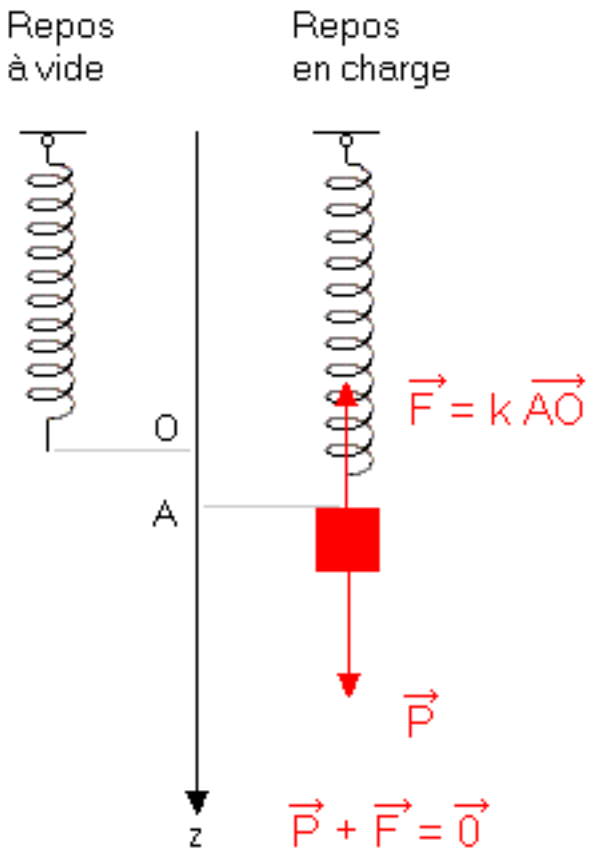
~10^{14} bacteria and ~10^{12} body cells

An choice between “tolerance” and “inflammation” in the face of mutualists and pathogens

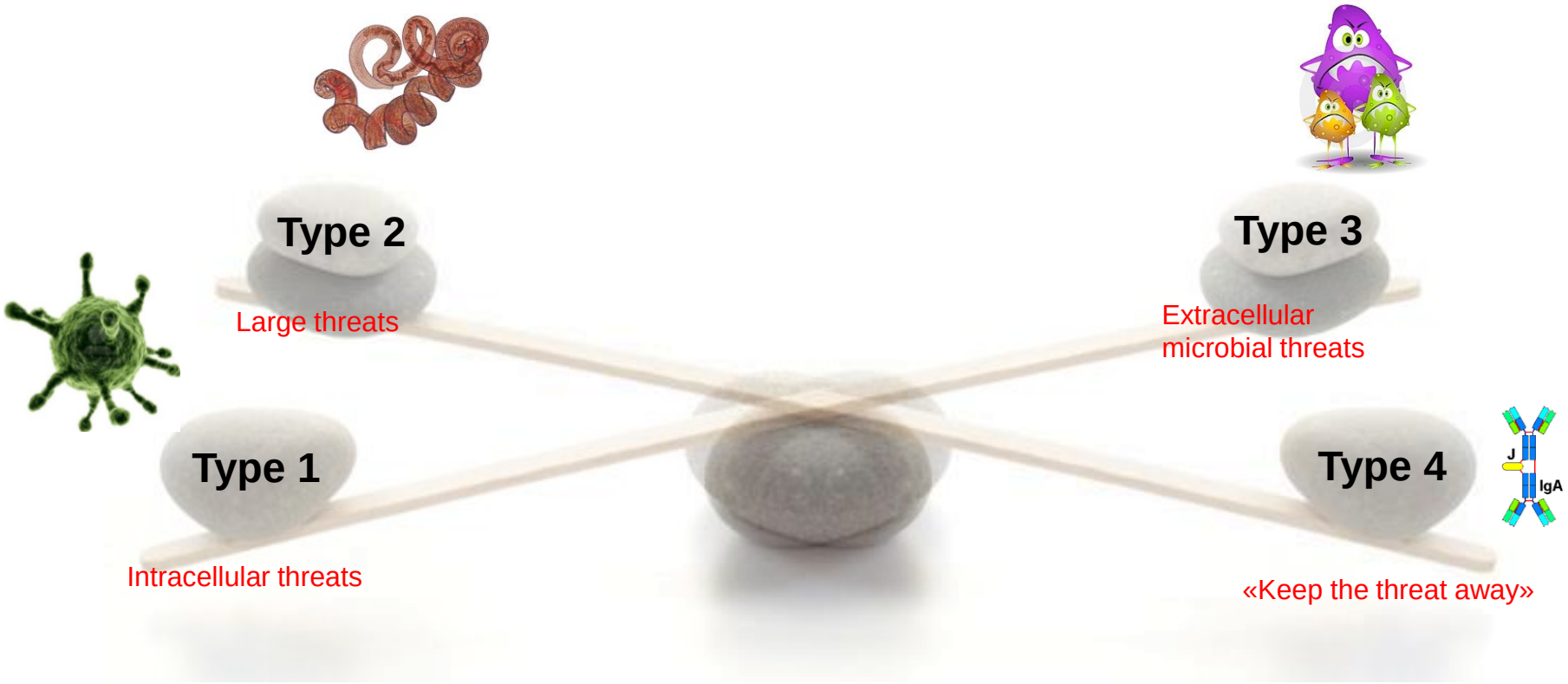




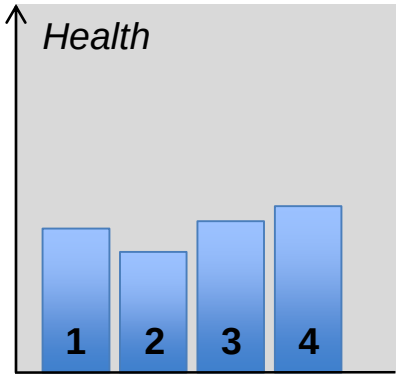
Or the immune system is just reacting…

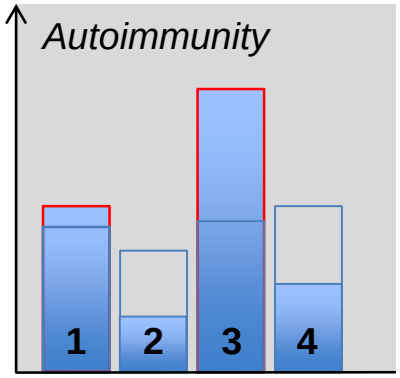


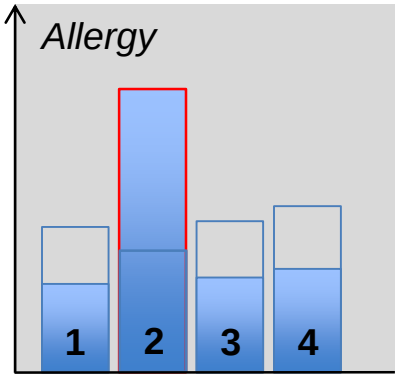
A fundamental equilibrium between the multiple forces of immunity (the Equilibrium Model of Immunity)



The “missing response” hypothesis







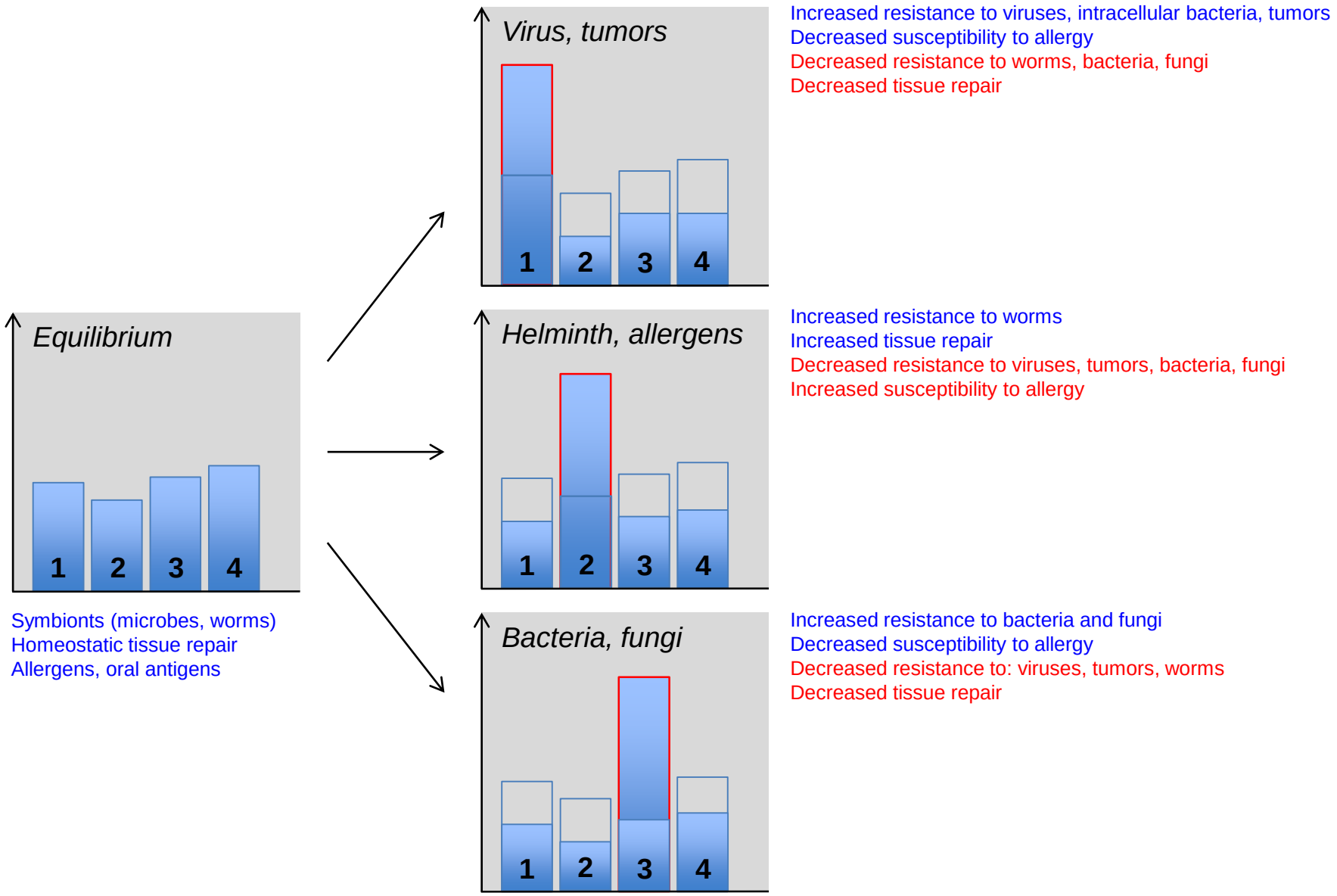

Equilibrium
1
2
3
4
Symbionts (microbes, worms)
Homeostatic tissue repair
Allergens, oral antigens
Virus, tumors
1
2
3
4
Increased resistance to viruses, intracellular bacteria, tumors
Decreased susceptibility to allergy
Decreased resistance to worms, bacteria, fungi
Decreased tissue repair
Helminth, allergens
1
2
3
4
Increased resistance to worms
Increased tissue repair
Decreased resistance to viruses, tumors, bacteria, fungi
Increased susceptibility to allergy
Bacteria, fungi
1
2
3
4
Increased resistance to bacteria and fungi
Decreased susceptibility to allergy
Decreased resistance to: viruses, tumors, worms
Decreased tissue repair

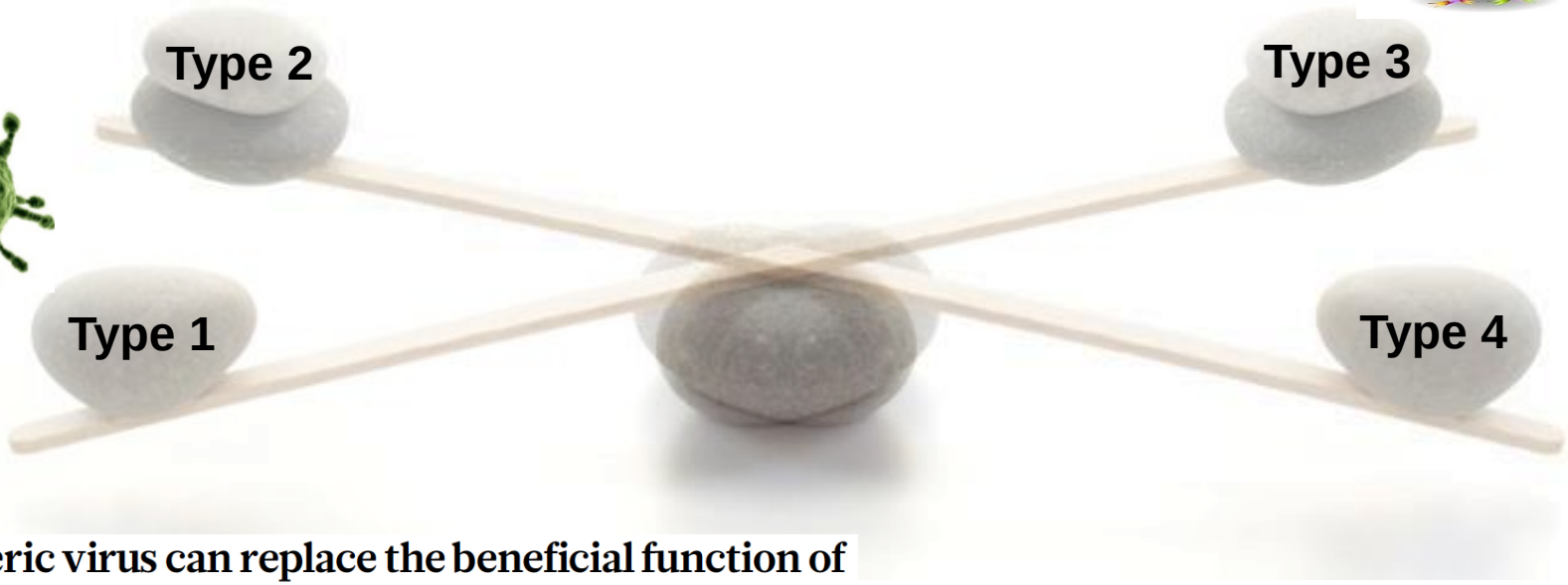
Figure 3

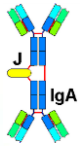
Virus-helminth coinfection reveals a microbiota-independent mechanism of immunomodulation

Lisa C. Osborne,[1,2] Laurel A. Monticelli,[1,2] Timothy J. Nice,[3] Tara E. Sutherland,[4] Mark C. Siracusa,[1,2*] Matthew R. Hepworth,[1,2,5] Vesselin T. Tomov,[5] Dmytro Kobuley,[1,2] Sara V. Tran,[1,2] Kyle Bittinger,[1] Aubrey G. Bailey,[1] Alice L. Laughlin,[1] Jean-Luc Boucher,[6] E. John Wherry,[2] Frederic D. Bushman,[1] Judith E. Allen,[4] Herbert W. Virgin,[3] David Artis[1,2,7†]

Commensal microbes and interferon-λ determine persistence of enteric murine norovirus infection

Megan T. Baldridge,[1] Timothy J. Nice,[1] Broc T. McCune,[1] Christine C. Yokoyama,[1] Amal Kambal,[1] Michael Wheadon,[1] Michael S. Diamond,[1,2] Yulia Ivanova,[1] Maxim Artyomov,[1] Herbert W. Virgin[1*]





An enteric virus can replace the beneficial function of commensal bacteria

Elisabeth Kernbauer[1,2], Yi Ding[3,4] & Ken Cadwell[1,2]

The Effect of Infections on Susceptibility to Autoimmune and Allergic Diseases

Jean-François Bach, M.D., D.Sc.

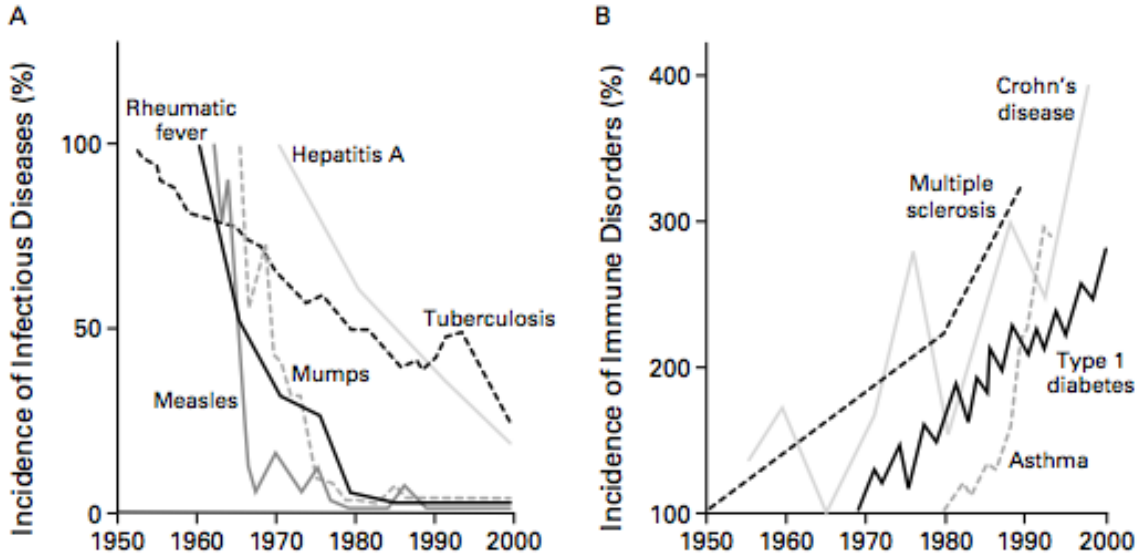


Figure 1. Inverse Relation between the Incidence of Prototypical Infectious Diseases (Panel A) and the Incidence of Immune Disorders (Panel B) from 1950 to 2000.

In Panel A, data concerning infectious diseases are derived from reports of the Centers for Disease Control and Prevention, except for the data on hepatitis A, which are derived from Joussemet et al.[12] In Panel B, data on immune disorders are derived from Swarbrick et al.,[10] Dubois et al.,[13] Tuomilehto et al.,[14] and Pugliatti et al.[15]

Guénolée Prioult
Cathryn Nagler-Anderson

Mucosal immunity and allergic responses: lack of regulation and/or lack of microbial stimulation?

Cell Host & Microbe
Article

Intestinal Microbial Diversity during Early-Life Colonization Shapes Long-Term IgE Levels

Julia Cahenzli,[1,2] Yasmin Köller,[1,2] Madeleine Wyss,[1] Markus B. Geuking,[1] and Kathy D. McCoy[1,*]
[1]Maurice Müller Laboratories (DKF), Universitätsklinik für Viszerale Chirurgie und Medizin Inselspital, Murtenstrasse 35, University of Bern,

Early life antibiotic-driven changes in microbiota enhance susceptibility to allergic asthma

Shannon L. Russell[1,2], Matthew J. Gold[3], Martin Hartmann[1,4], Benjamin P. Willing[2], Lisa Thorson[2], Marta Wlodarska[1,2], Navkiran Gill[2], Marie-Renée Blanchet[5], William W. Mohn[1,4], Kelly M. McNagny[3+] & Brett B. Finlay[1,2++]

Microbial Exposure During Early Life Has Persistent Effects on Natural Killer T Cell Function

Torsten Olszak,[1*] Dingding An,[2*] Sebastian Zeissig,[3] Miguel Pinilla Vera,[4] Julia Richter,[5] Andre Franke,[6] Jonathan N. Glickman,[7] Reiner Siebert,[5] Rebecca M. Baron,[4] Dennis L. Kasper,[2†‡] Richard S. Blumberg[1†‡]

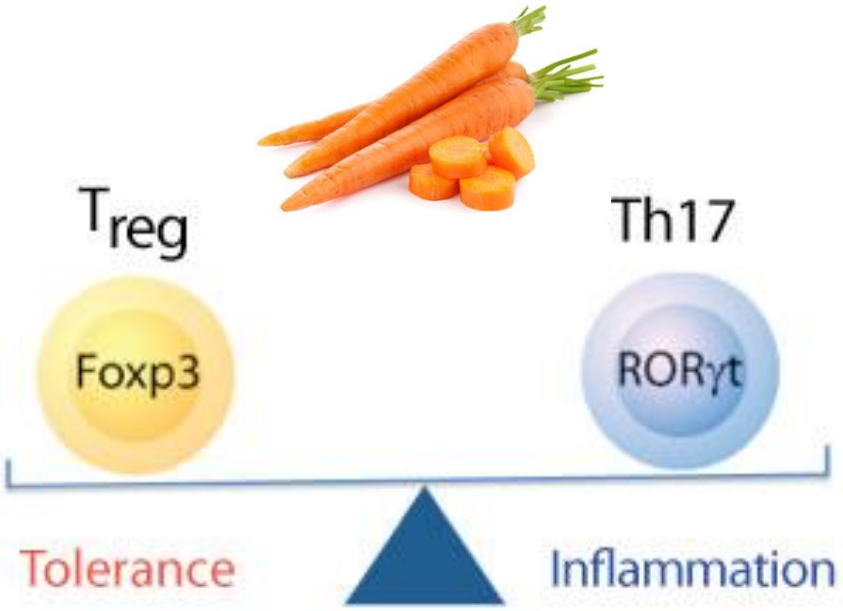
Regulation of type 2 responses by microbiota and RORγt+ cells

Caspar Ohnmacht

C. Ohnmacht, Science 2015

An equilibrium between Th17 and Treg cells regulated by retinoic acid

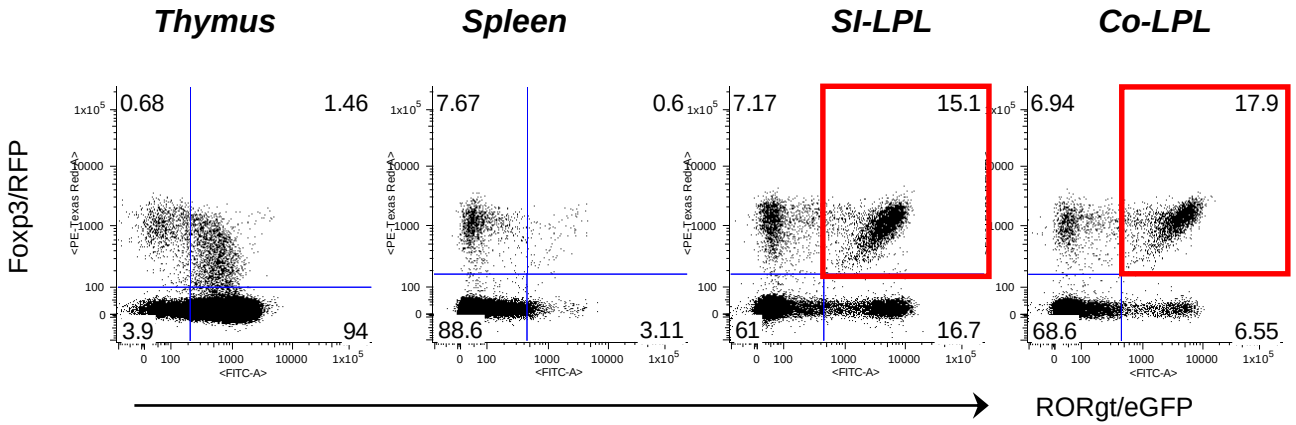
Joo Hong Park



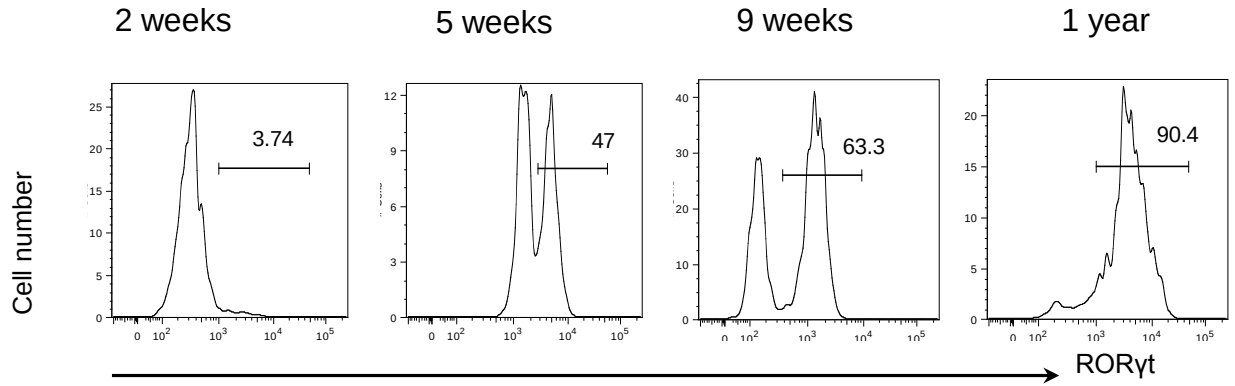
Type 3

C. Ohnmacht, Science 2015

RORγt^{+} Tregs in the intestine



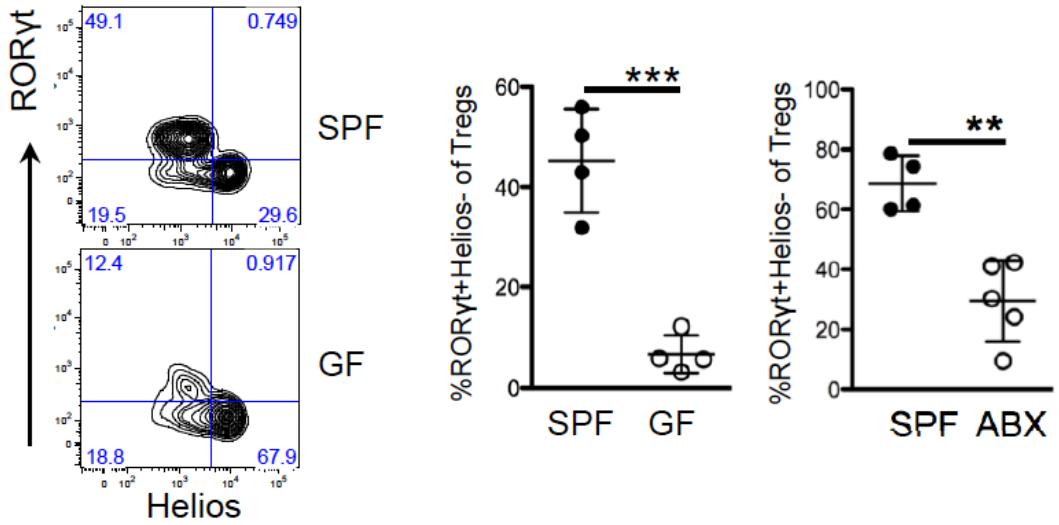
CD4+ T cells

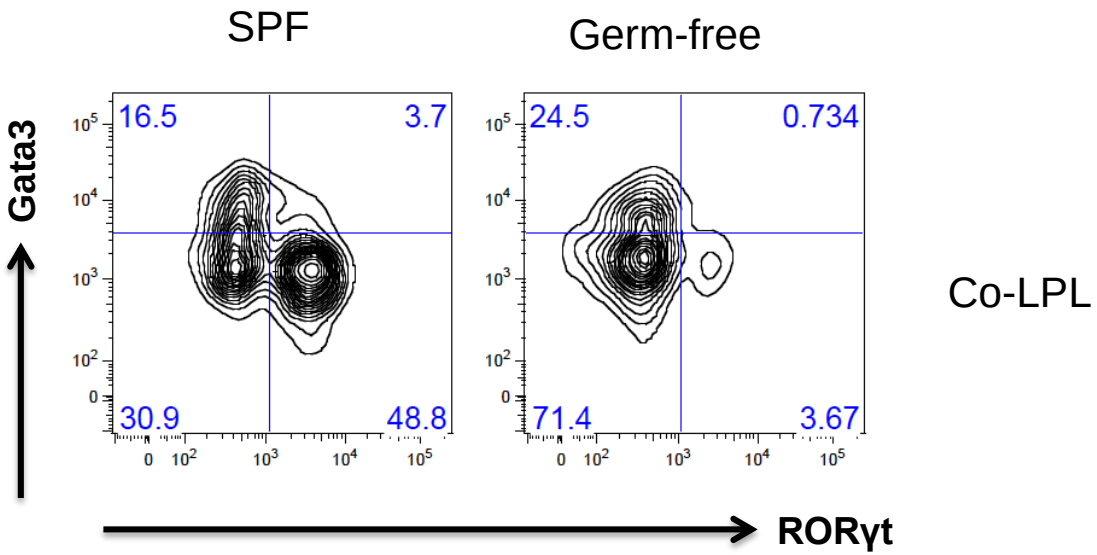


FoxP3+ T cells

C. Ohnmacht, Science 2015

Type 3 Tregs are induced by microbiota





Co-LPL

C. Ohnmacht, Science 2015

Cell Host & Microbe
Article

Specific Microbiota Direct the Differentiation of IL-17-Producing T-Helper Cells in the Mucosa of the Small Intestine

Ivaylo I. Ivanov,[1] Rosa de Llanos Frutos,[5] Nicolas Manel,[1] Keiji Yoshinaga,[3,7] Daniel B. Rifkin,[3,4] R. Balfour Sartor,[6] B. Brett Finlay,[5] and Dan R. Littman[1,2,*]
[1]The Kimmel Center for Biology and Medicine of the Skirball Institute, Departments of Microbiology and Pathology
[2]Howard Hughes Medical Institute, Departments of Microbiology and Pathology
[3]Department of Cell Biology
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New York University School of Medicine, New York, NY 10016, USA
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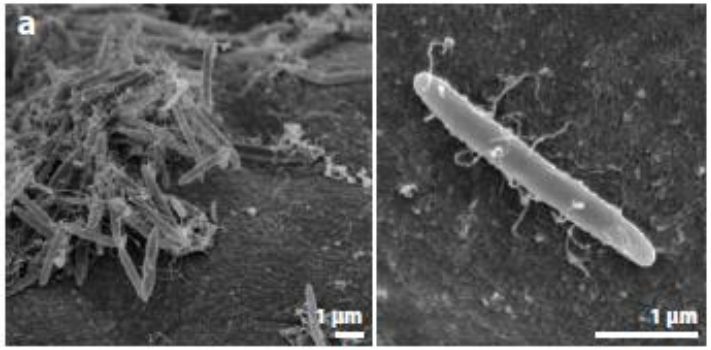
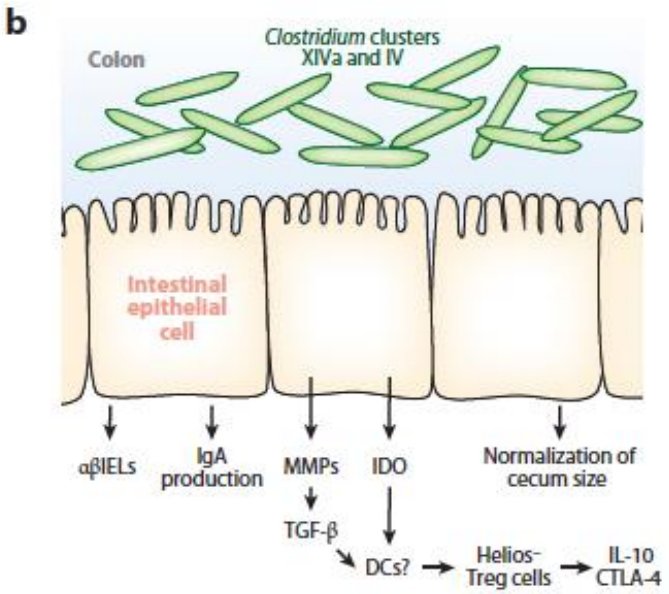
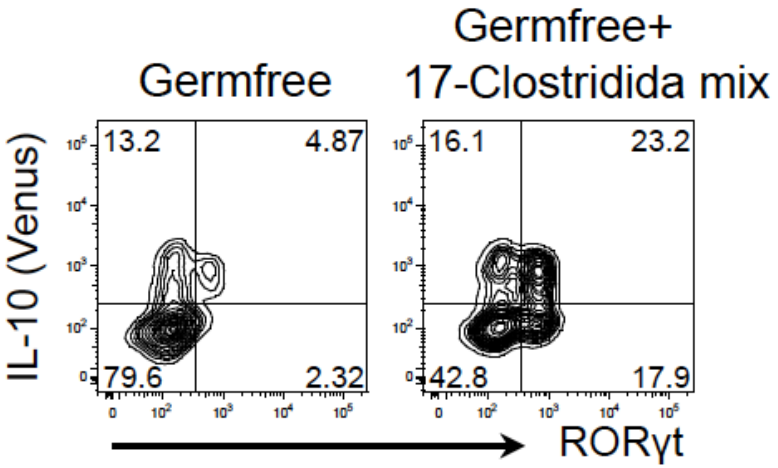
[6]Department of Medicine, and Department of Microbiology and Immunology, Center for Gastrointestinal Biology and Disease, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599, USA
[7]Present address: Department of Surgery and Science, Kyushu University, 3-1-1 Maidashi Higashiku, Fukuoka 812-8582, Japan
*Correspondence: littman@saturn.med.nyu.edu
DOI 10.1016/j.chom.2008.09.009

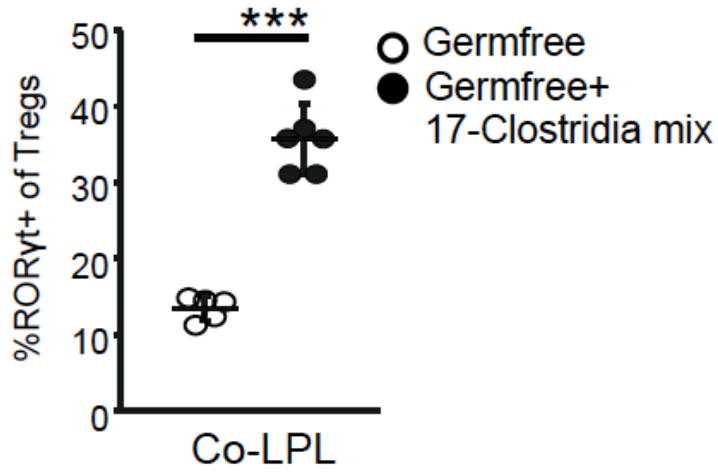
Type 3 Tregs are induced by Clostridia

Honda et al., 2012









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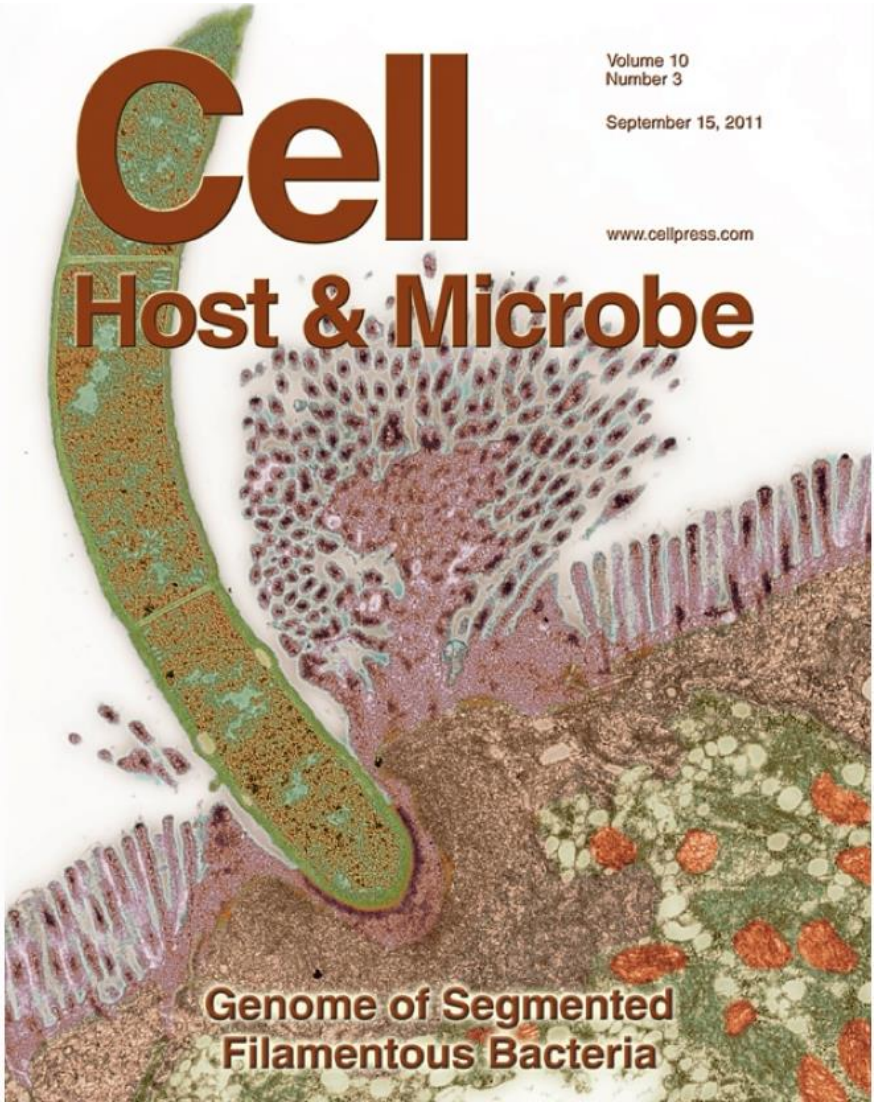
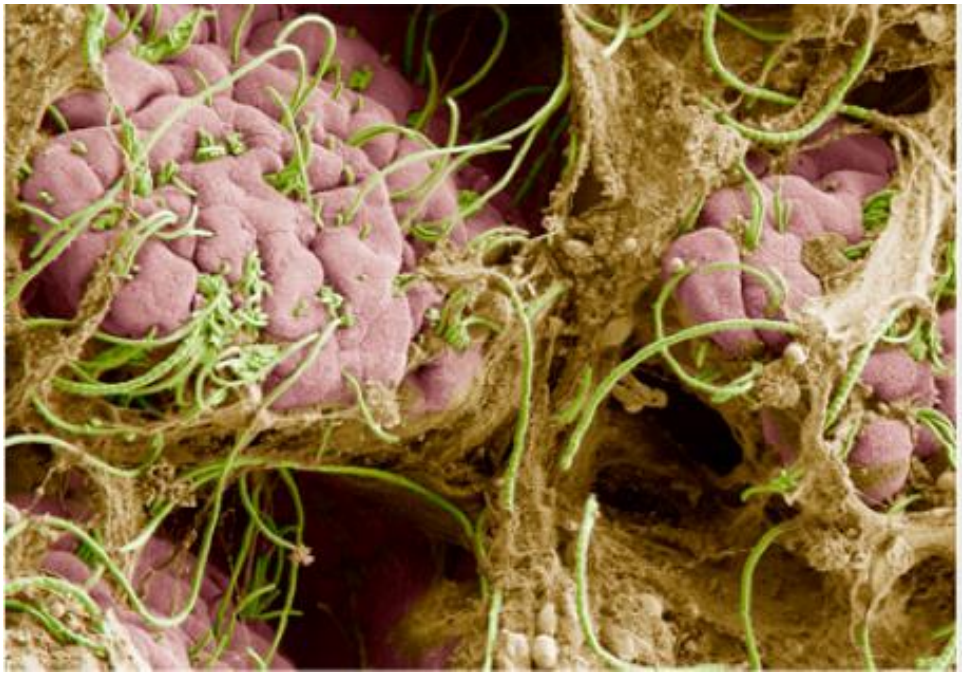
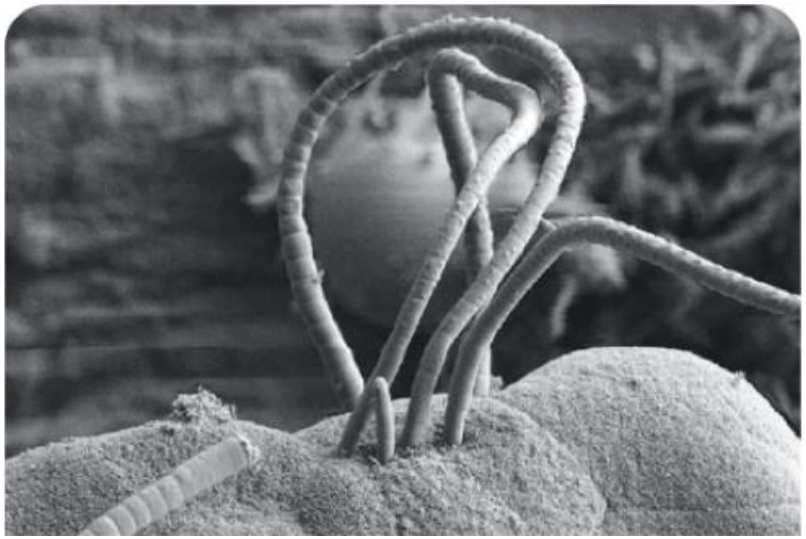
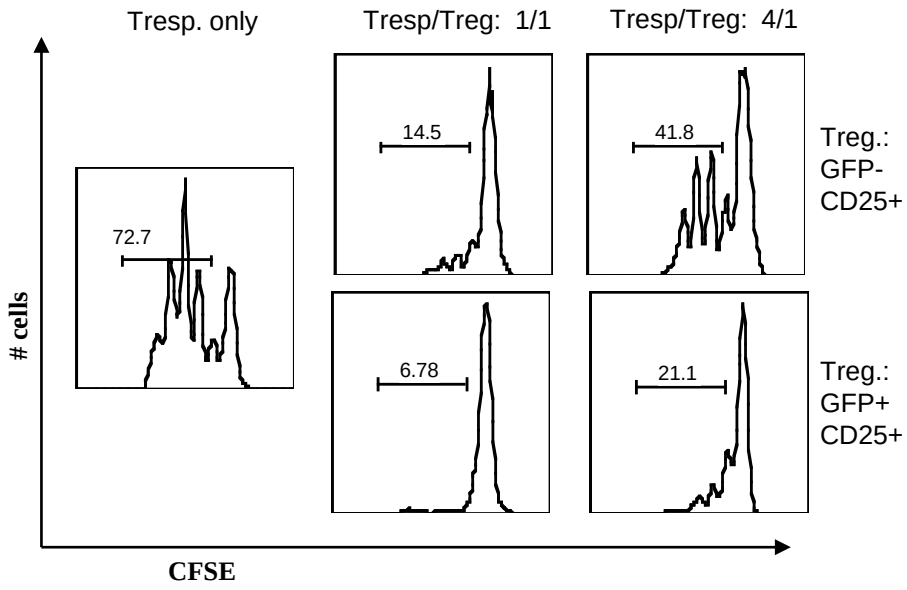
Bactéries Segmentées Filamenteuses (SFB)

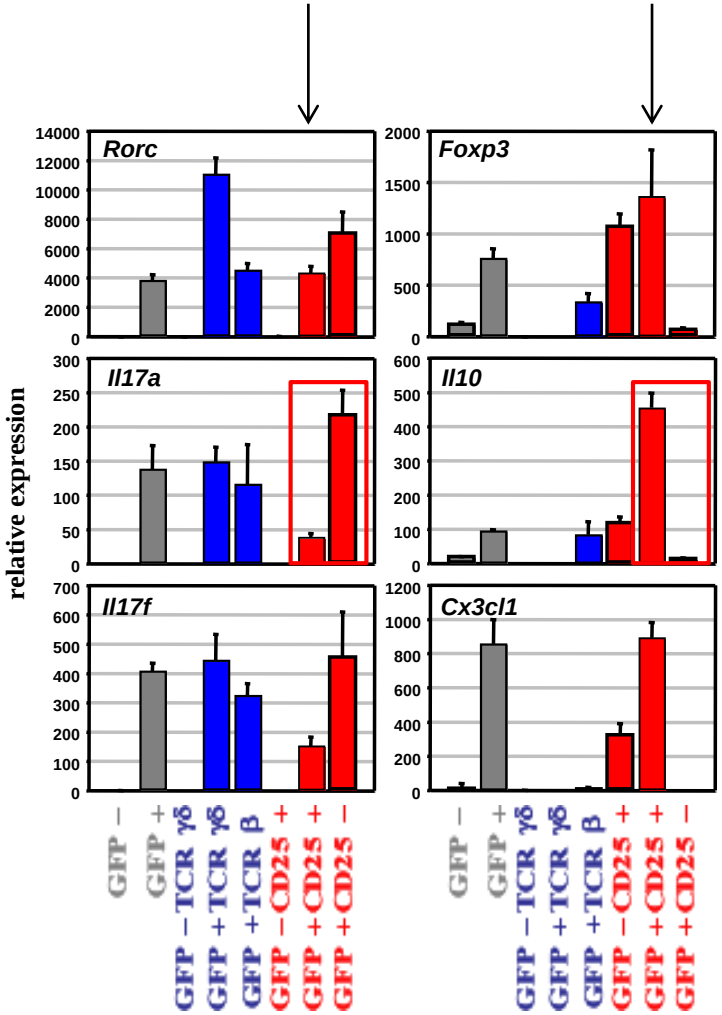






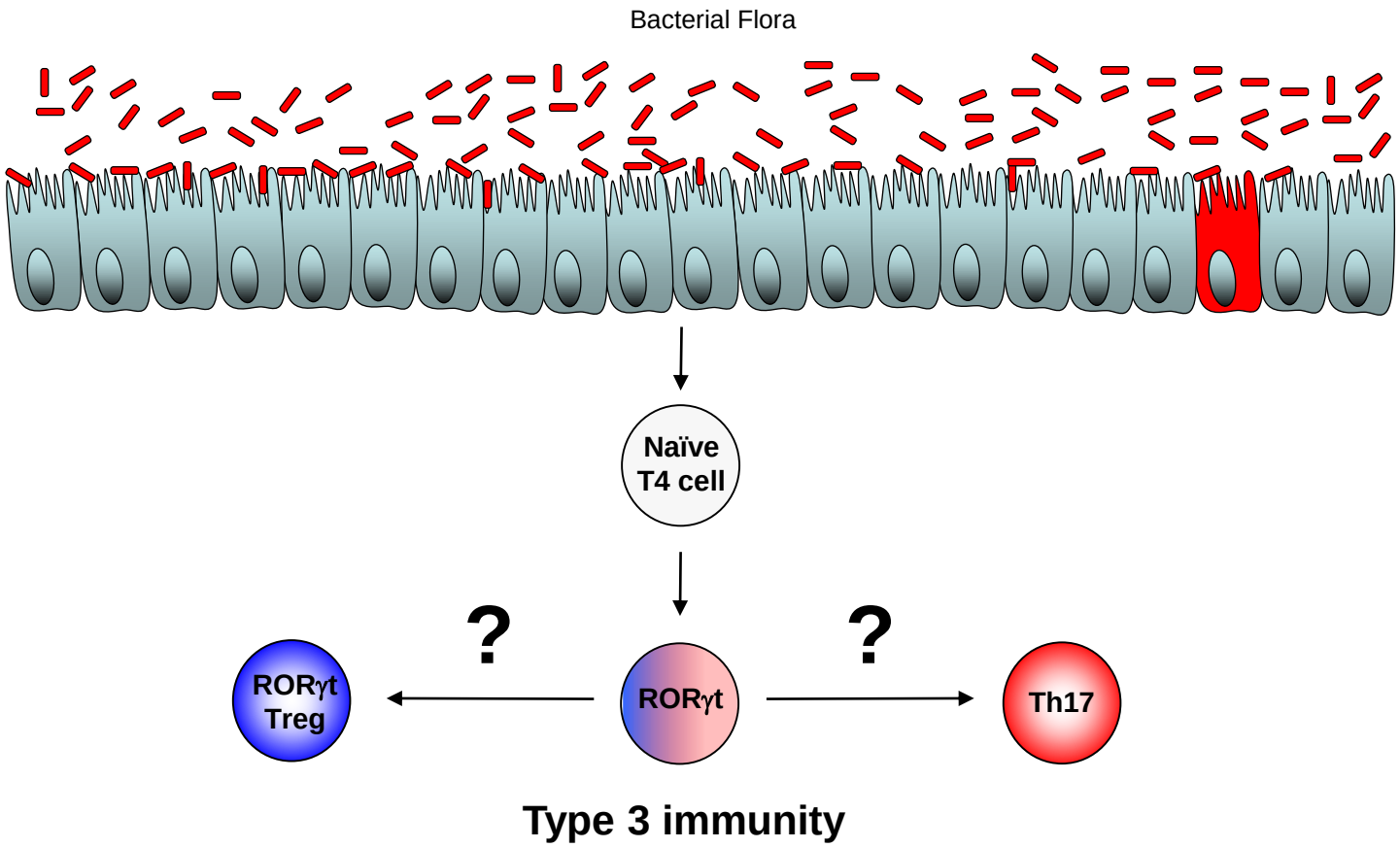
Type 3 Tregs in the intestine





M. Lochner, J. Exp. Med. 2008

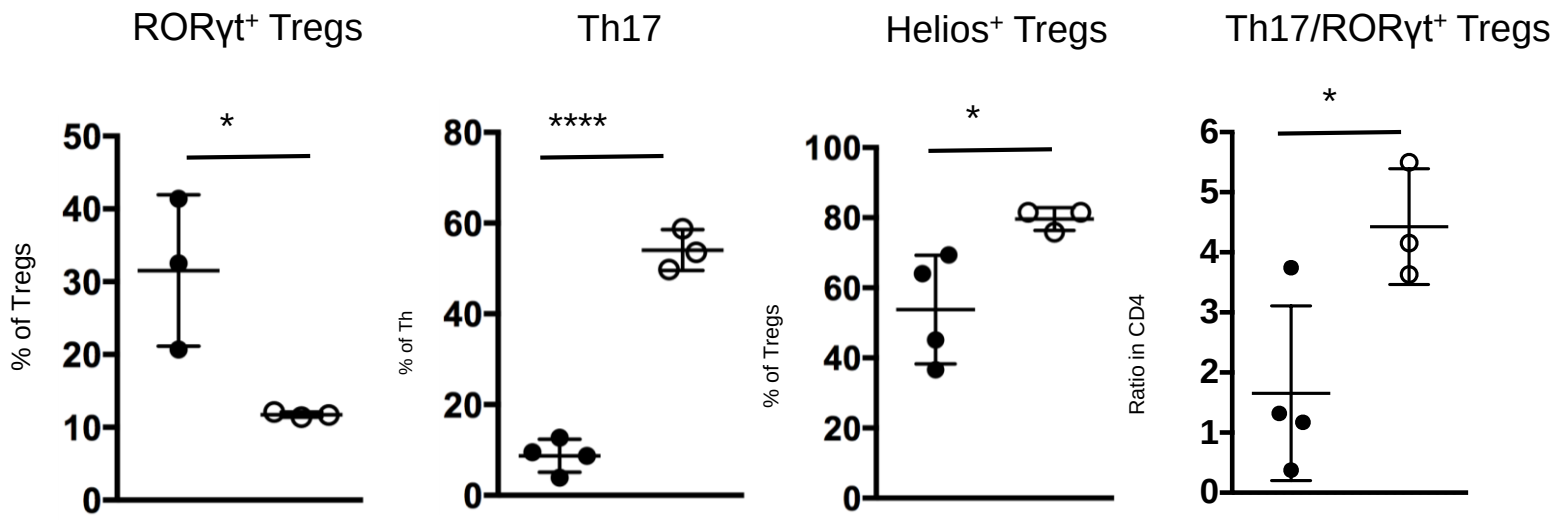
Generate type 3 Tregs or Th17 cells?



Retinoic acid favors Type 3 Tregs over Th17 cells

● Control diet

○ VitA-deficient diet



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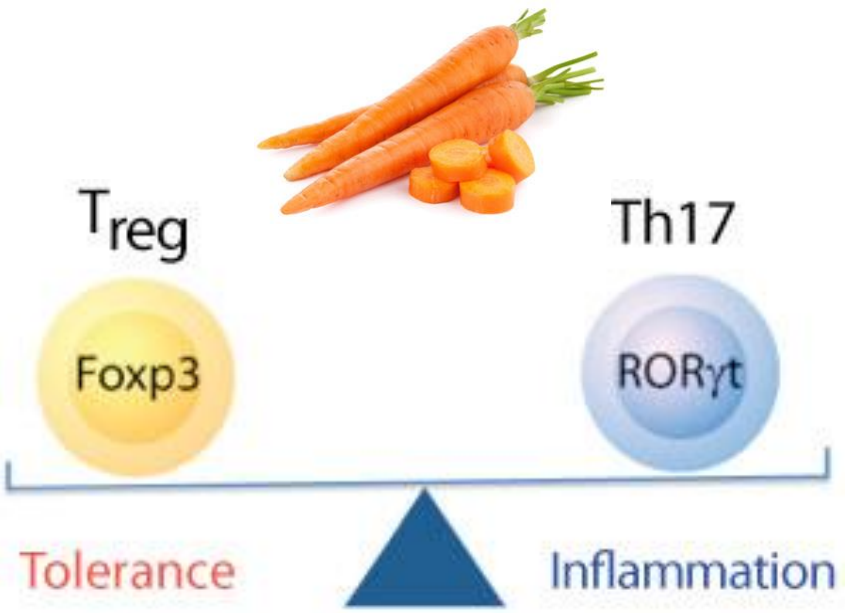
An intestinal equilibrium between Th17 and Treg cells regulated by retinoic acid at steady state

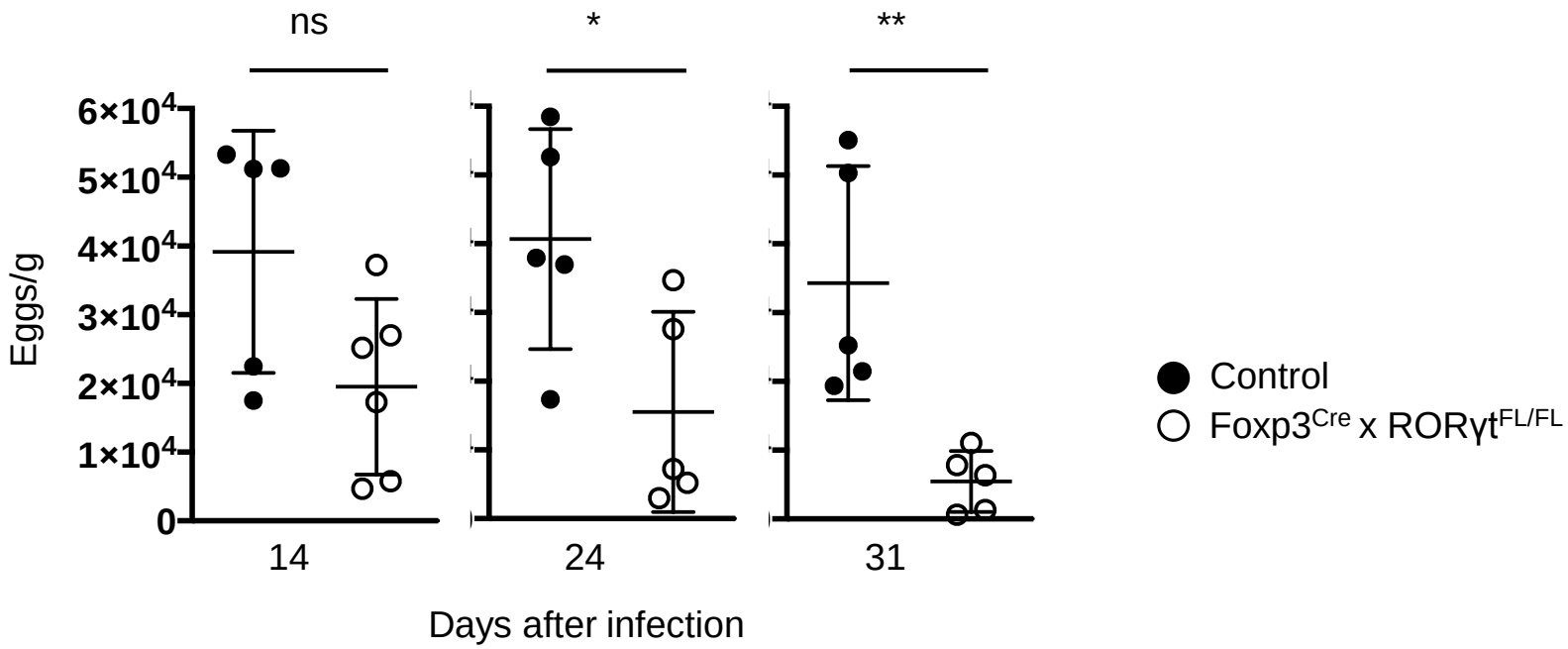


Type 3

Intestinal equilibrium between type 3 and type 2 responses regulated by microbes

Type 3 Tregs control type 2 responses

Heligmosomoides polygyrus infection



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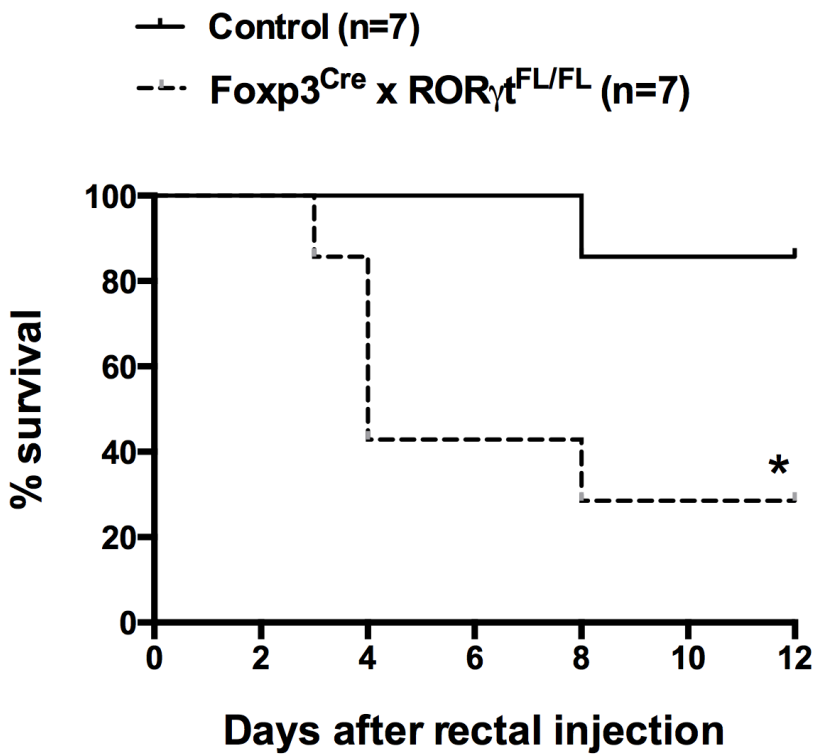
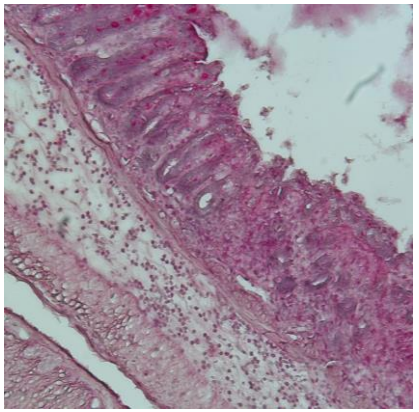
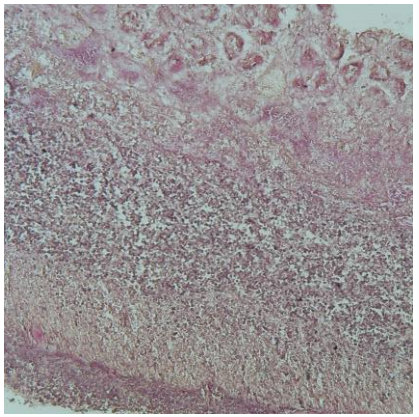
Type 3 Tregs control type 2 responses

Oxazolone colitis (Type 2)



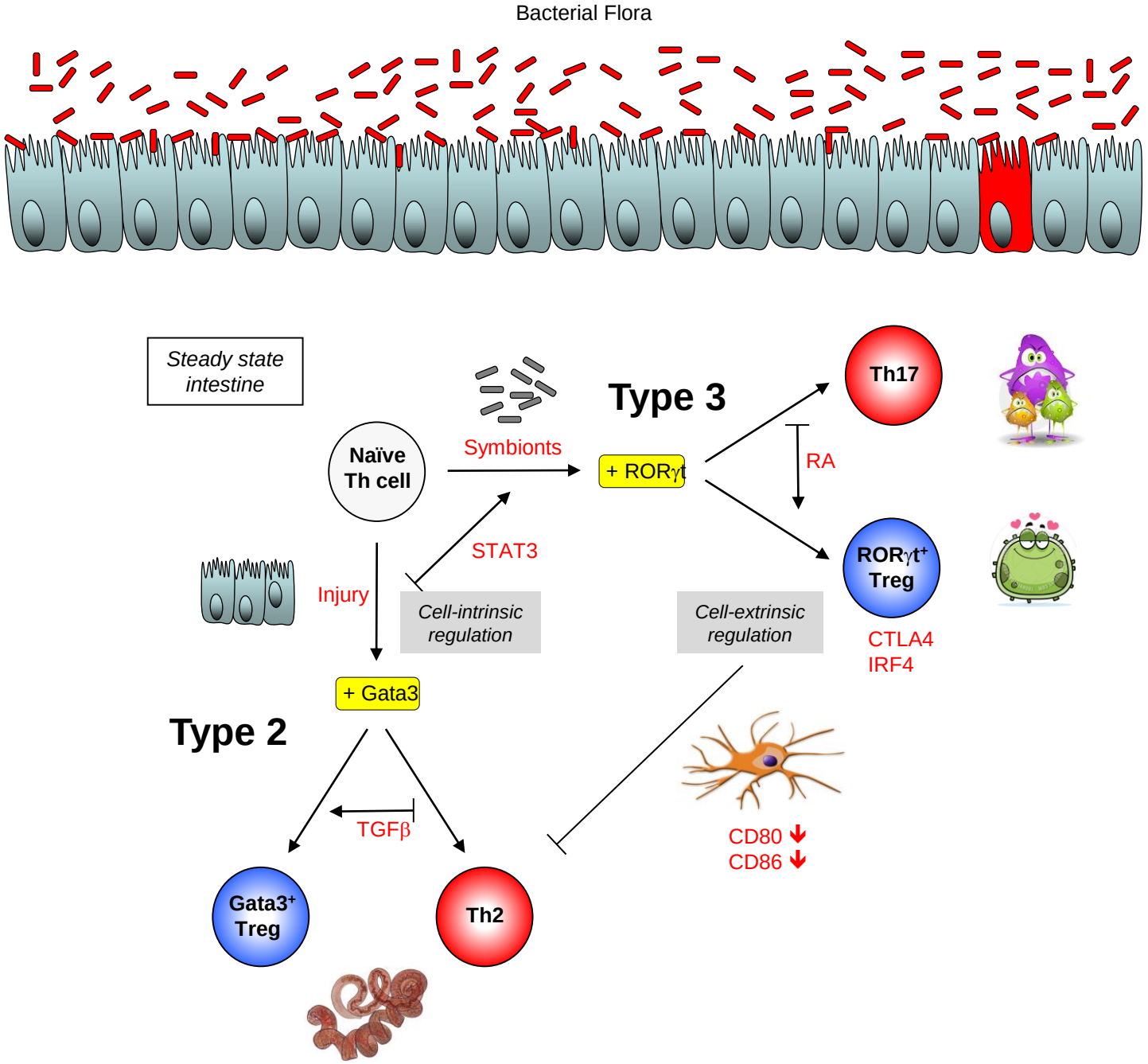


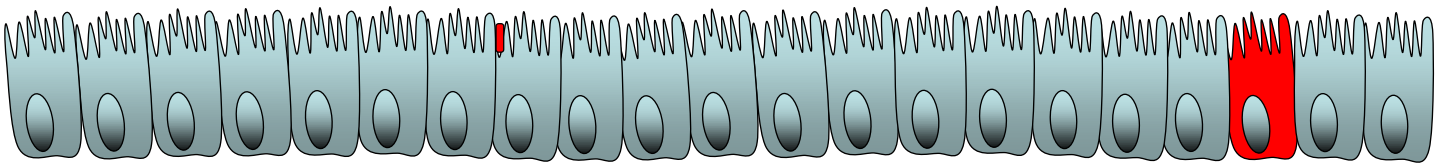
Control

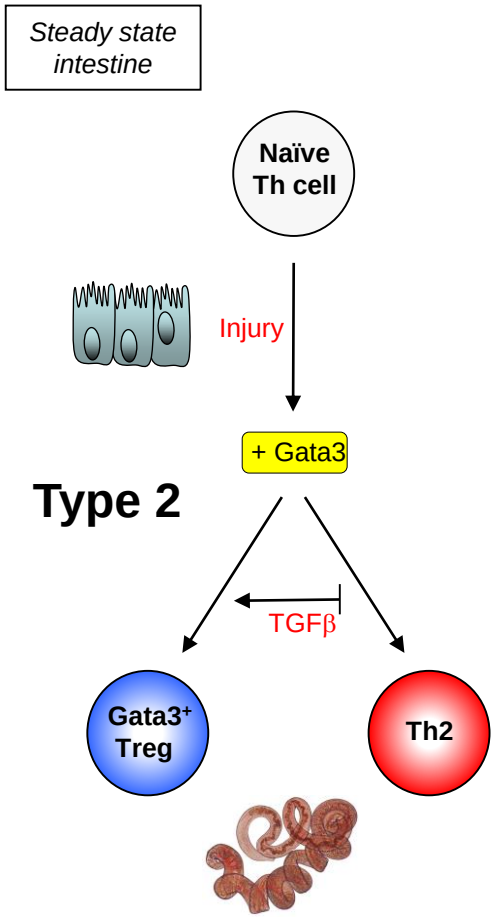


Foxp3^{Cre} x RORγt$^{FL/Fl}$

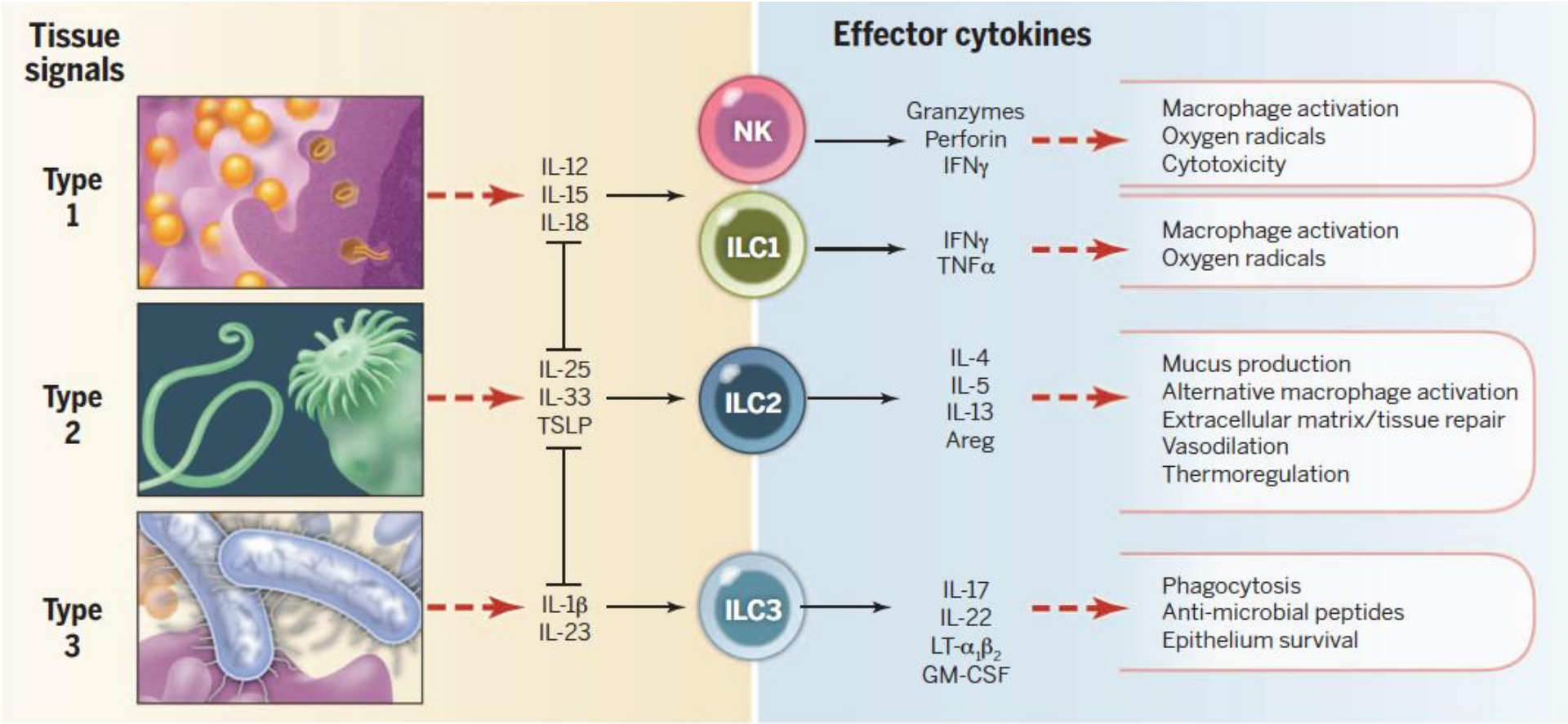
C. Ohnmacht, Science 2015


Bacterial Flora
Steady state intestine
Naïve Th cell
Symbionts
Type 3
+ RORγt
Th17
RA
RORγt+ Treg
CTLA4
IRF4
STAT3
Injury
Cell-intrinsic regulation
Cell-extrinsic regulation
+ Gata3
Type 2
TGFβ
Gata3+ Treg
Th2
CD80
CD86




Steady state intestine
Naïve Th cell
Injury
+ Gata3
Type 2
TGFβ
Gata3+ Treg
Th2

Innate Lymphoid Cells



Eberl et al, Science, 2015

Microenvironment & Immunity Unit

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Universitätsklinikum Erlangen

David Vöhringer

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Meinrad Busslinger