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The first recorded death from an insect allergy was King Menes of Egypt, who, according to the hieroglyphics on his tomb, died of a wasp sting in 2621 B.C.



A typical family history of atopy

Emperor Augustus: suffered from bronchial asthma, seasonal rhinitis and atopic eczema

Emperor Claudius: perennial rhinoconjunctivitis

Britannicus: horse dander allergy



King Richard III (1452-1485) used his allergy to strawberries to arrange the murder of Lord William Hastings.

He ate some strawberries and developed acute urticaria.

He then accused Hastings of putting a curse on him, an action that demanded the head of Hastings on a plate.

Regulatory/suppressor cells

Suppressor mechanism

T cells

Tr1

IL-10, TGF- β

Th3

TGF- β

CD4⁺ CD25⁺ T_{Reg}

IL-10, TGF- β , CTLA-4,
PD-1, GITR

CD8⁺ CD25⁺

Same as CD4⁺ CD25⁺

CD28⁻ T_{Reg}

Qa-1-dependent CD8⁺

Qa-1-specific TCR

CD4⁻ CD8⁻ T_{Reg}

induction of apoptosis

TCR $\gamma\delta$ T_{Reg}

IL-10, TGF- β

B cell subset

B_{reg}

IL-10

DC

DC_{Reg}

IL-10

NK cell subset

NK_{Reg}

IL-10

Macrophages

IL-10, TGF- β

Resident tissue cells

IL-10, TGF- β

IPEX syndrome

FOX P 3 mutations

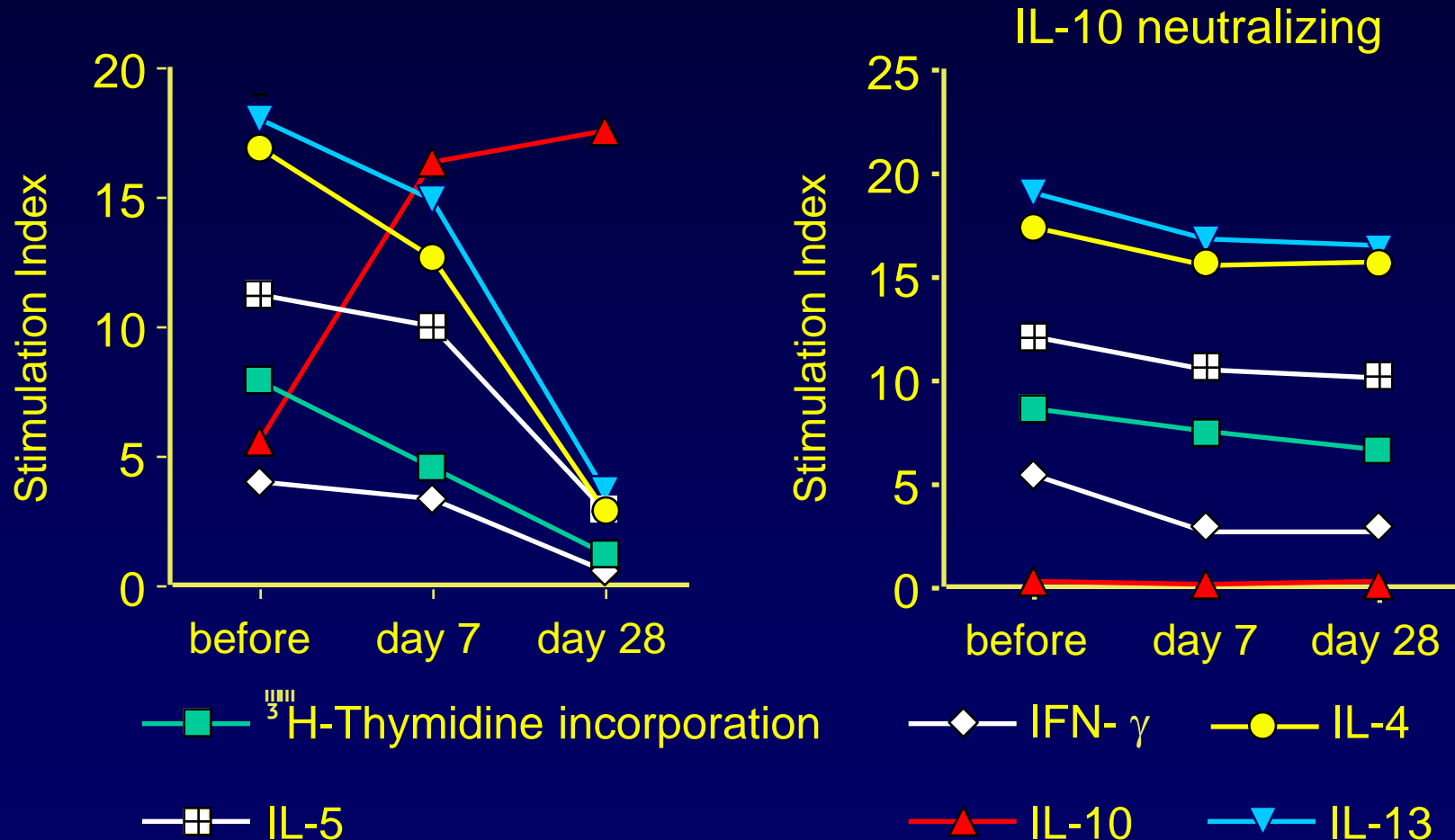
Hyper IgE

Eczema

Autoimmunity

Increased Th1 and Th2

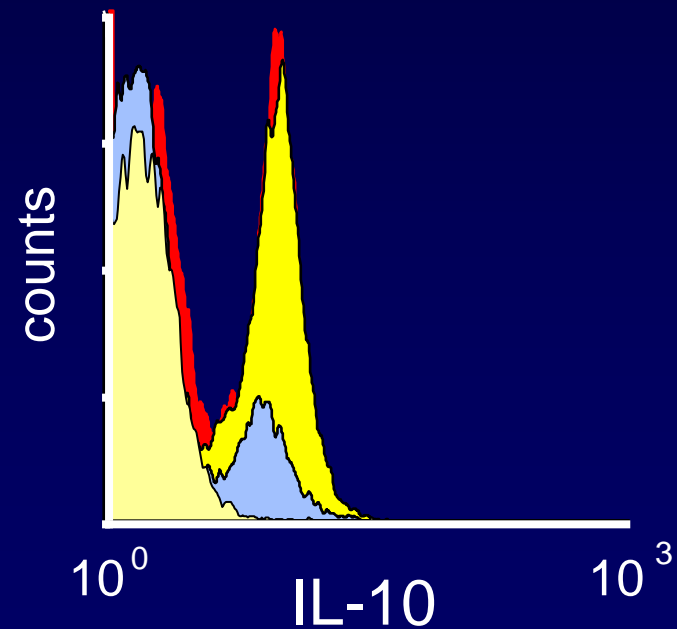
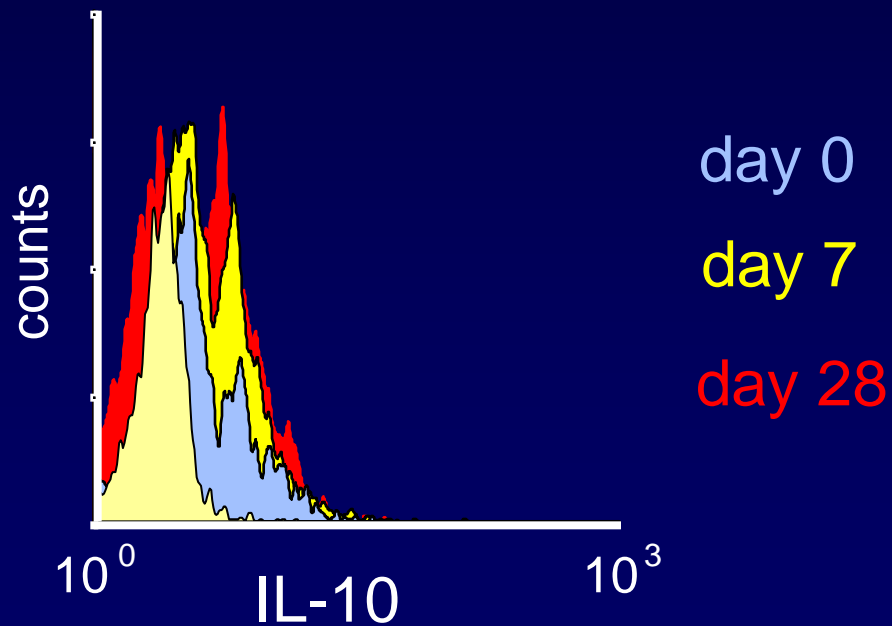
IL-10-induced peripheral T cell tolerance in bee venom specific-immunotherapy



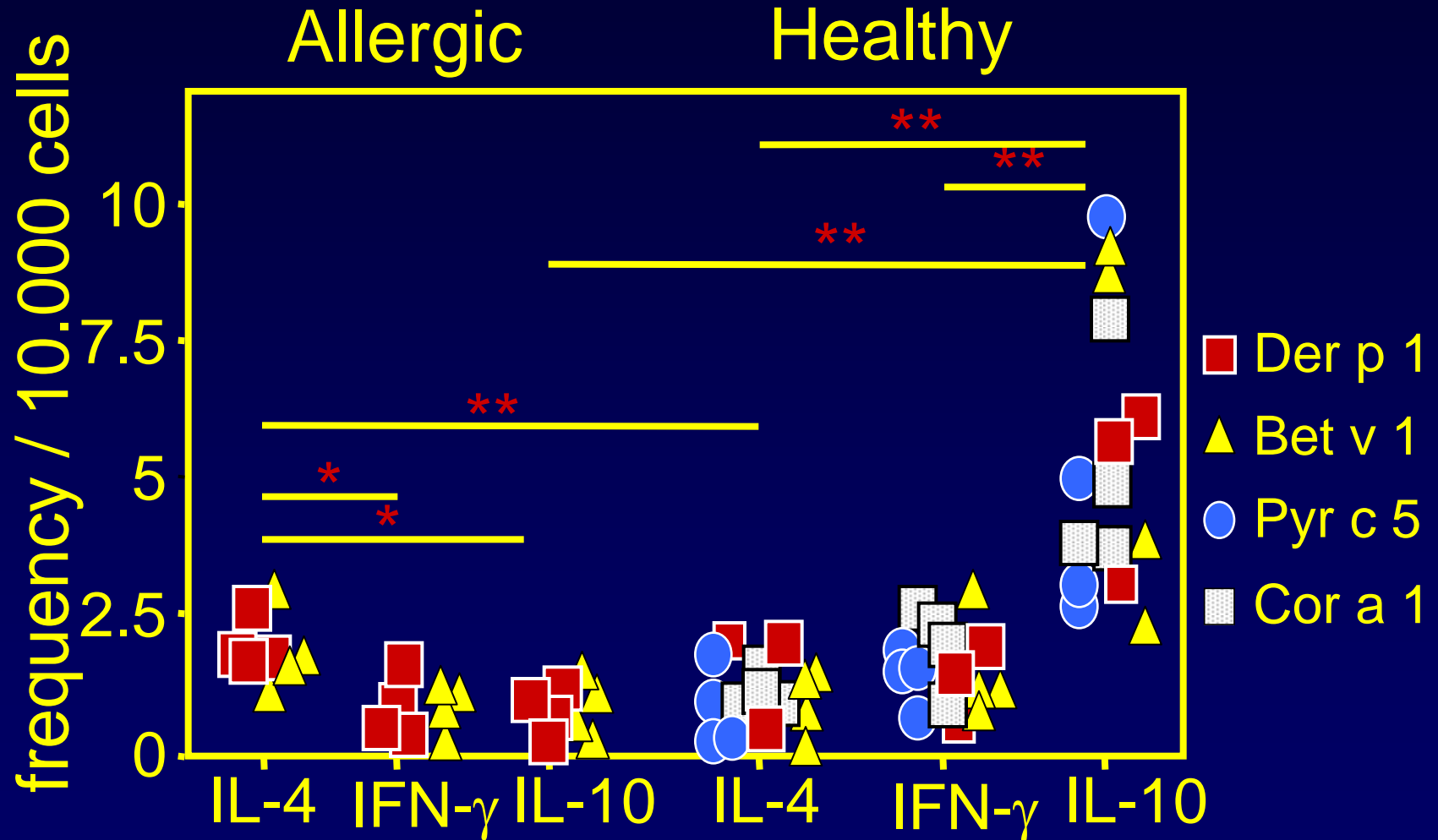
IL-10 production in T cells during specific immunotherapy

CD4⁺ CD25⁺ T cells

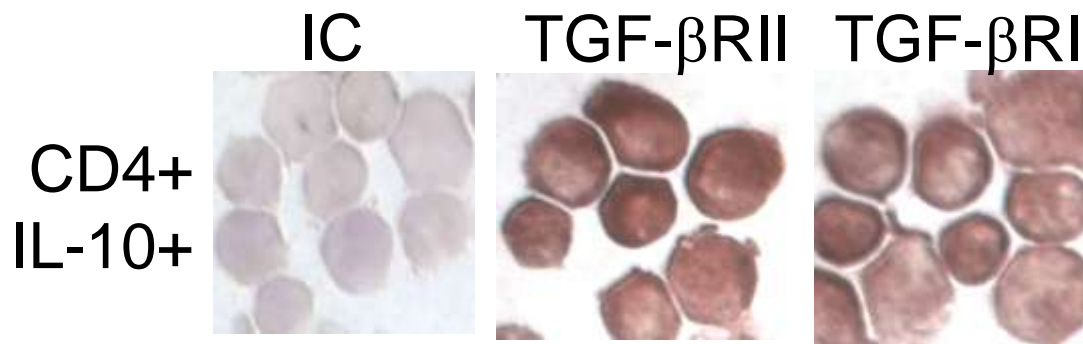
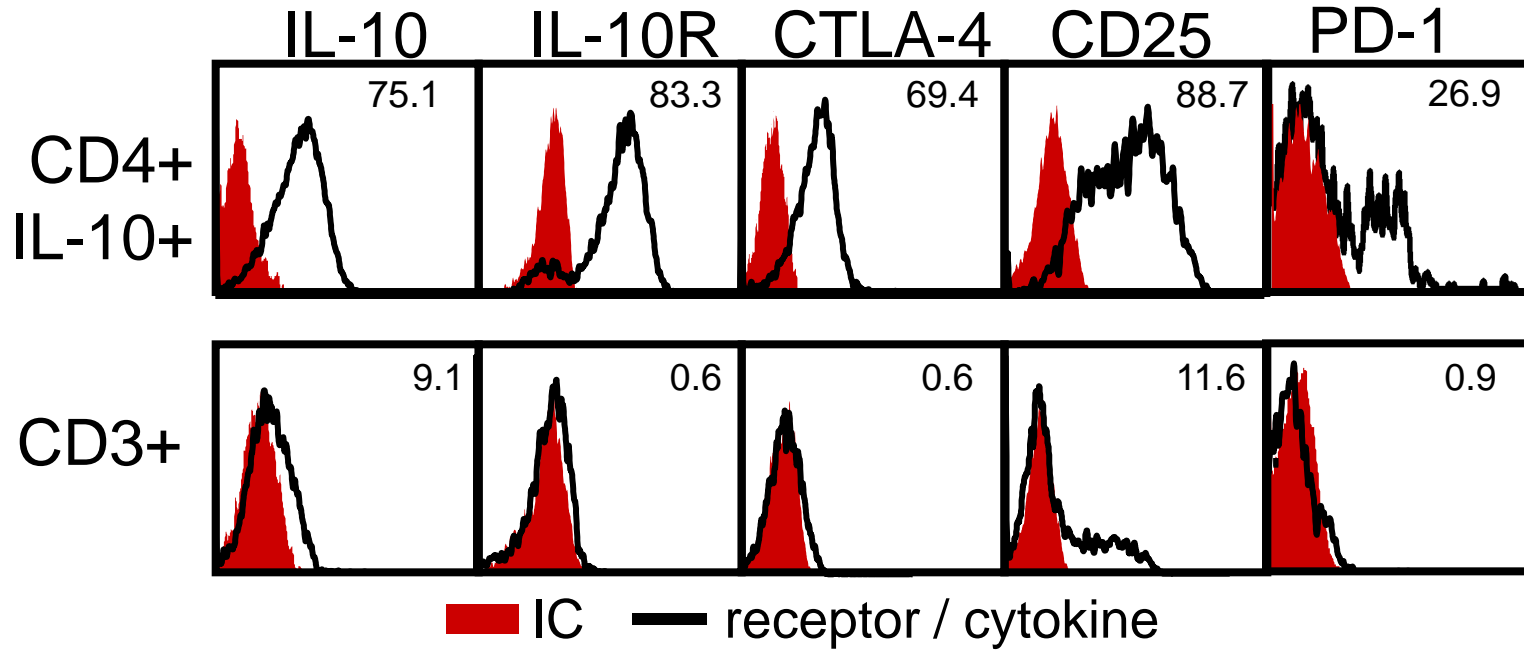
PLA-stimulated T cells



Aeroallergen-specific T cell frequency in health and allergy



T_{Reg} cells in allergy: multiple suppressor factors



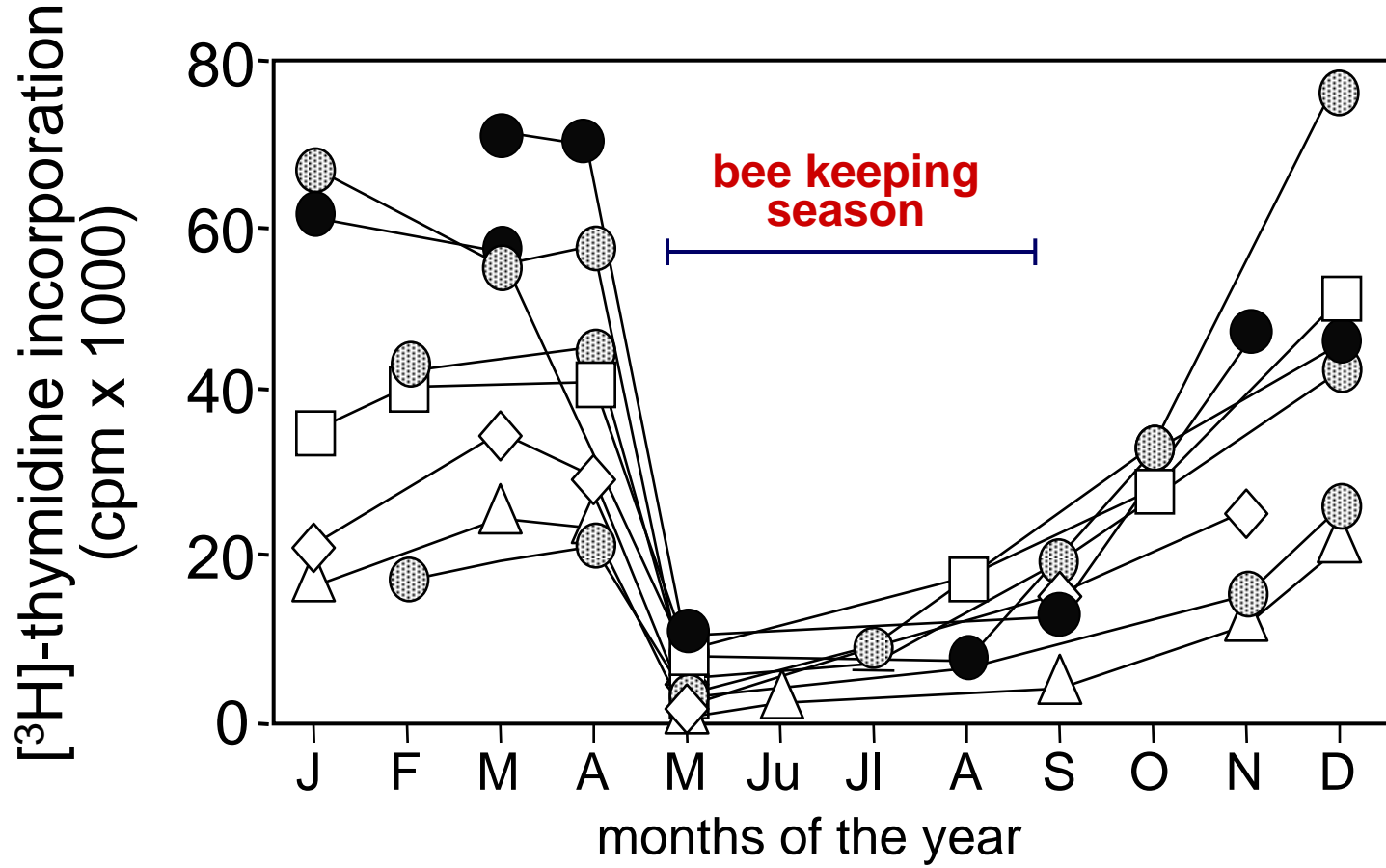
IL-10-mediated peripheral T cell
tolerance during natural bee stings

a model for
natural high dose antigen/allergen
exposure

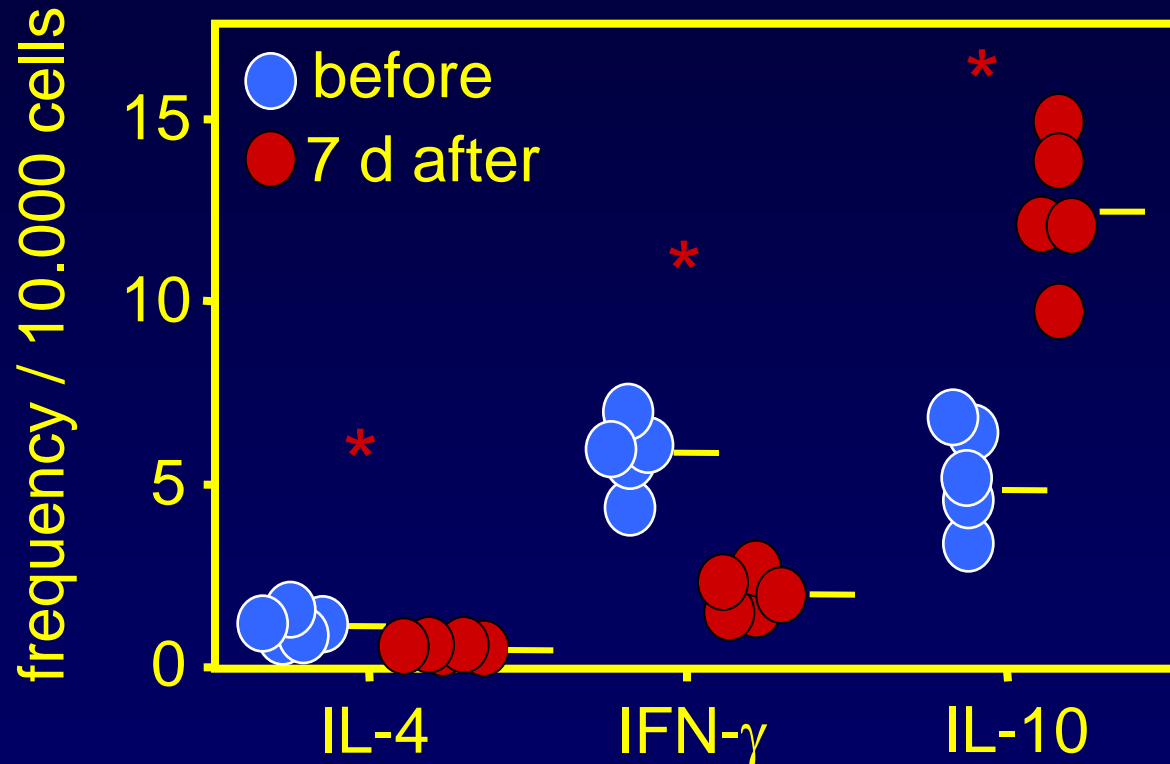
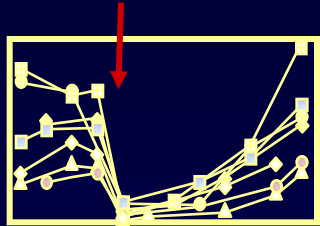
more than 20 bee stings in one week



Antigen-specific peripheral T cell tolerance



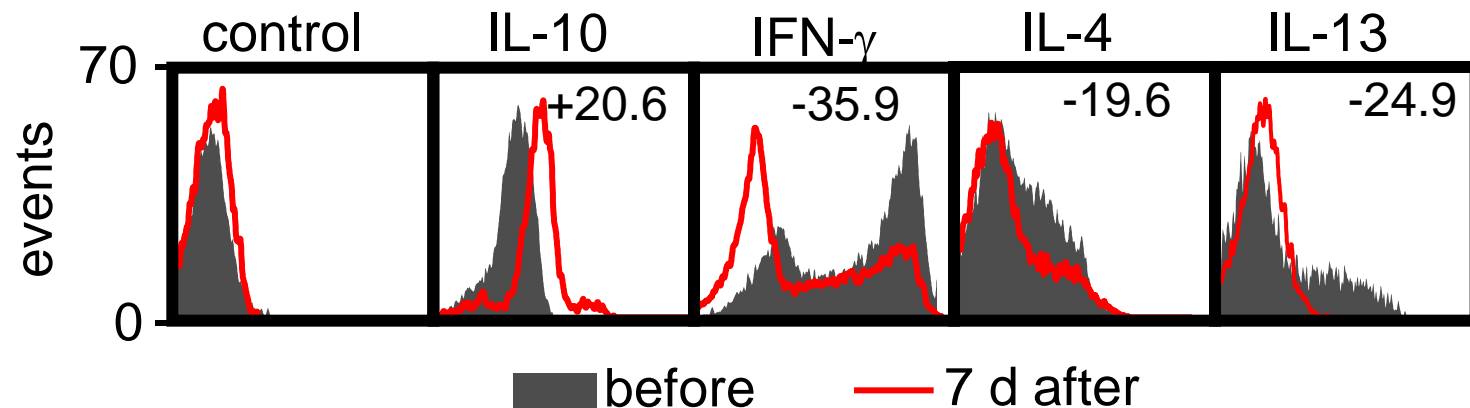
Frequency of PLA-specific cytokine secreting T cells before and after live bee stings



Decreased frequency of PLA-specific IL-4- and IFN- γ -secreting T cells, increased frequency of IL-10-secreting T cells is observed 7 days after ≥ 20 bee stings

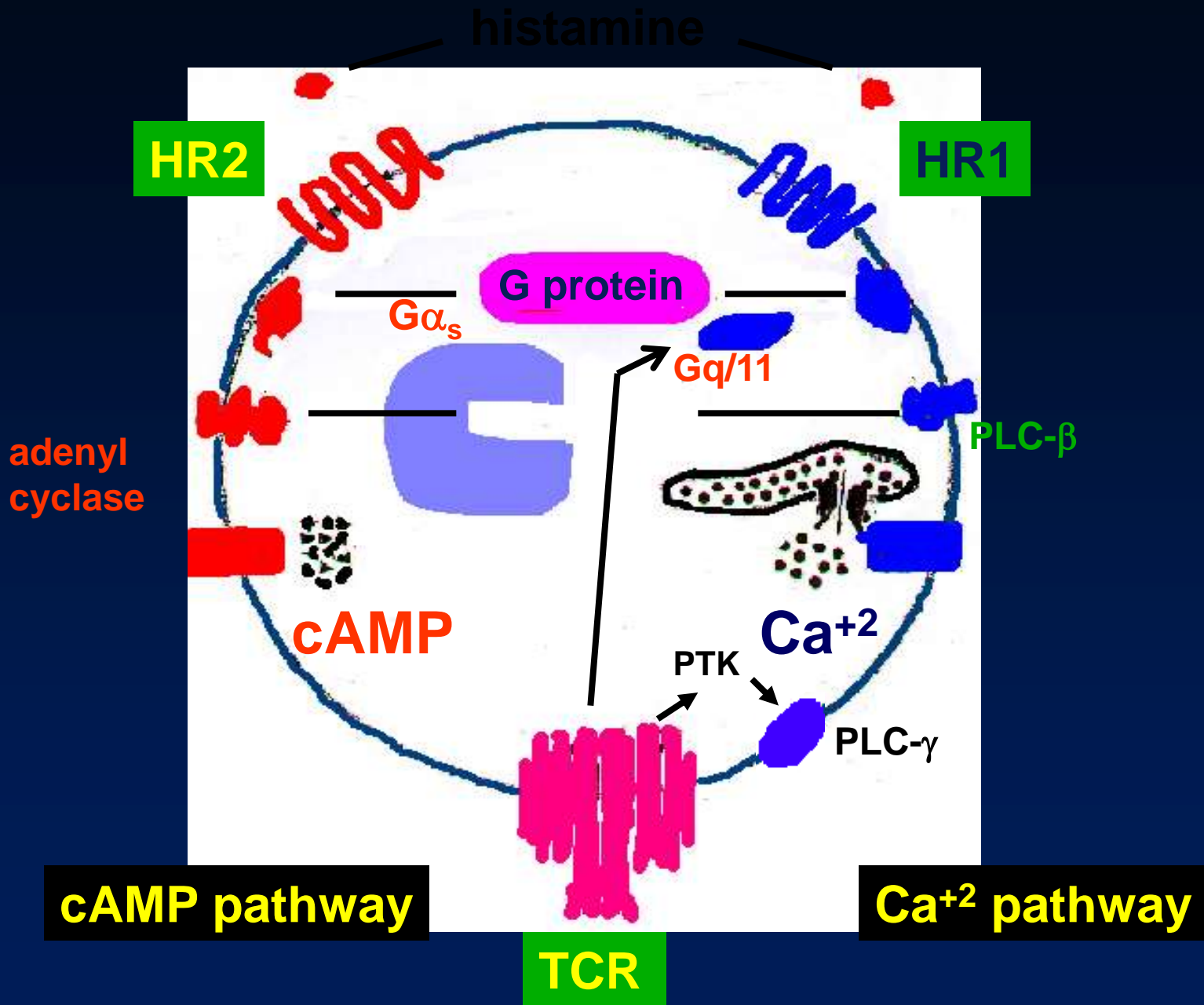
*: p < 0.001
n: 5 beekeepers

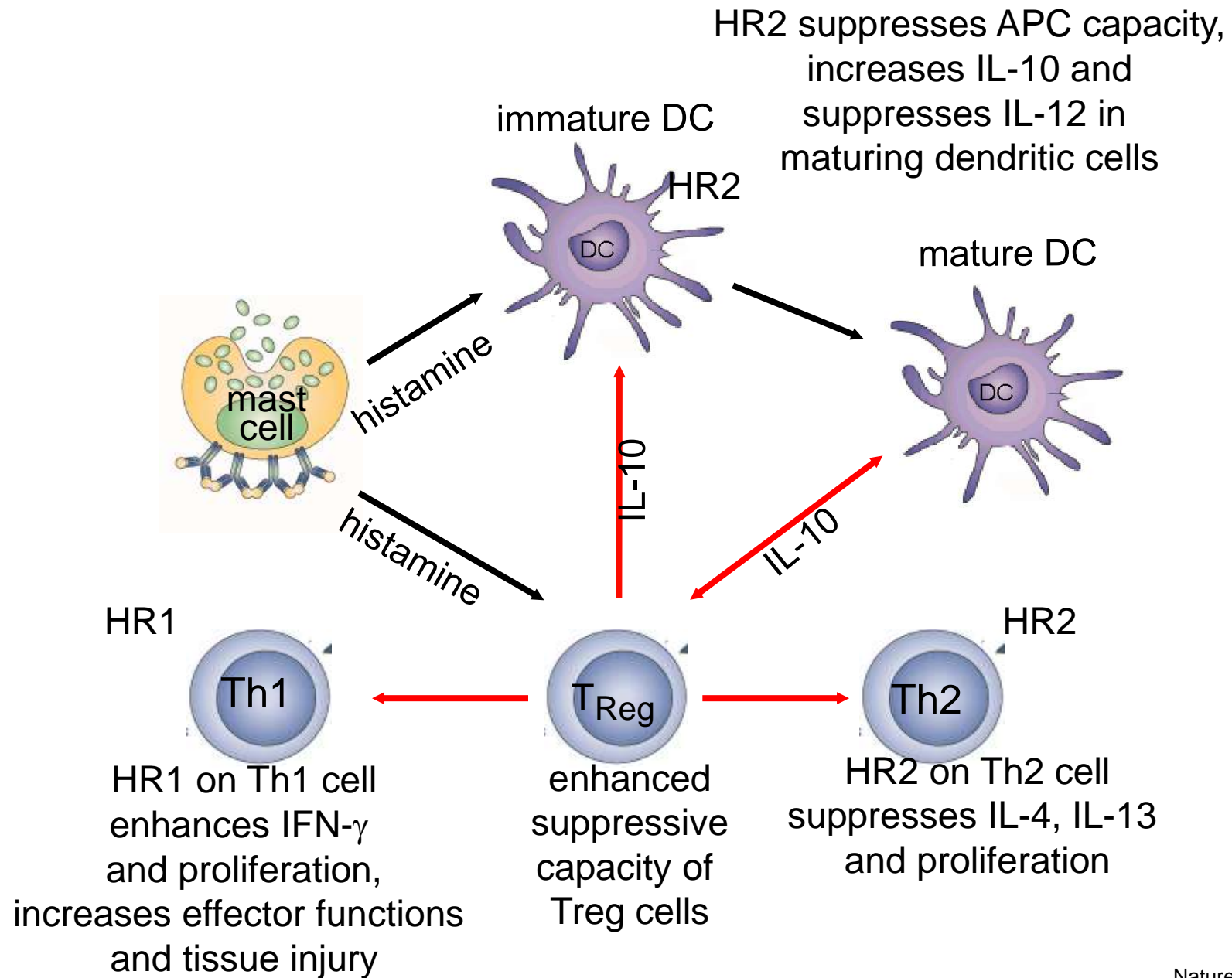
Increased IL-10, suppressed IL-4, IL-13, IFN- γ in PLA-specific cells after bee stings



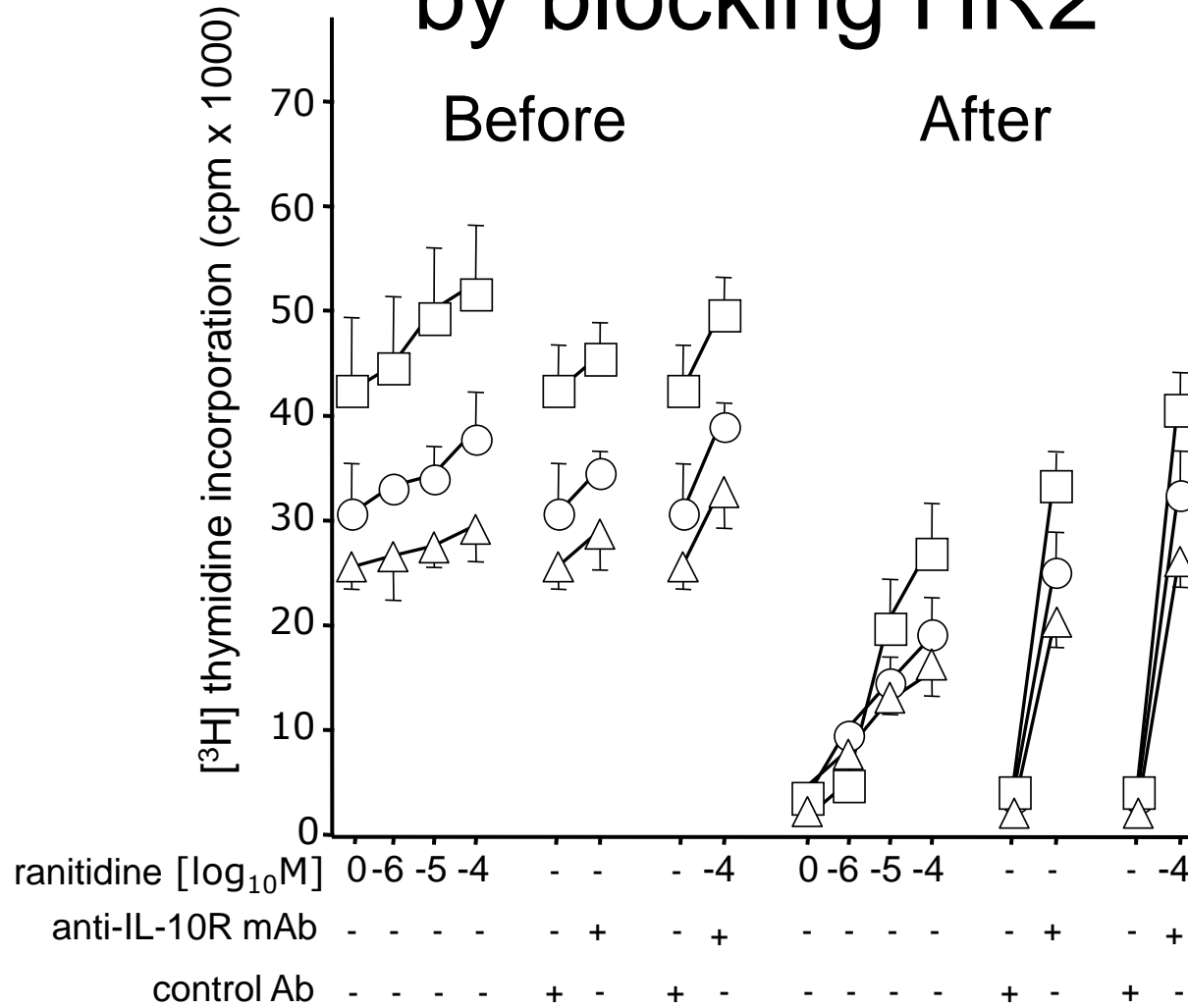
Mechanisms of Immune Tolerance to Allergens - III

role of histamine receptor 2





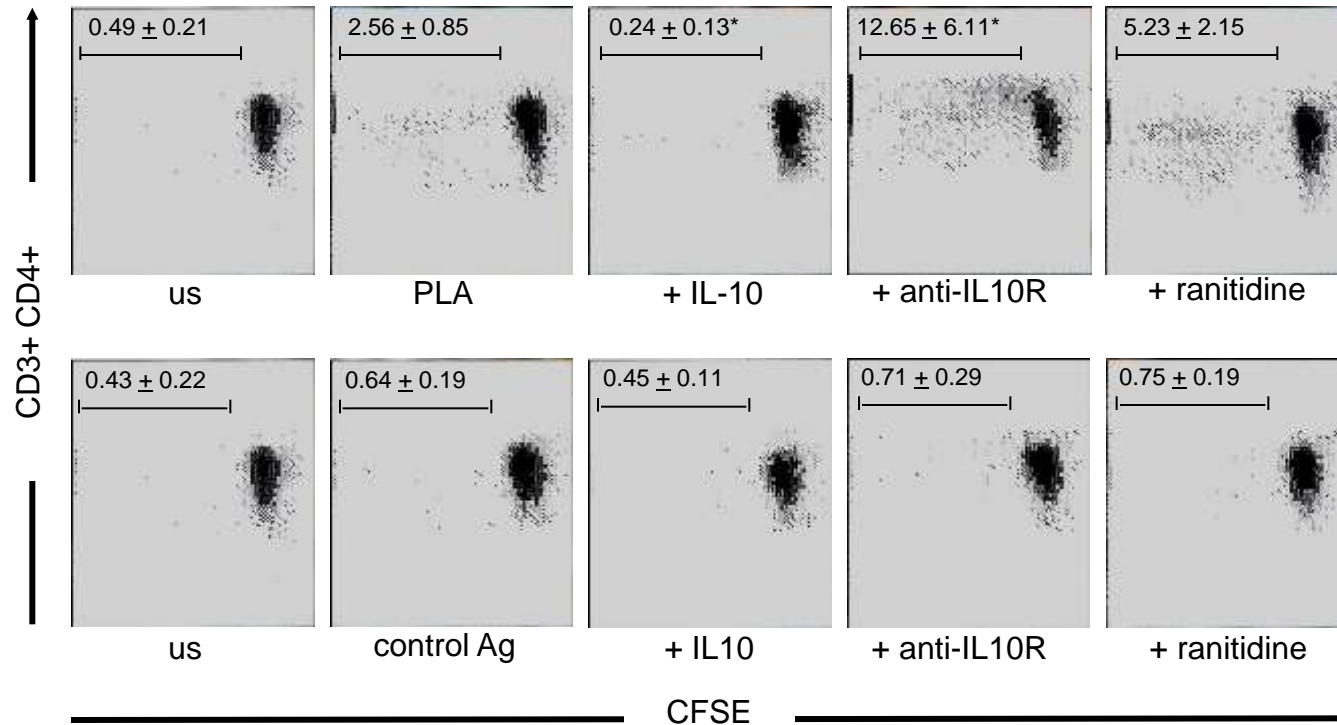
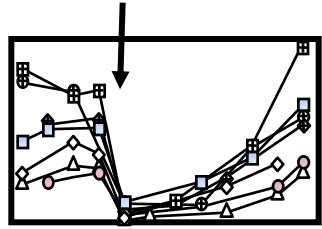
Recovery from peripheral T cell tolerance by blocking HR2



PBMC of 3 beekeepers before and after natural stings were stimulated with $0.3\mu\text{M}$ PLA and different doses of ranitidine

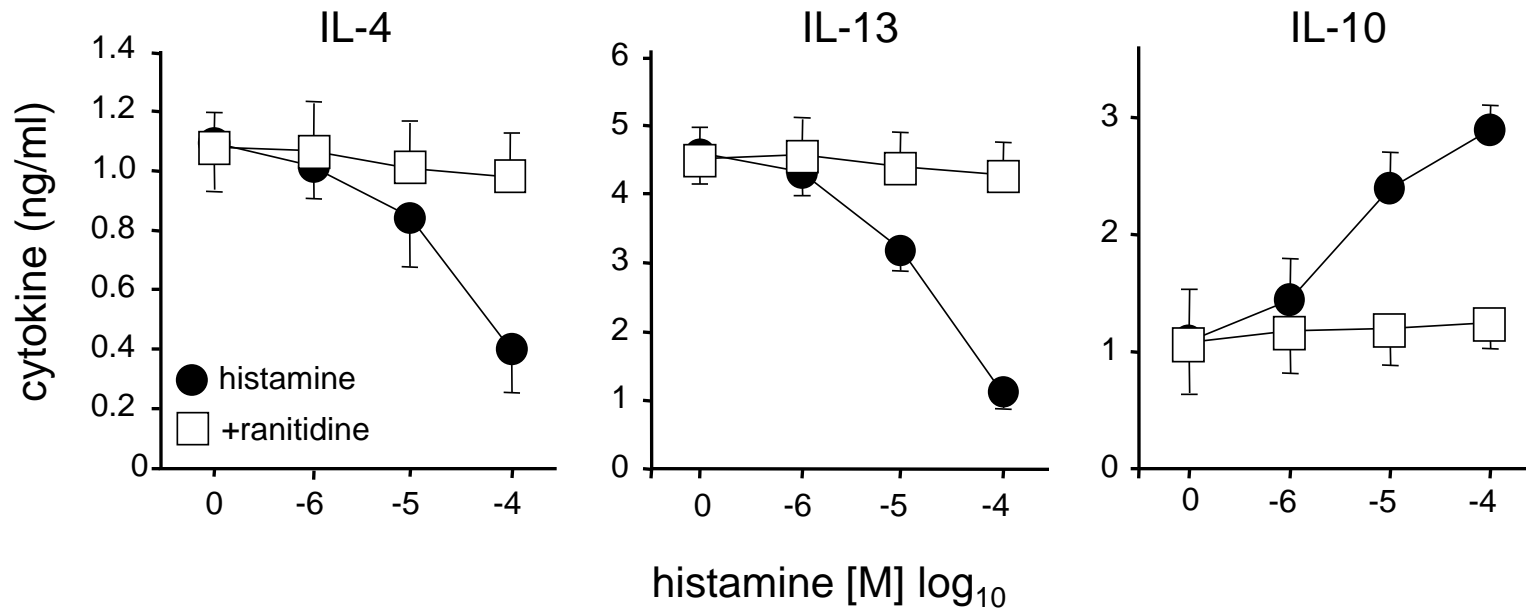
^3H -thymidine incorporation was determined at day 5

Breaking of peripheral T cell tolerance by blocking IL-10R and HR2

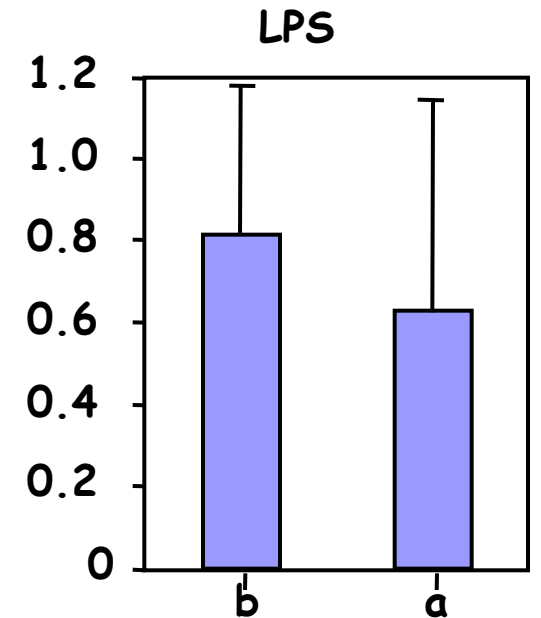
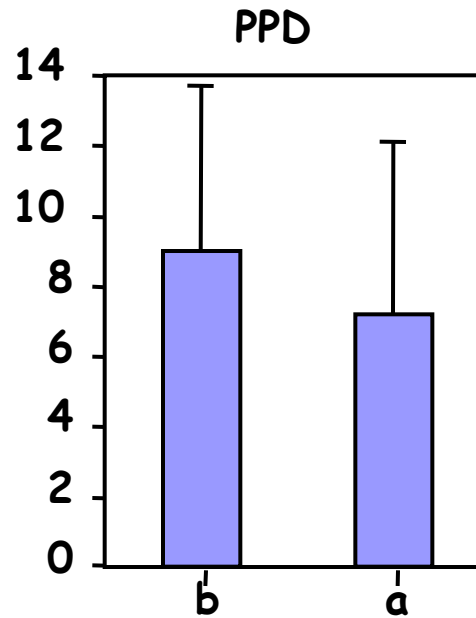
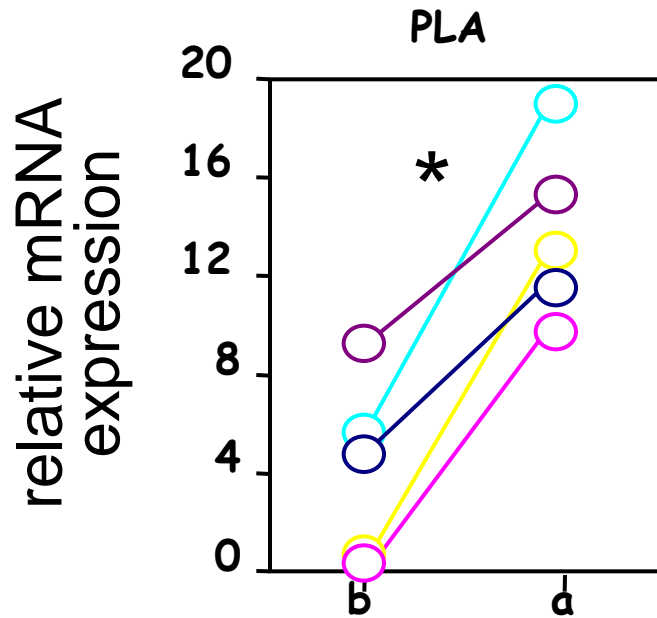
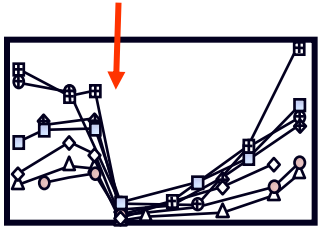


active suppression by IL-10 and histamine via HR2 after multiple bee stings

Histamine enhances IL-10 production by Th2 cells via HR2

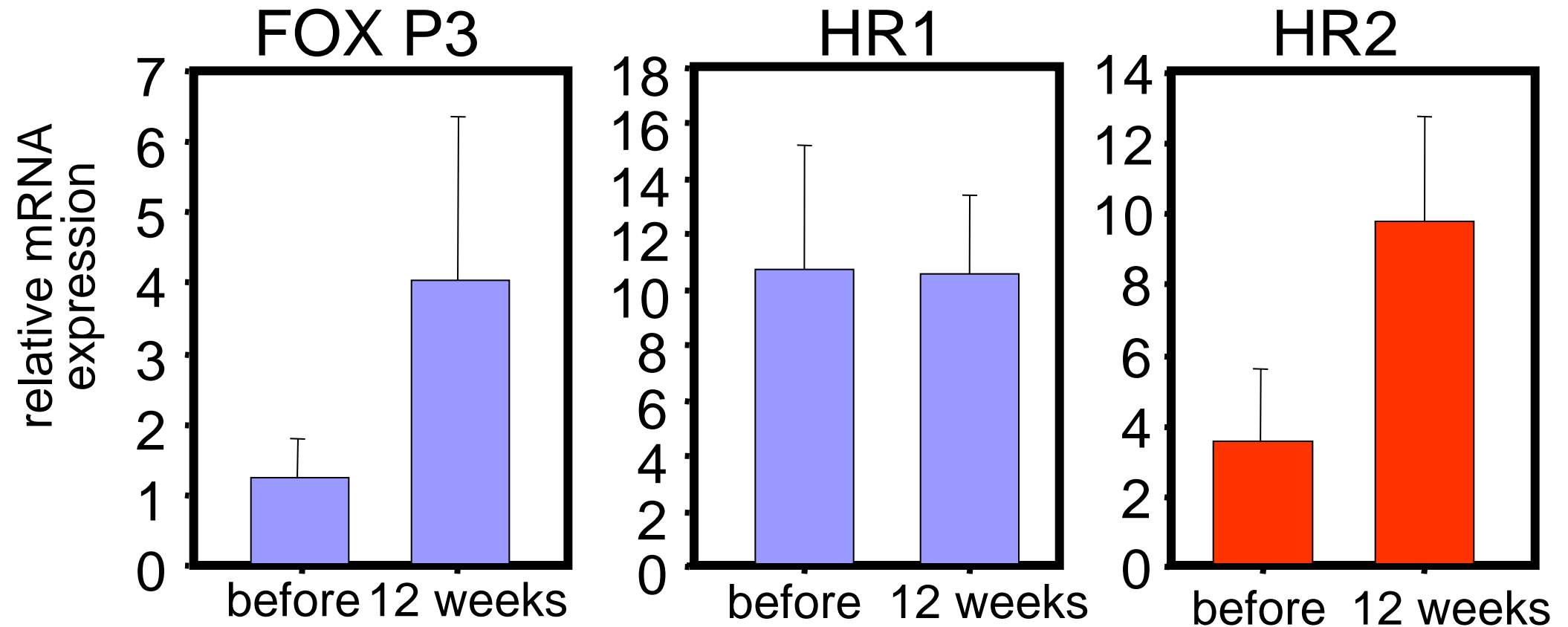


Upregulation of HR2 on allergen-specific T cells by natural bee stings



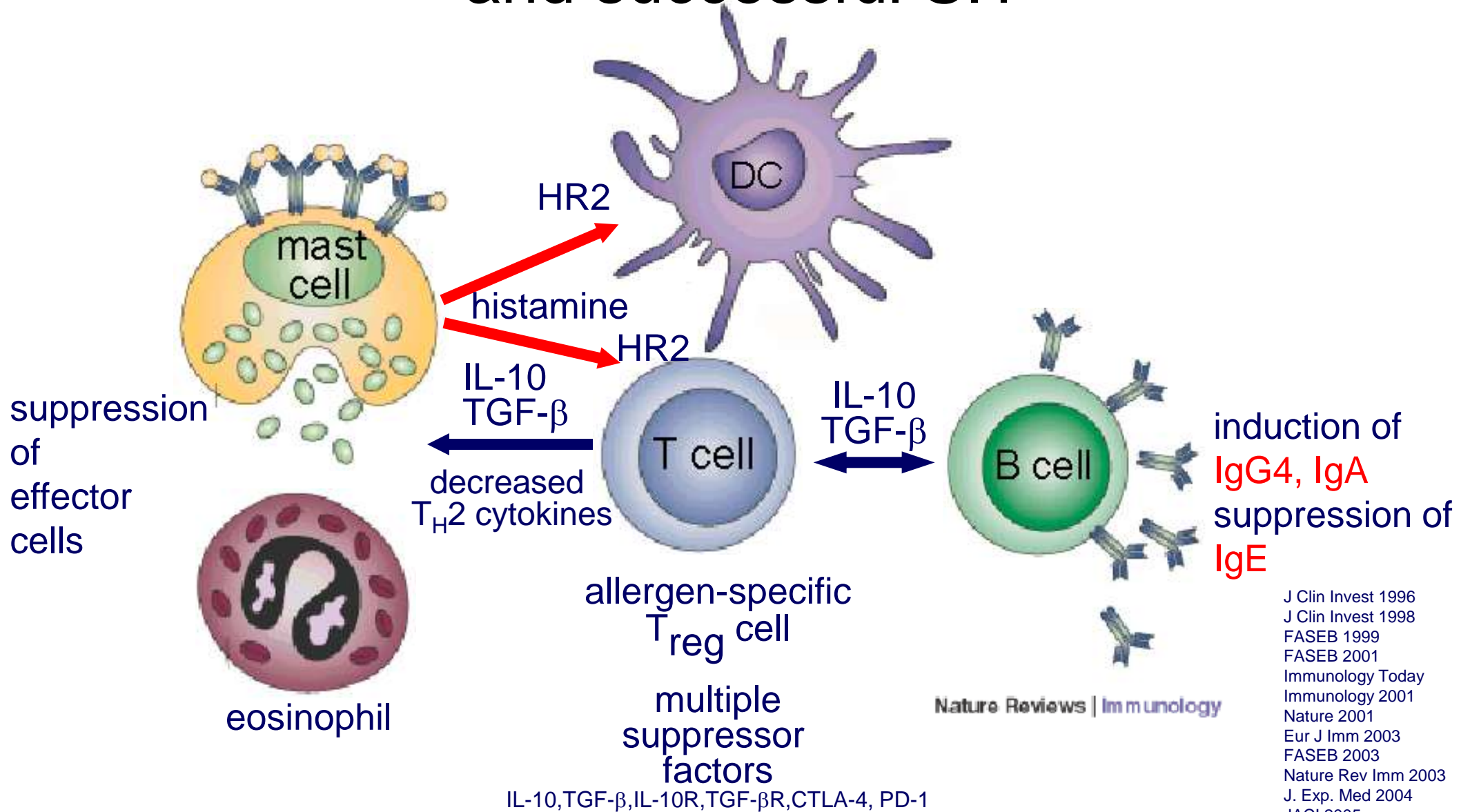
2-ddCT 18s versus HR2 in 12 day expanded allergen, PPD or LPS activated cultures
Analysed mRNAs are HR1, HR2, HR4, CIS1, FOX P3, SOCS 1, SOCS 3, SOCS 5

Induction of HR2 and FOXP3 on specific T cells by PLA peptide immunotherapy



n=7, 0.1, 1, 5, 25, 50, 50, 100, 100, 100 μ g weekly PLA peptides, PBMC + PLA, d5 IL-12, d12 anti-CD2/CD28

Tolerance in healthy immune response and successful SIT



J Clin Invest 1996
 J Clin Invest 1998
 FASEB 1999
 FASEB 2001
 Immunology Today
 Immunology 2001
 Nature 2001
 Eur J Imm 2003
 FASEB 2003
 Nature Rev Imm 2003
 J. Exp. Med 2004
 JACI 2005
 Curr Opin Immunol 2006

Philosophy of the meeting

As ever, immune regulation is the hottest issue in basic and clinical sciences. No question that we need to gather and get inspired. With an outstanding list of speakers in this field, „Immune Regulation – Davos“ becomes the key event of the year 2007, being big enough to learn from other disciplines and small enough to personally meet the experts.

Davos has been stimulating not only for scientists, but also for other meetings such as the World Economic Forum, held every year in the same conference center. There will be long lunch breaks, allowing to digest attended symposia, to talk with colleagues, while enjoying the winter sports and landscape. The evening sessions will give young researchers the opportunity to meet senior scientists. As at other Davos meetings, we will come together for poster sessions with desserts and drinks providing a relaxed and stimulatory atmosphere for scientific exchange.



Practical workshops

A practical course on flow cytometric and Treg analysis will be performed at the Swiss Institute of Allergy and Asthma Research. This course will provide first-hand expertise on Treg-analysis facilitating your research. The course is planned both for scientific fellows and technical assistants. It will be an ideal complementation for the theoretical background provided by the meeting and will be supported by flowcytometer experts as well as researchers from SIAF. Several other workshops are being planned and details will be announced on our website.



Organisator:
Cezmi Akdis
Organizing comitee:
Carsten Schmidt-Weber
Mübeccel Akdis
Reto Cramer

In:
Davos, congress center
Abstract submission:
15 January 2007 - 15 February 2007
Early registration deadline:
15 December 2006

Meeting style:
Symposium & workshop, practical workshops

Meeting organization:
This meeting is organized by the Swiss Institute of Allergy and Asthma Research (SIAF), a non-profit, University associated foundation
SIAF, Obere Str. 22, CH-7270 Davos
Treg.meeting.Davos@siaf.unizh.ch

Registration Fee:
500.- Swiss Francs
Fellows in training: 200.- Swiss Francs

SIAF



GALEN
Network of Excellence

World Immune Regulation Meeting

Special focus on regulatory cells

11 - 15 April 2007
Davos - Switzerland

<http://www.siaf.unizh.ch/WTM/index.html>



Immune tolerance

- Judith Zumkehr
- Sven Klunker
- Alison Taylor
- Johan Verhagen
- Flurina Meiler
- Christian Karagiannidis

- U. Müller, Bern
- B. Wüthrich, Zurich
- M. Jutel, Wroclaw, SIAF
- R. Valenta, Vienna
- S. Viehls, Langen
- H. Fiebig, Reinbek
- C. Heusser, Basel
- S. Durham, London
- M. Larche, London
- B. Ballmer-Weber, Zurich

Effector Mechanisms

- Reto Crameri
- Carsten Schmidt-Weber
- Cezmi A. Akdis
- Kurt Blaser

- R. Disch
- B. Wüthrich
- P. Schmid-Grendelmeier
- W. Kneist
- M. Schliz
- D. Kleeman
- W. Deglmann
- G. Menz

