

# ***Host-Parasite Co-Evolution... To whose advantage?***

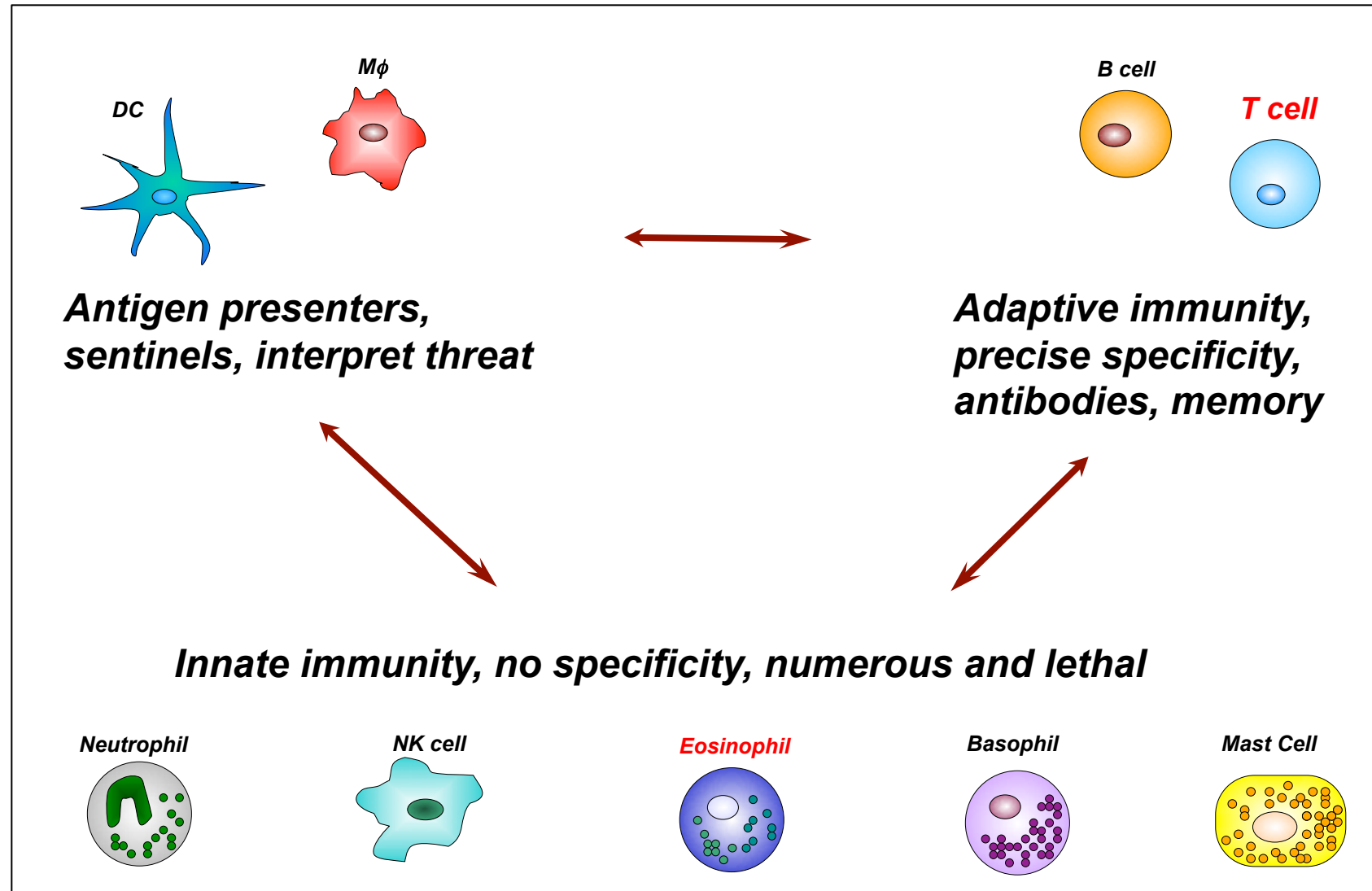
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University of Edinburgh***

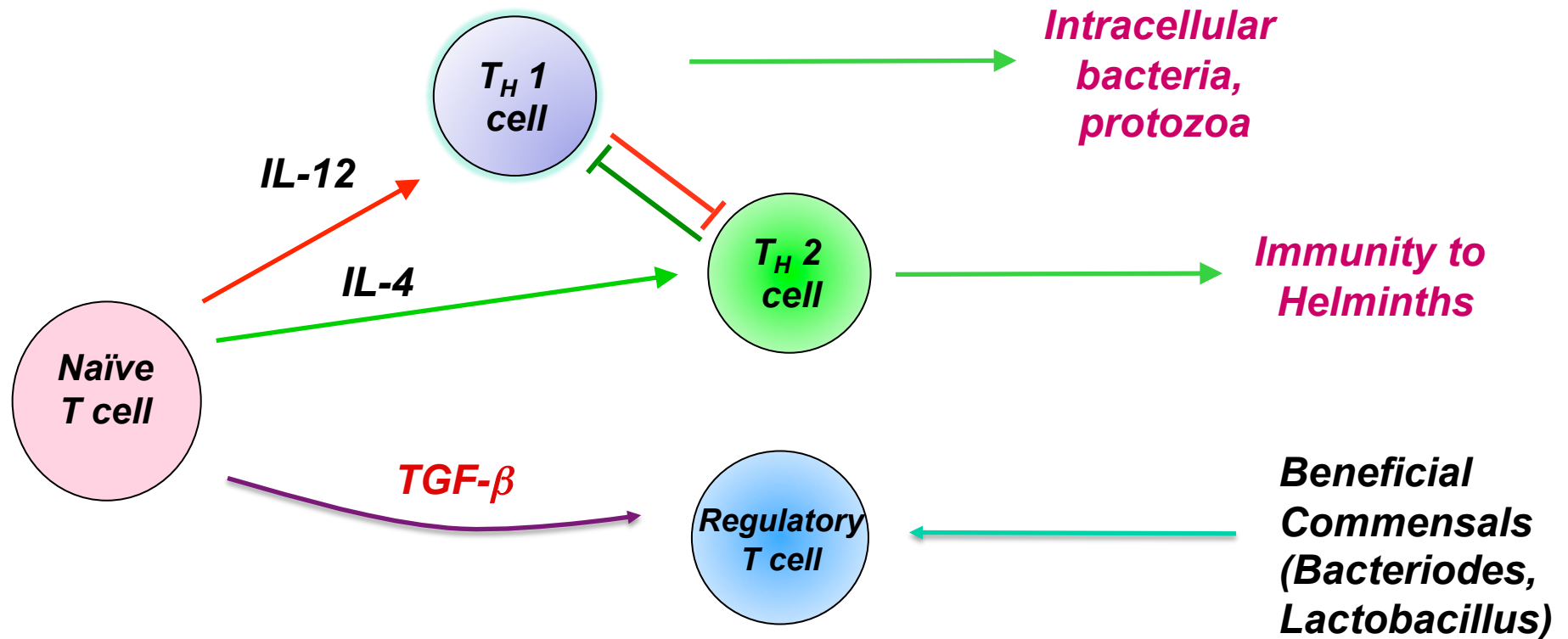
*<http://maizelsgroup.biology.ed.ac.uk/>*



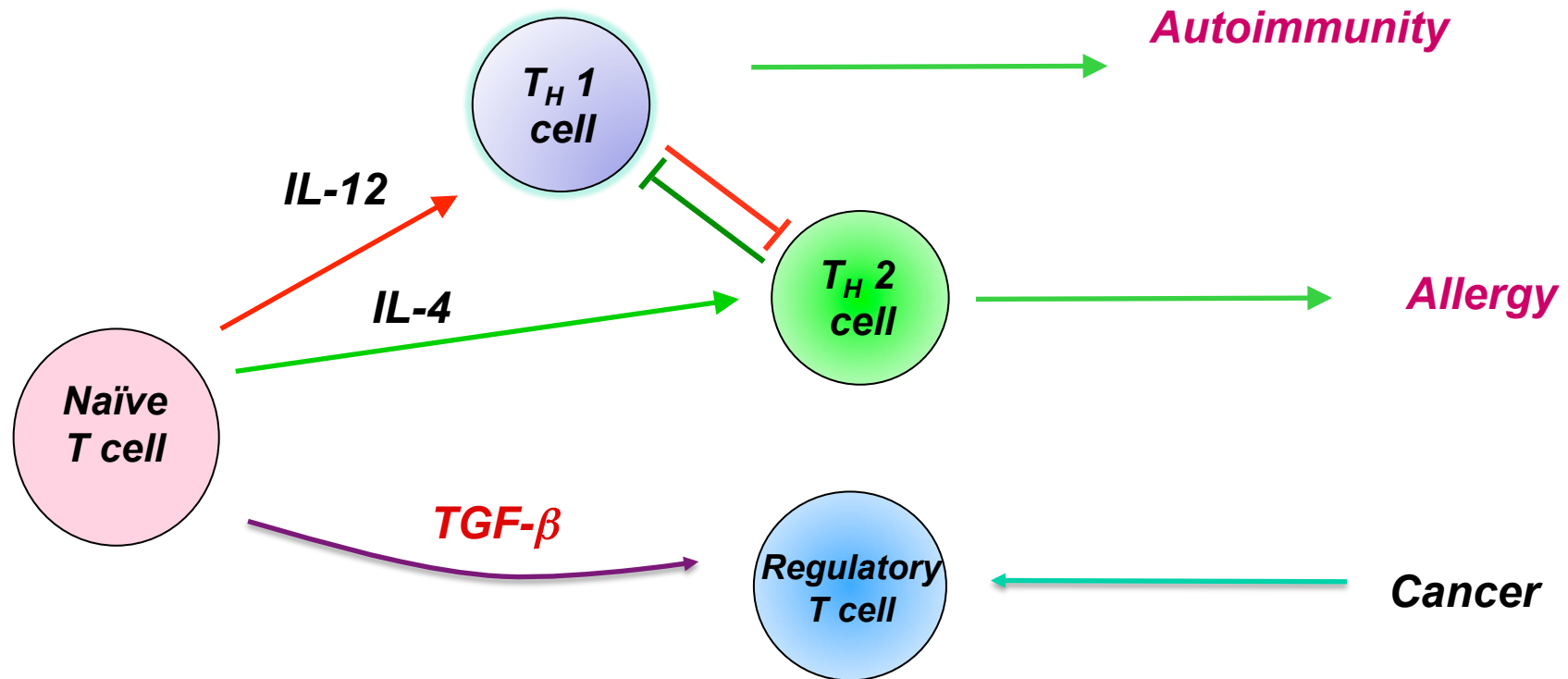
## Immune system has evolved complexity of cell types



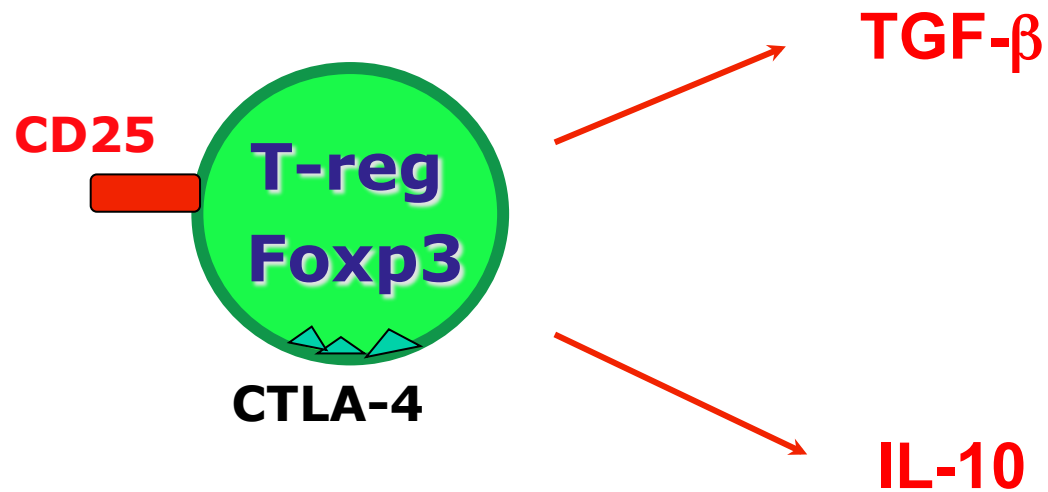
# The immune system evolved to fight many enemies



## The immune system also makes mistakes

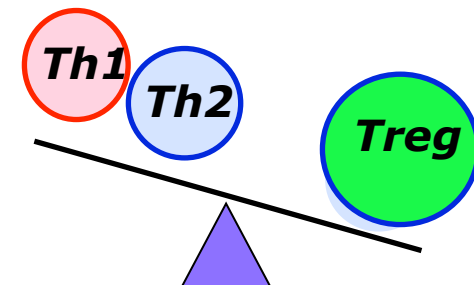


# Regulatory T Cells

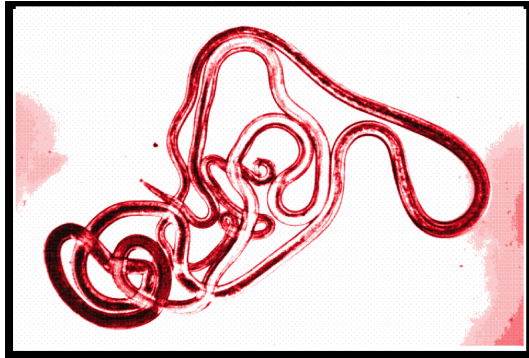


Block Th1 autoimmunity  
- Enforce Self-tolerance  
Maintain food tolerance  
Block Th2 Allergies

But...  
may block immunity to infection, tumours



## Long lived parasites

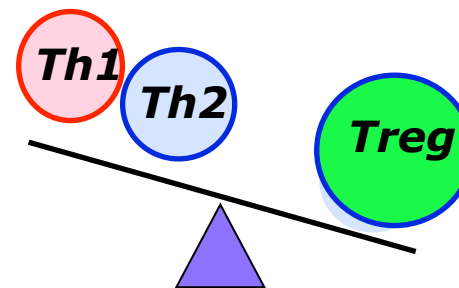


**Filarial nematodes** eg *Brugia malayi*  
inhabiting human lymphatics and  
blood

**Schistosomes** eg *Schistosoma  
mansoni*, living in hepatic  
vasculature



**Like Self antigens ?**  
**Induce Immune System's own Down-  
Regulatory Mechanisms**



# Helminth Parasites Infect 25% of the Human Population

<i>Species</i>	<i>No. infected</i>
<i>Schistosoma mansoni</i> and other schistosome species	200 million
<i>Lymphatic Filaria</i> ( <i>Brugia malayi</i> and <i>Wuchereria bancrofti</i> )	140 million
<i>Trichuris trichiura</i>	795 million
<i>Ancylostoma</i> and other hookworms	740 million
<i>Ascaris lumbricoides</i>	1221 million

Figures from  
Elliott et al (2007)  
Int J Parasitol  
37:457



Current  
global  
population  
6,850 million

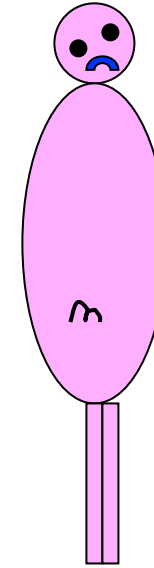
# Spectrum of outcomes in helminth infections



*Uninfected  
despite exposure*



*Infected  
no pathology*



*Infected  
pathology*

*Frequency*

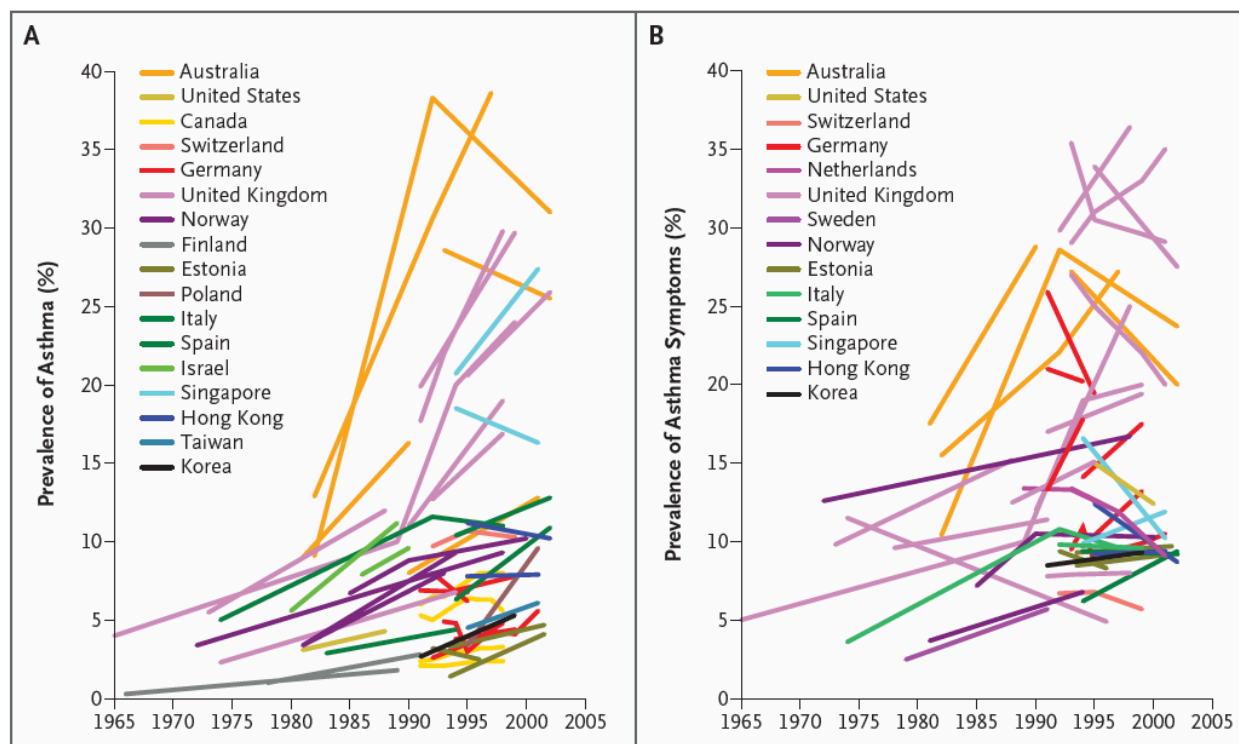


REVIEW ARTICLE

CURRENT CONCEPTS

# The Asthma Epidemic

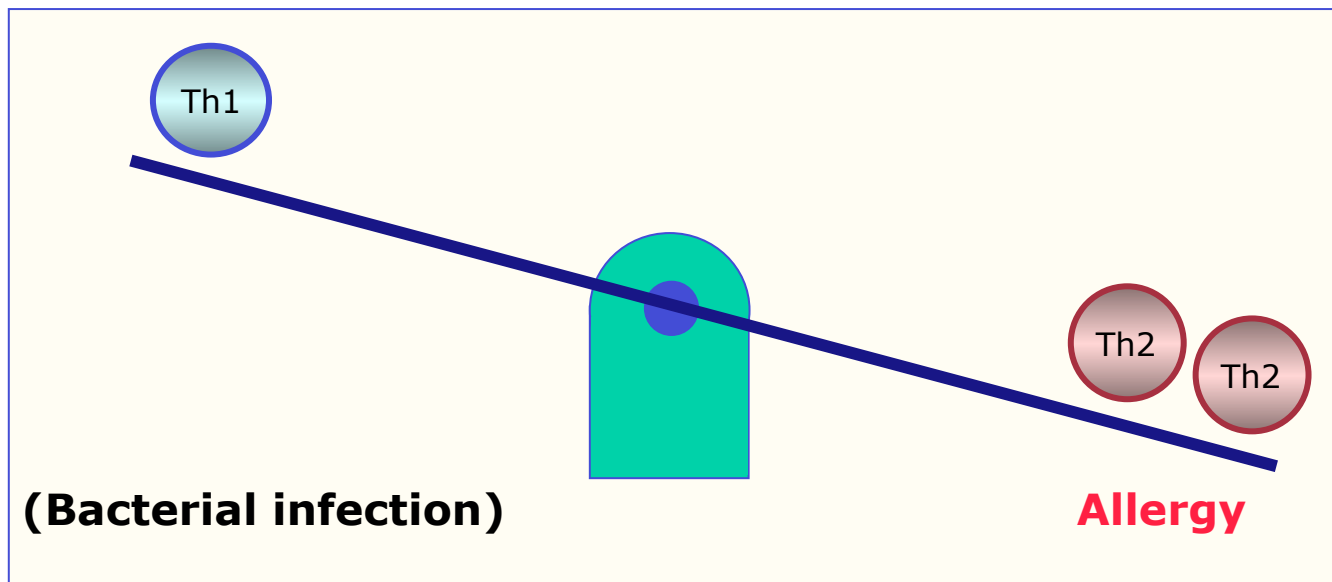
Waltraud Eder, M.D., Markus J. Ege, M.D., M.P.H., and Erika von Mutius, M.D.



**Figure 1.** Changes in the Prevalence of Diagnosed Asthma and Asthma Symptoms over Time in Children and Young Adults.

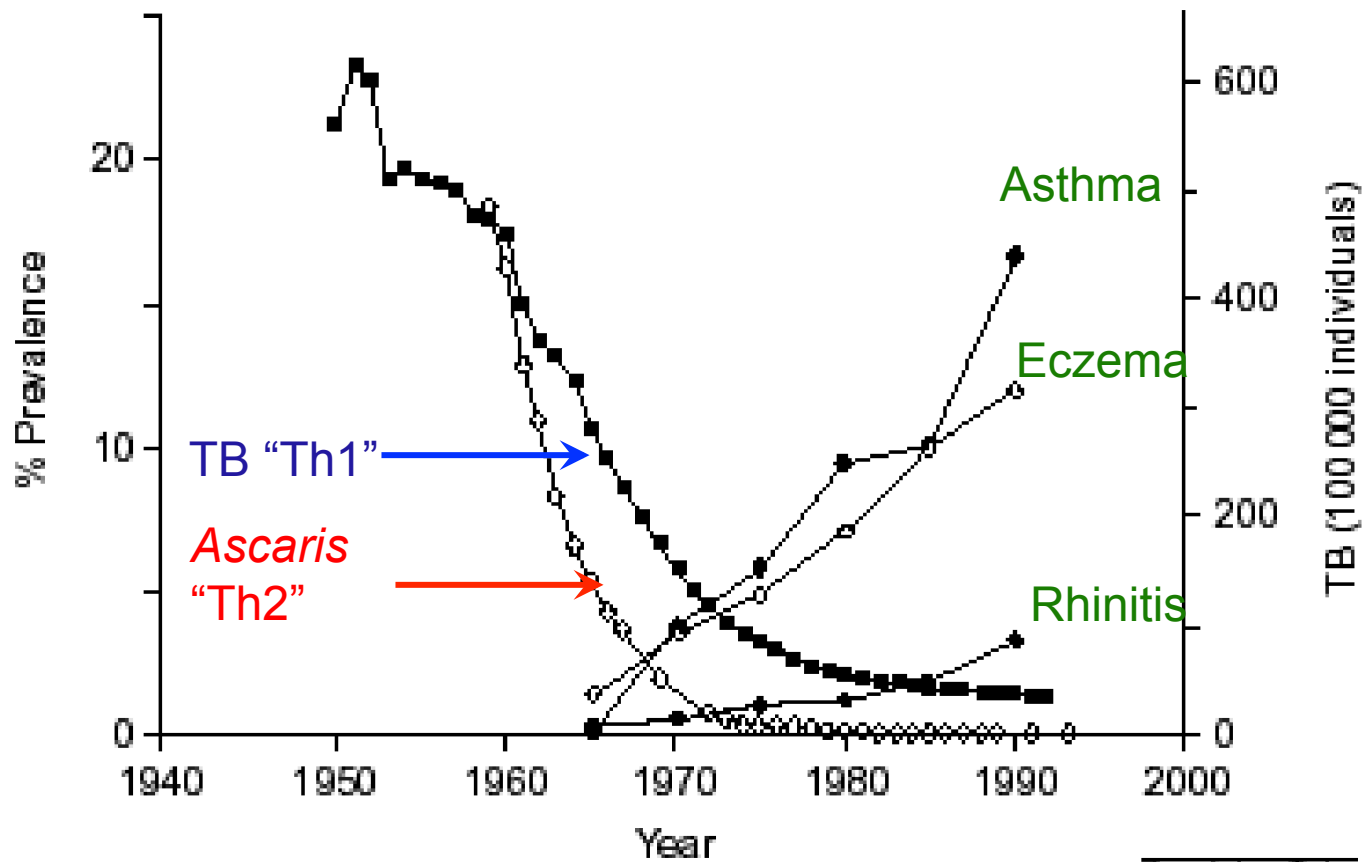
# "The Hygiene Hypothesis", 1990's

First mooted by Strachan (1989, BMJ 299:1259)  
*"Hay fever, hygiene and household size"*



Reduced exposure to microbial infections in developed countries has resulted in exaggerated Th2 responsiveness - and the allergy epidemic

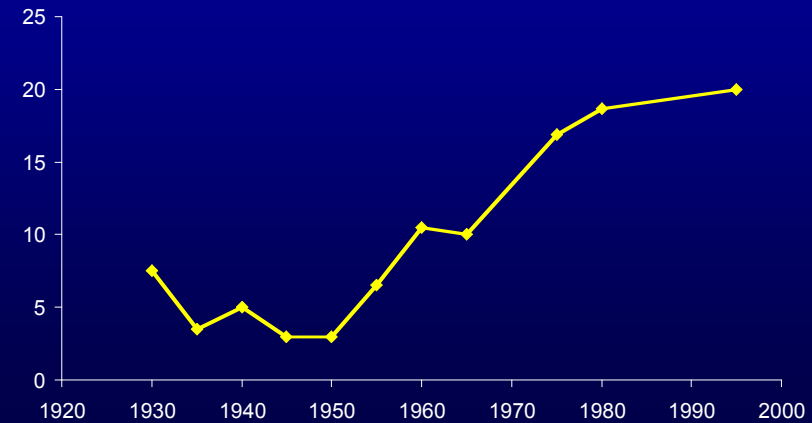
## But... Th2-driving infections also fell in developed countries



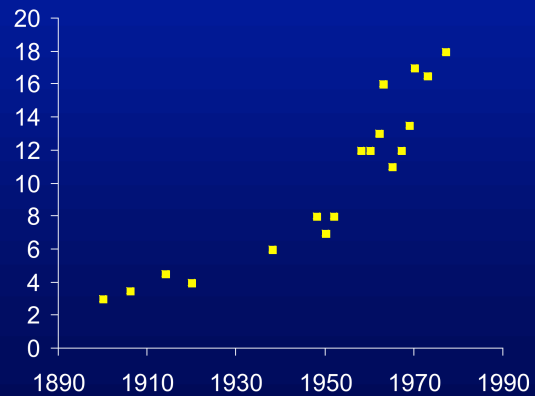
Parasitology Today

**... and Th1  
autoimmune  
diseases also  
rising**

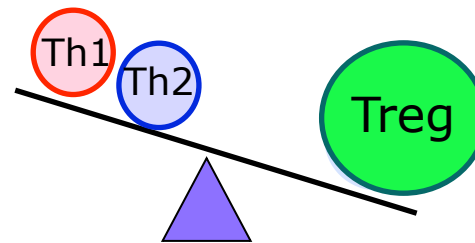
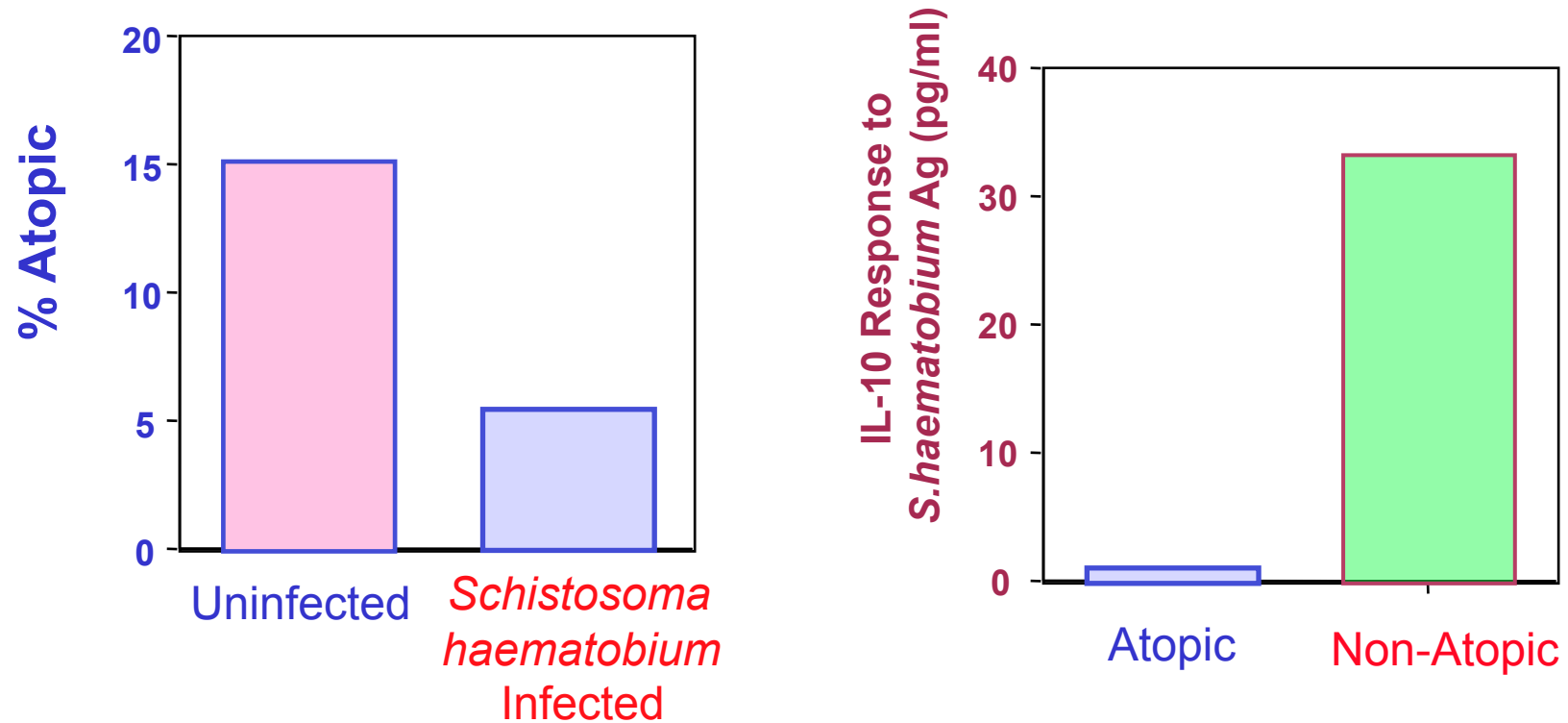
### **Childhood diabetes in Norway 0-10 years, 1925-1995**



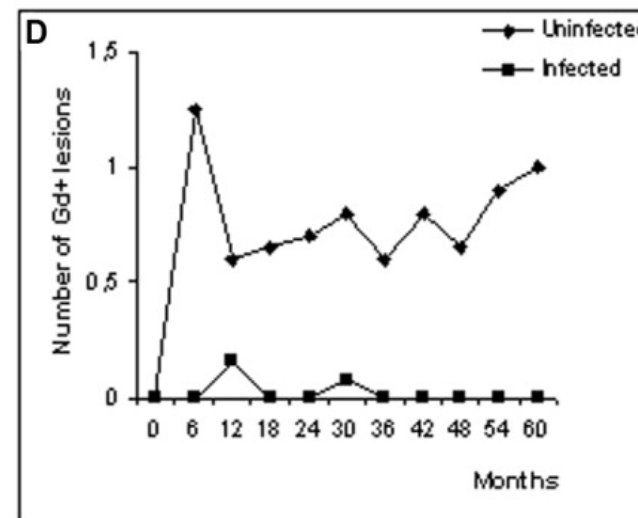
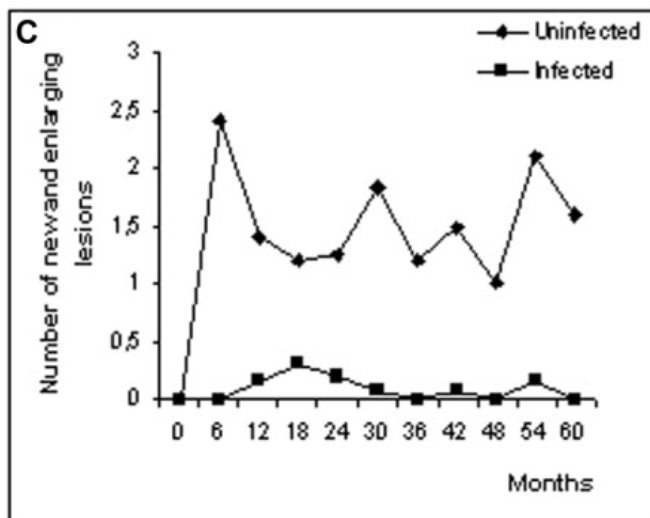
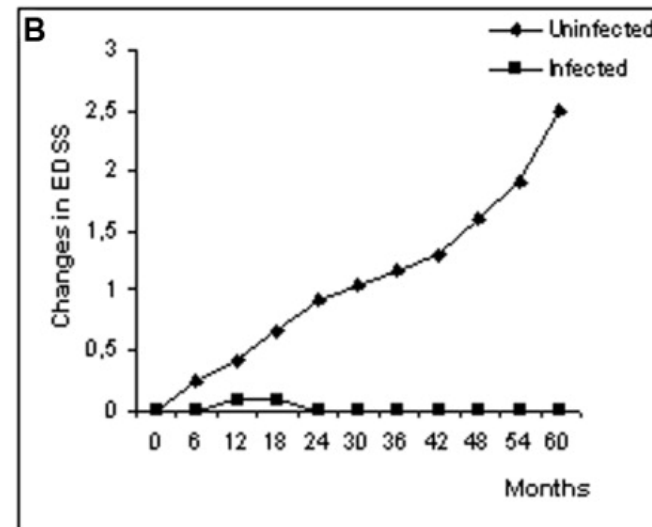
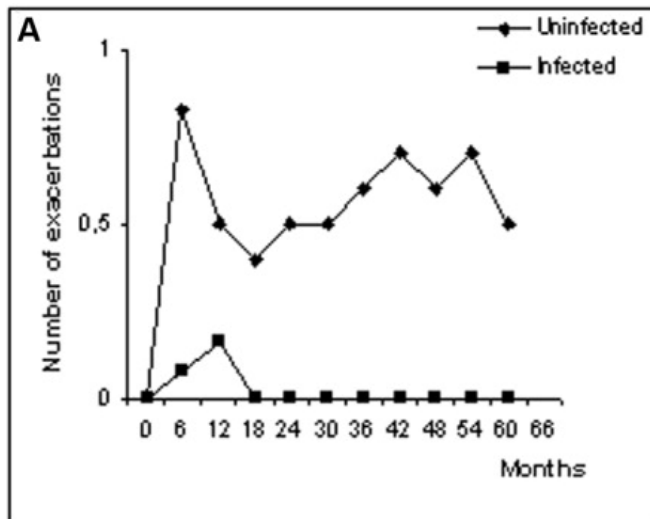
### **Incidence of type 1 diabetes in the USA 1900-1976**



## Helminth (Th2)-infected children have *less* allergy\*



# Helminths may mitigate multiple sclerosis



## Helminths as therapy ?



<http://www.ovamed.org/>

Clinical treatments are now being offered using live *Trichuris suis* to alleviate chronic inflammatory diseases of Ulcerative Colitis and Crohn's Disease

Trials now under way for *Necator americanus* therapy, and for helminth therapy of multiple sclerosis and allergic rhinitis

Summers et al (2005) Gut 54: 87-90

Summers et al (2005) Gastroenterology 128: 825-832

Bager et al (2010) J Allergy Clin Immunol 125:123-30

Feary et al (2010) Clin Exp Allergy 40: 299-306

## Infection with *H. polygyrus*



*H. polygyrus* - model system  
gut nematode in mice

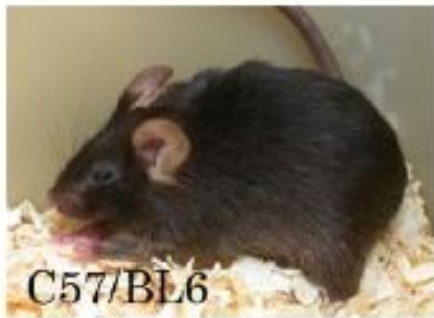
- Natural parasite of mice
- Establishes chronic infection in most strains
- Entirely enteric - does not transit lungs



## Models of airway allergy

### Model 1

C57BL/6 mice sensitised and challenged with Der p1 from *Dermatophagoides pteronyssinus*



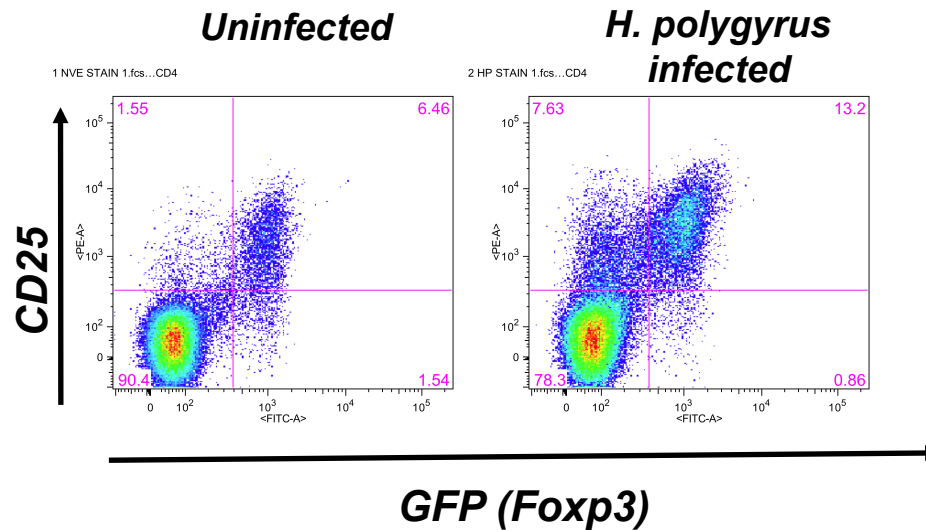
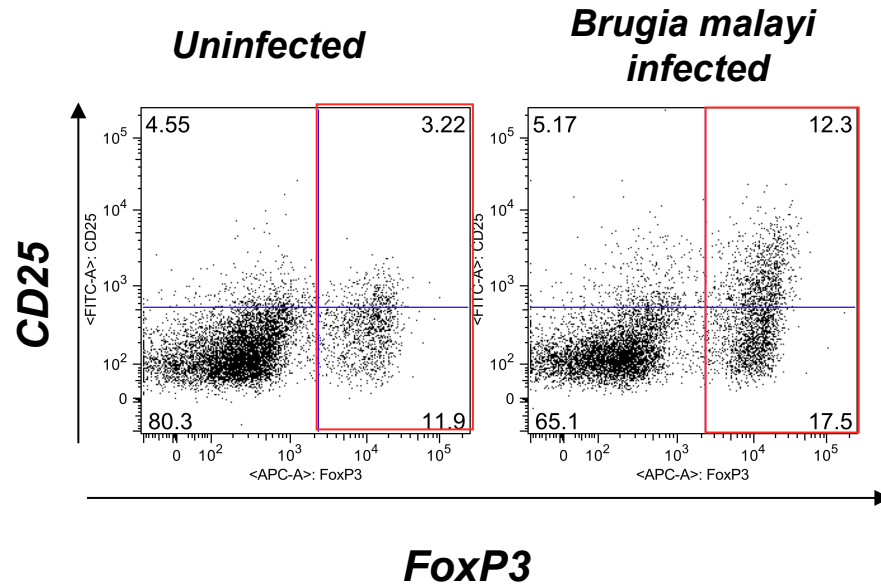
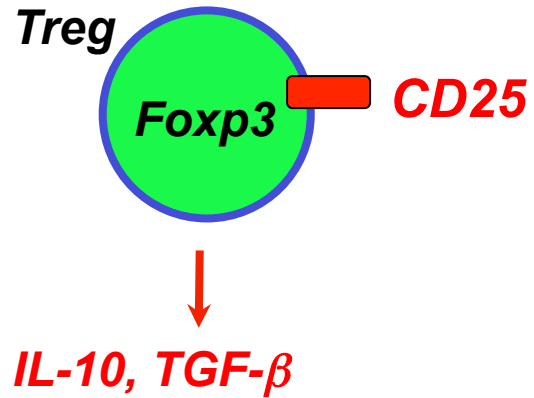
### Model 2

BALB/c mice sensitised and challenged with Ovalbumin (OVA).

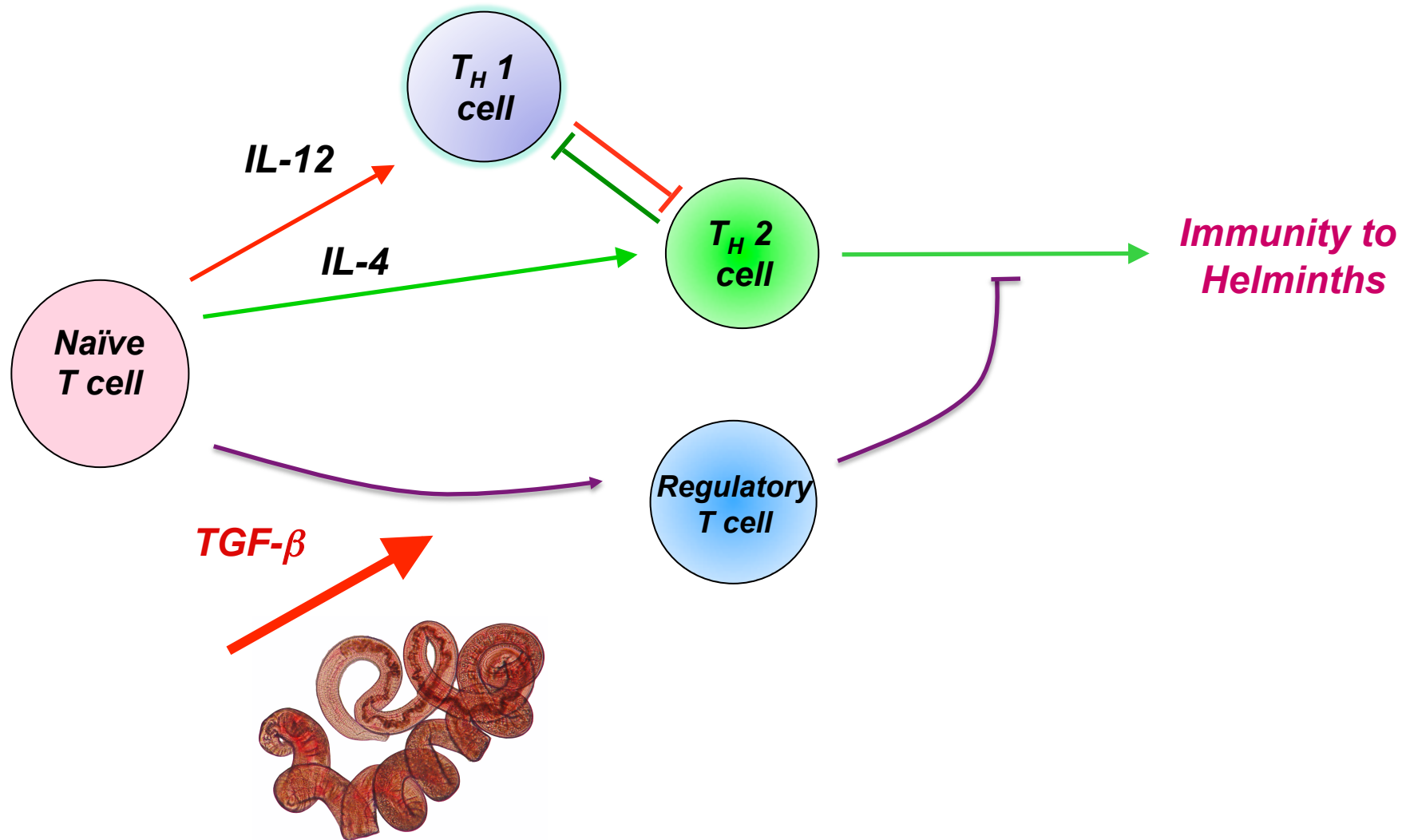




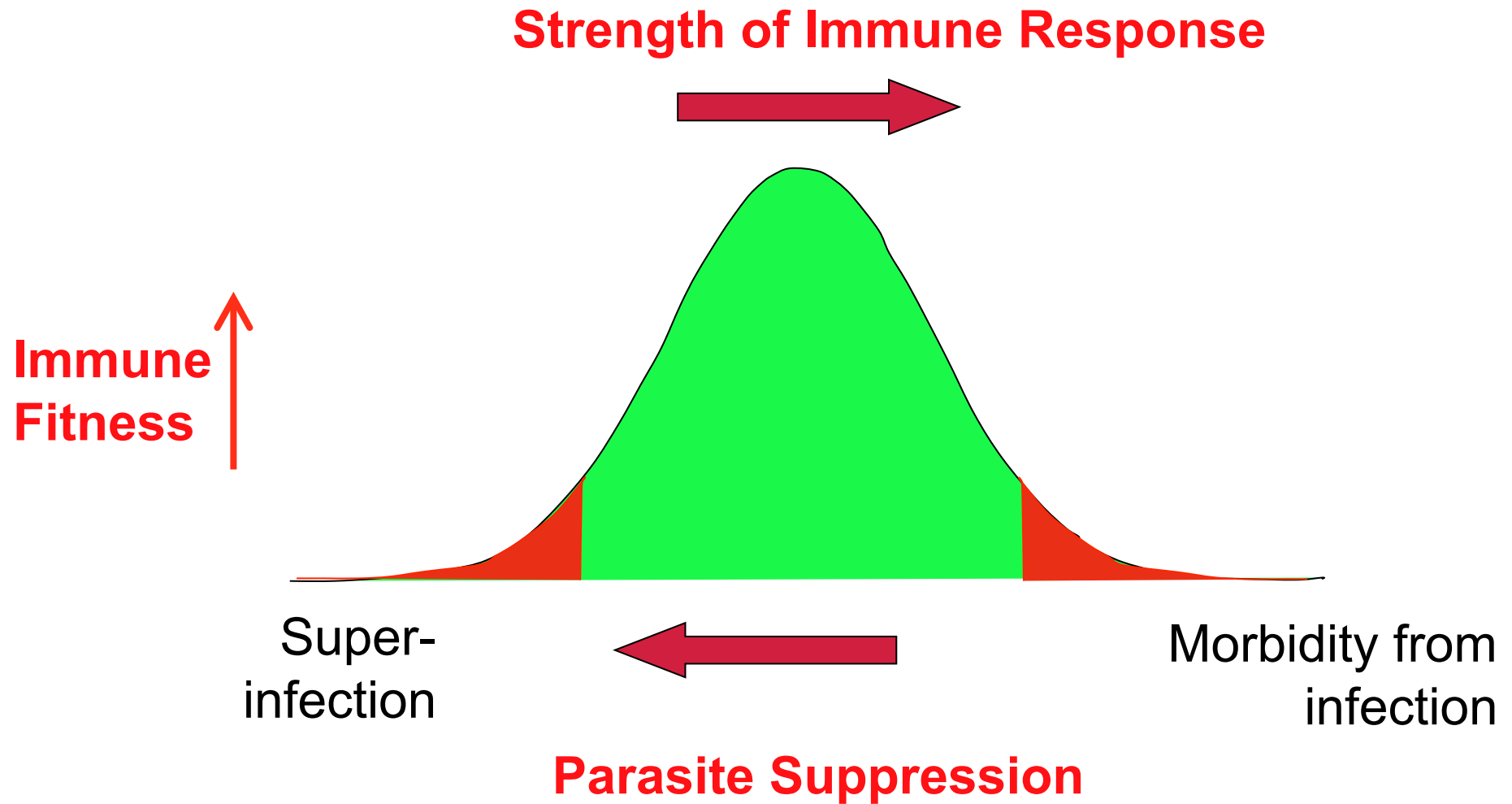
# Helminths induce Regulatory T cells



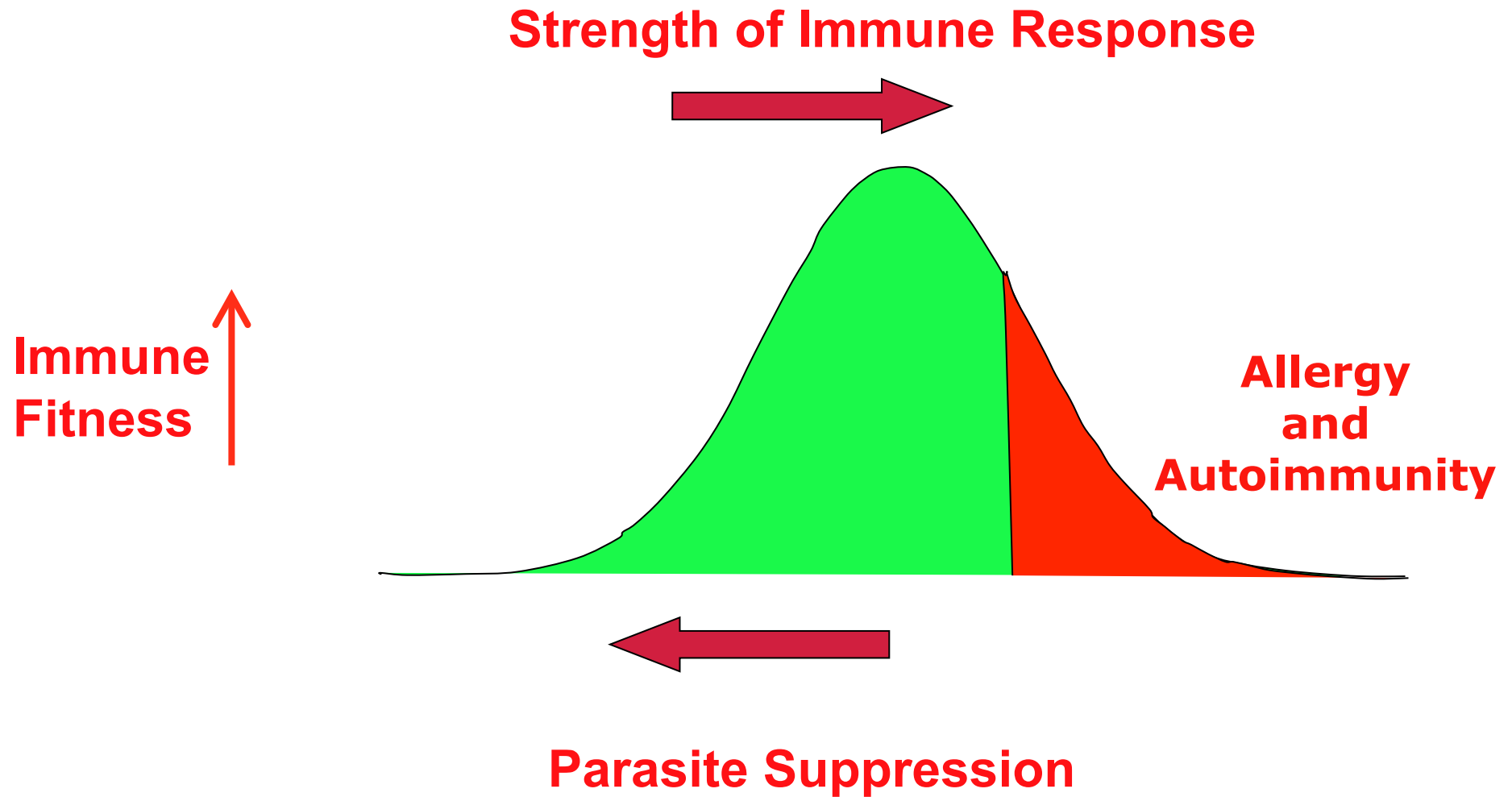
## Helminths mimic $TGF\beta$ to exploit host pathway



**If parasites dampen the immune system,  
we will have evolved to compensate**



# In absence of parasites...



## ***Helminths may promote immune polymorphism***

Parasites represent a major selective force for interleukin genes and shape the genetic predisposition to autoimmune conditions

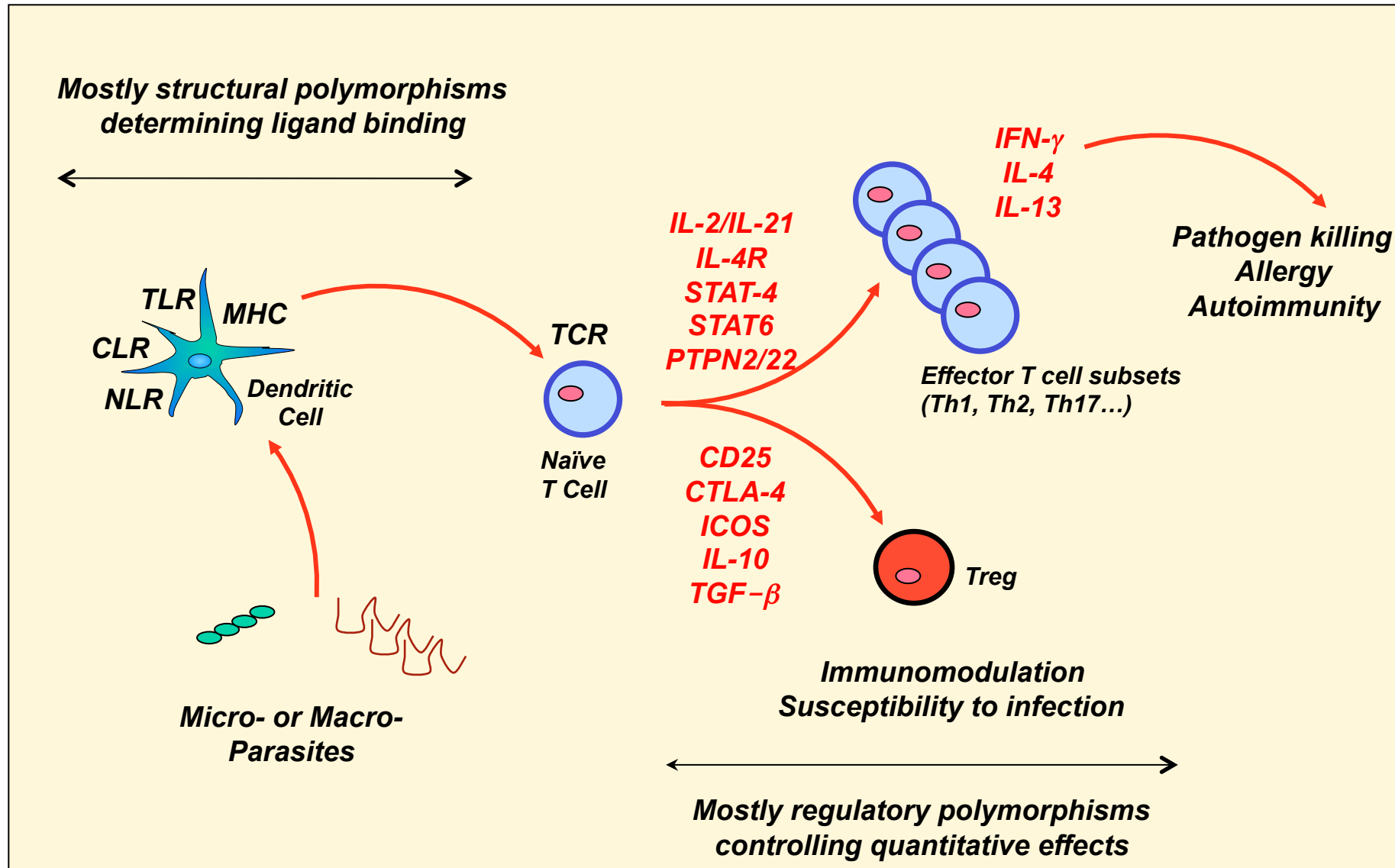
Matteo Fumagalli,<sup>1,2</sup> Uberto Pozzoli,<sup>1</sup> Rachele Cagliani,<sup>1</sup>  
Giacomo P. Comi,<sup>3</sup> Stefania Riva,<sup>1</sup> Mario Clerici,<sup>4,5</sup> Nereo Bresolin,<sup>1,3</sup>  
and Manuela Sironi<sup>1</sup>

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***J Exp Med 206 : 1395 (2009)***

- Populations with greater helminth species diversity have greater immune gene polymorphism
- Greater parasite “species richness” associated with 6/9 CD/IBD predisposition alleles

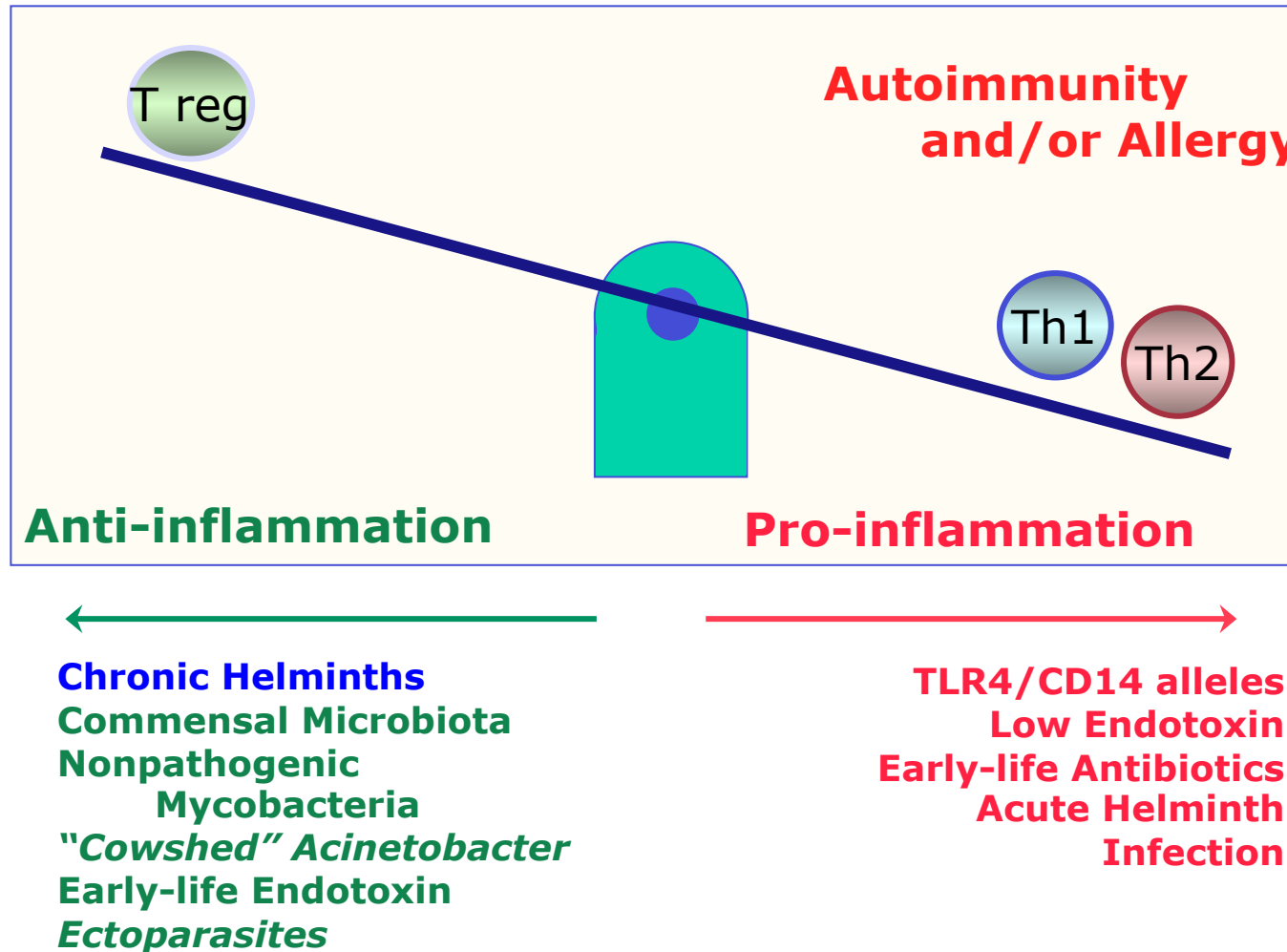
# Immune polymorphisms – mostly fine tuning





# Expanded Hygiene Hypothesis, 2010

Regulatory T cells (Tregs) can control immune pathologies of Th1 autoimmunity *and* Th2 allergy



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**David Knox, Moredun**

**Alexander Rudensky : Foxp3-GFP**