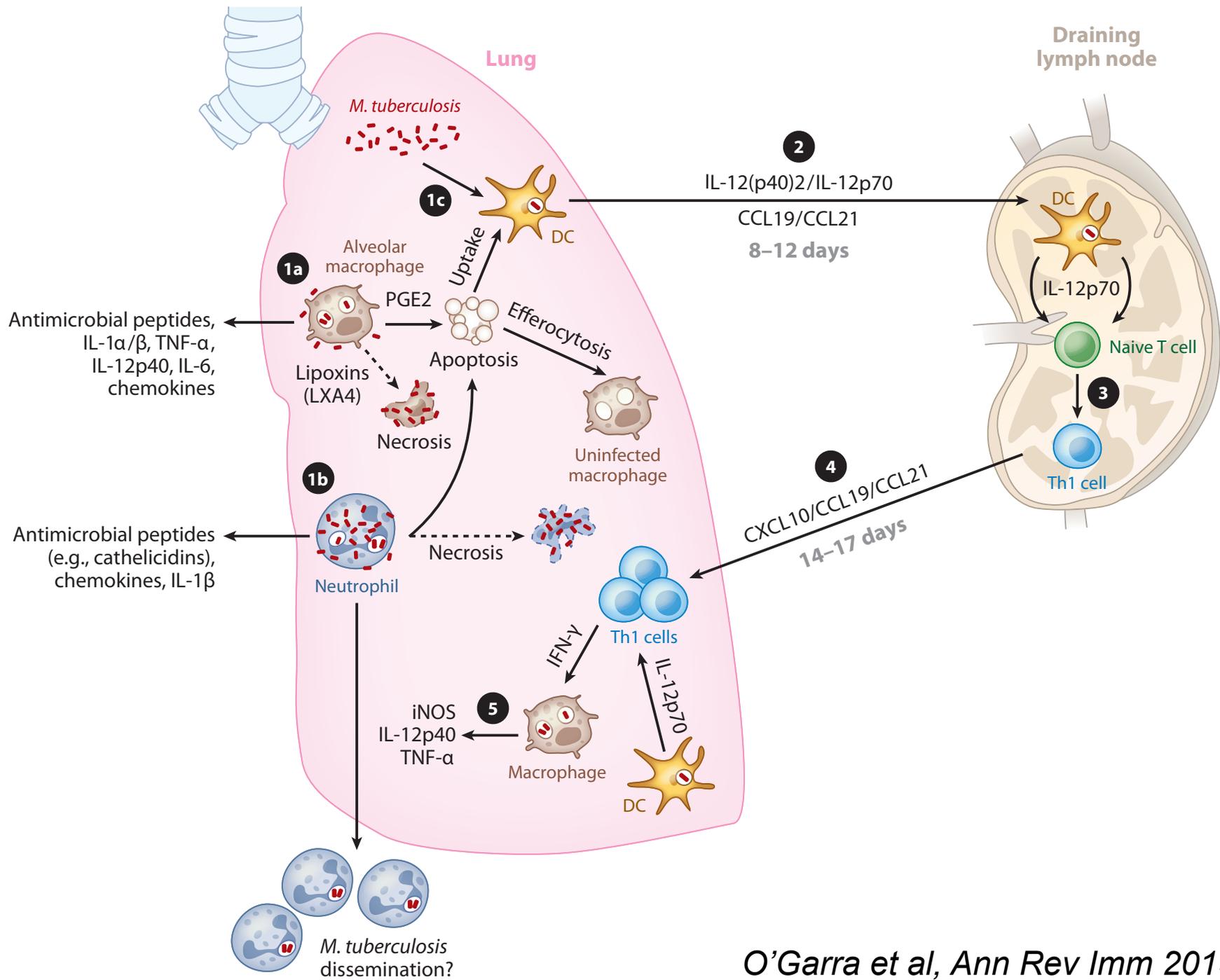




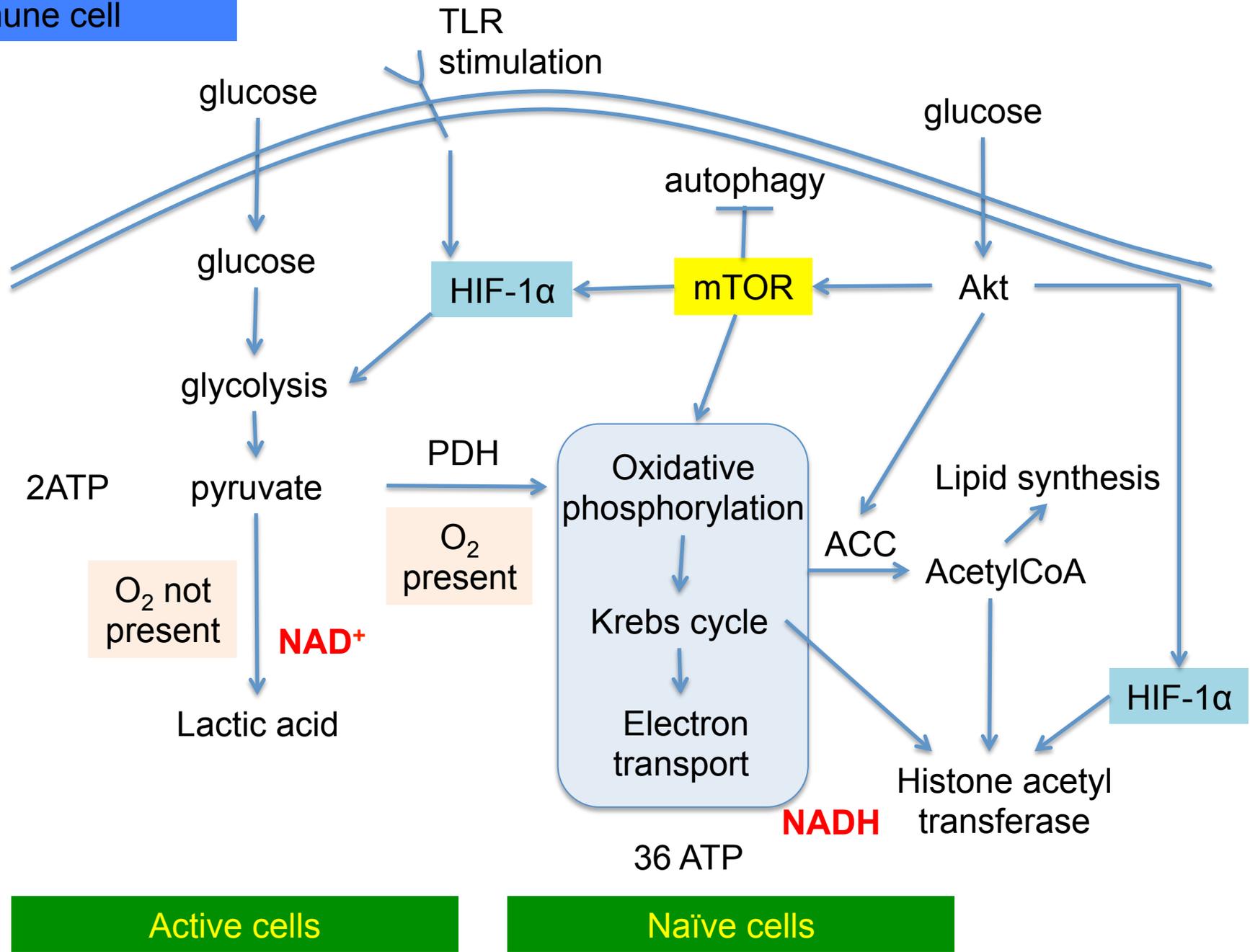
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Immunometabolic circuits in host defense

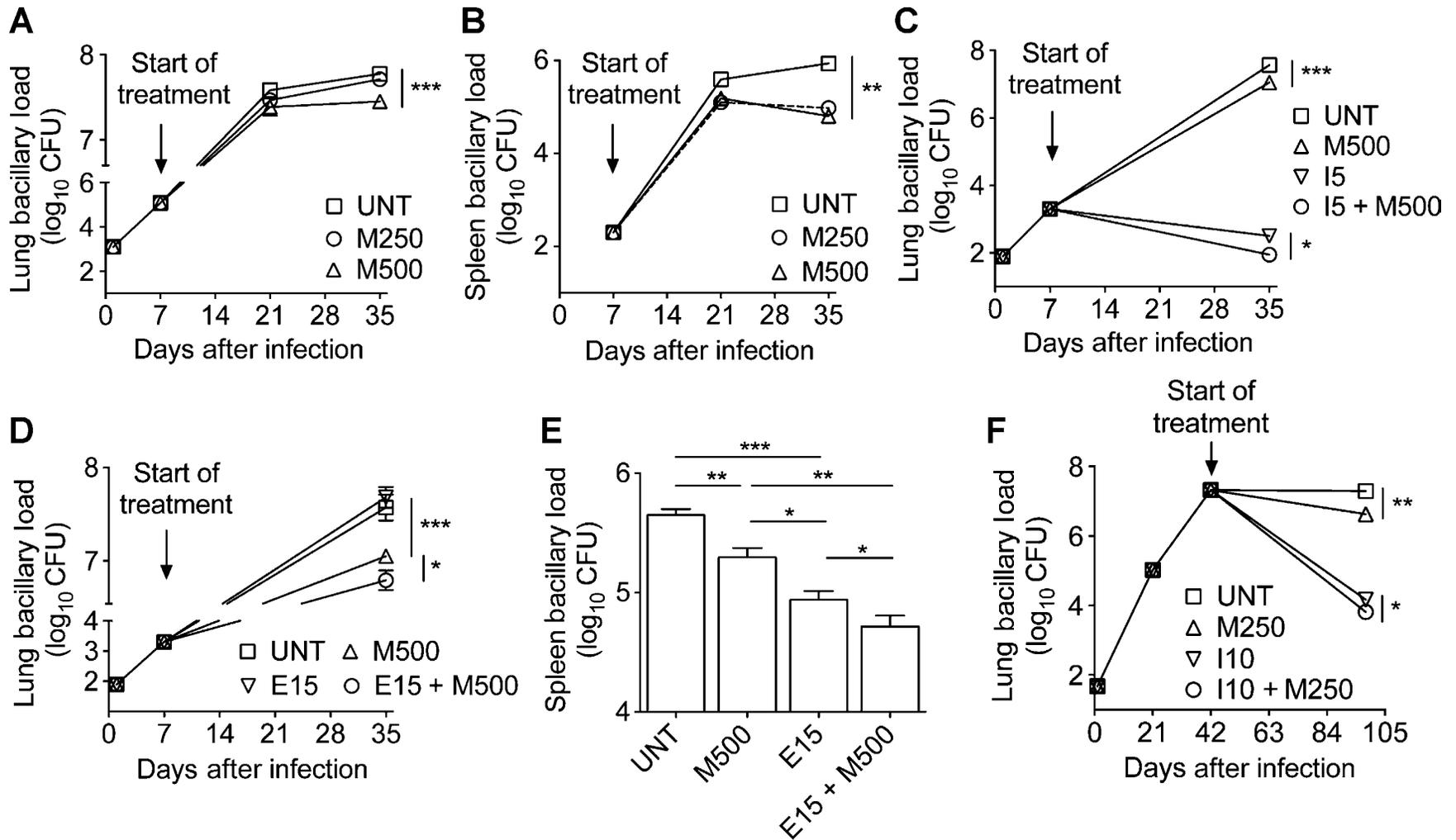
Mihai G. Netea



Immune cell



Metformin and host-directed therapy in tuberculosis

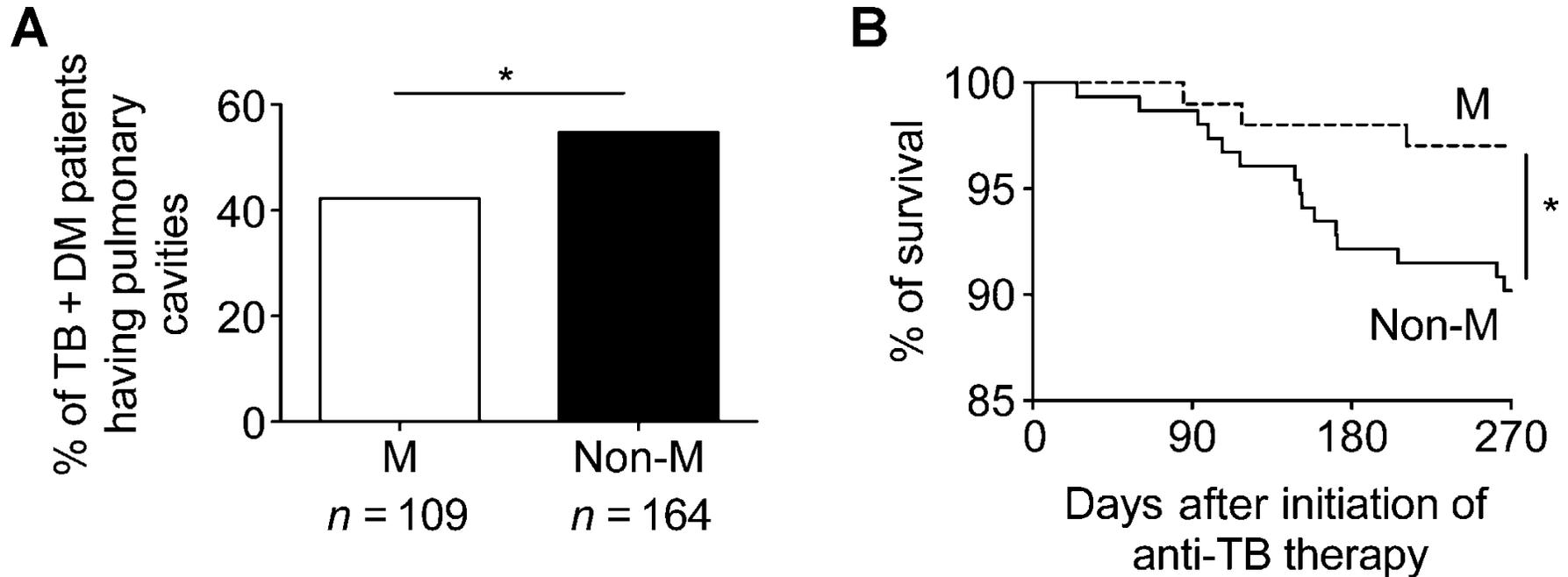


TUBERCULOSIS

Metformin as adjunct antituberculosis therapy

Amit Singhal,^{1*} Liu Jie,^{1†} Pavanish Kumar,^{1†} Gan Suay Hong,² Melvin Khee-Shing Leow,^{3,4} Bhairav Paleja,¹ Liana Tsenova,^{5,6} Natalia Kurepina,⁵ Jinmiao Chen,¹ Francesca Zolezzi,¹ Barry Kreiswirth,⁵ Michael Poidinger,^{1,7} Cynthia Chee,² Gilla Kaplan,^{5,8} Yee Tang Wang,² Gennaro De Libero^{1,9*}

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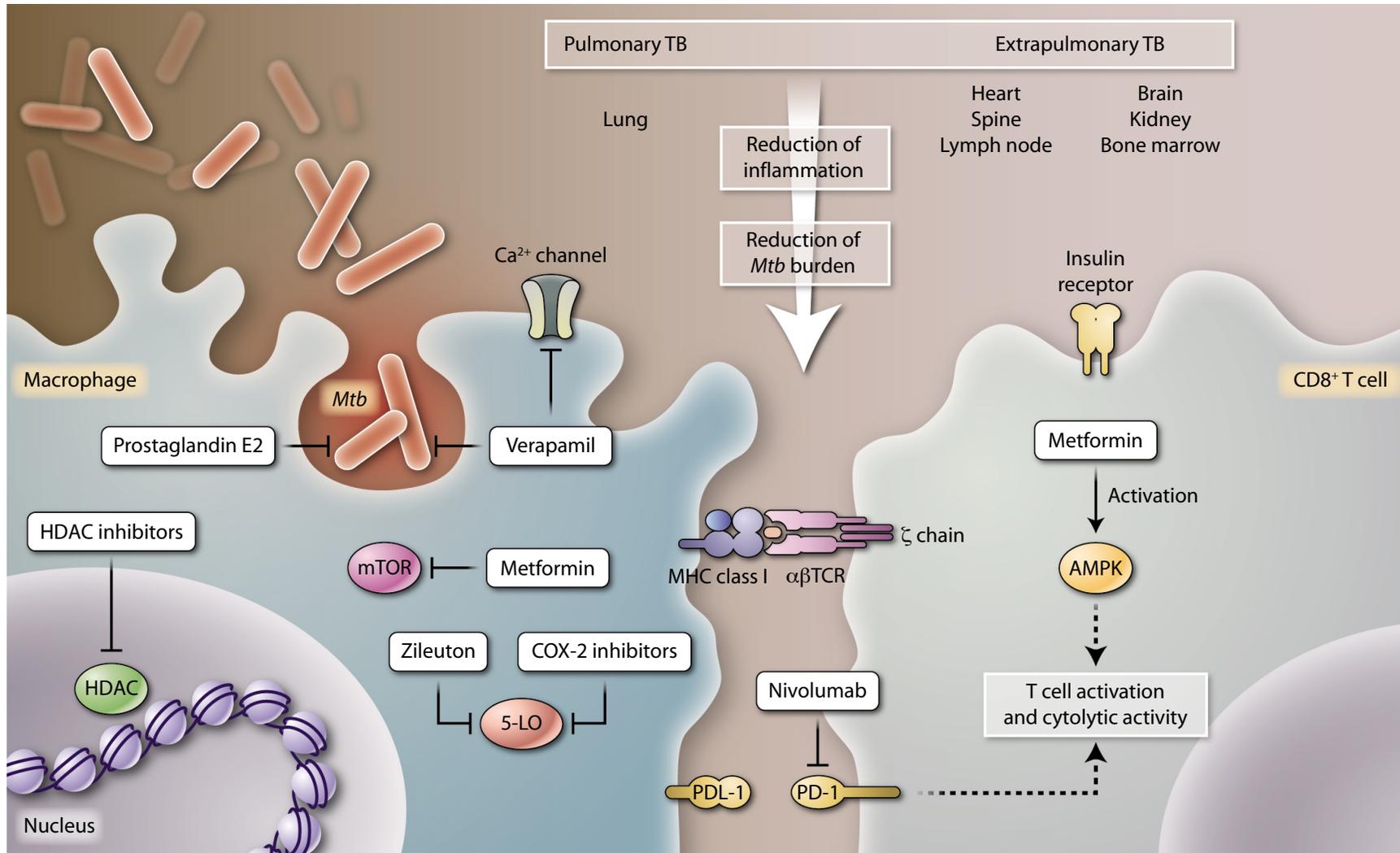


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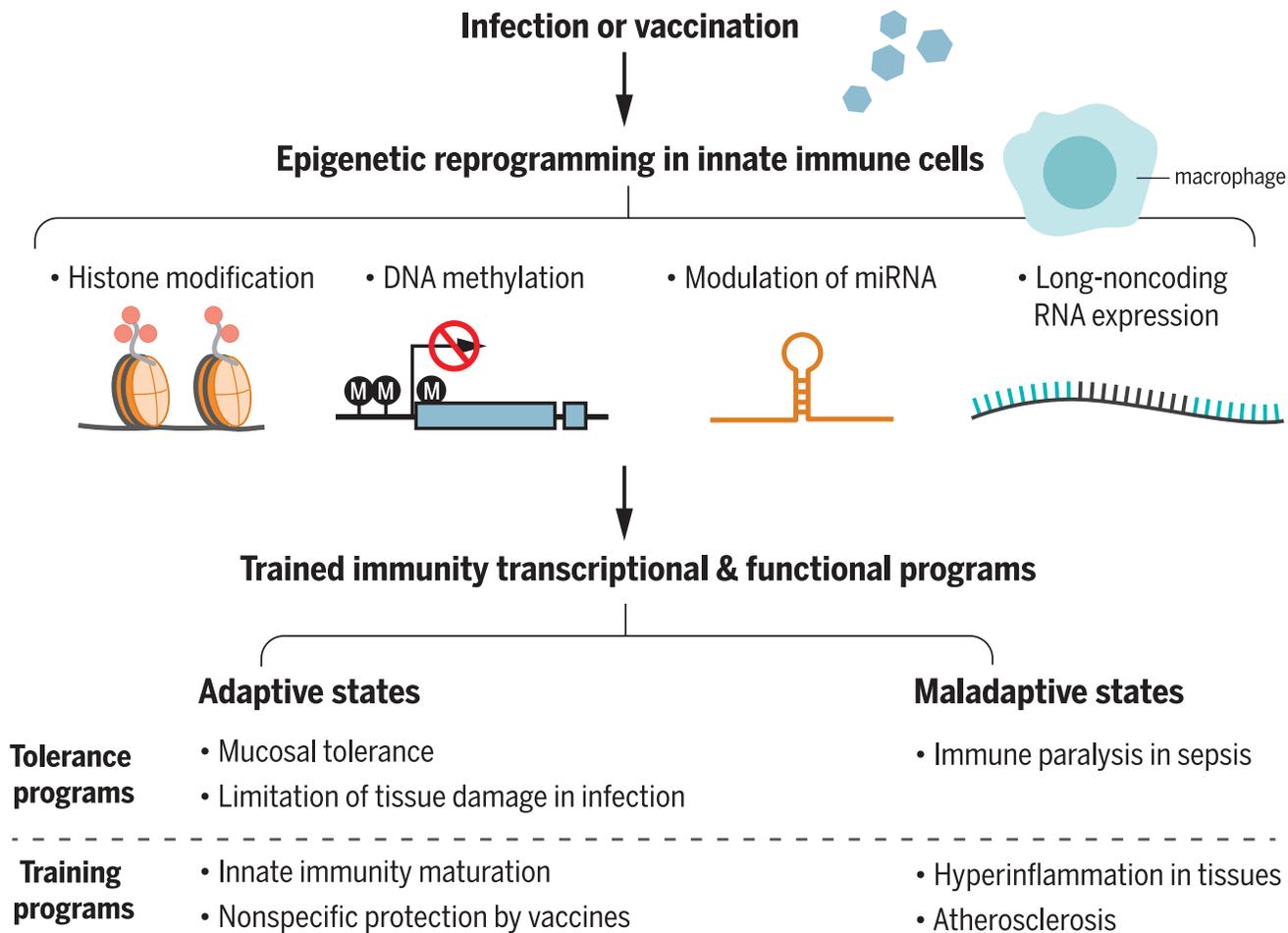
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Trained immunity versus tolerance





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Trained immunity in humans

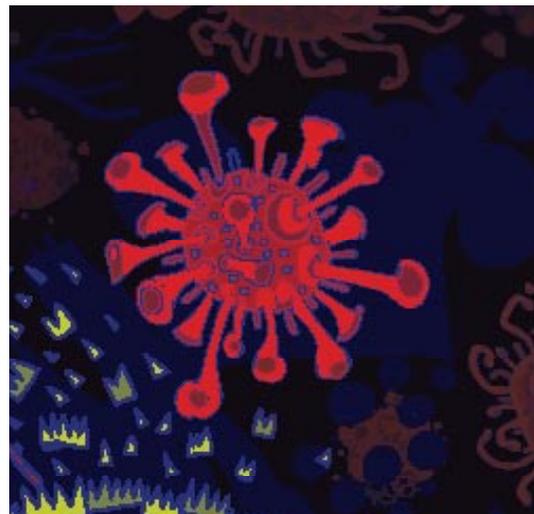
Pediatr Allergy Immunol 2008; 19: 438–448
DOI: 10.1111/j.1399-3038.2007.00869.x

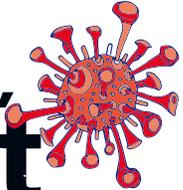
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PEDIATRIC ALLERGY AND
IMMUNOLOGY

Potential health effects from non-specific
stimulation of the immune function in early
age: The example of BCG vaccination

New Scientist
Aug. 2013



Small shot,
big impact 

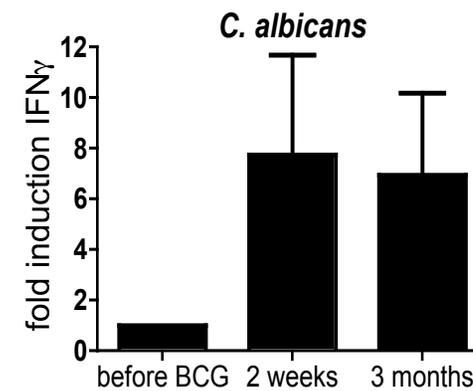
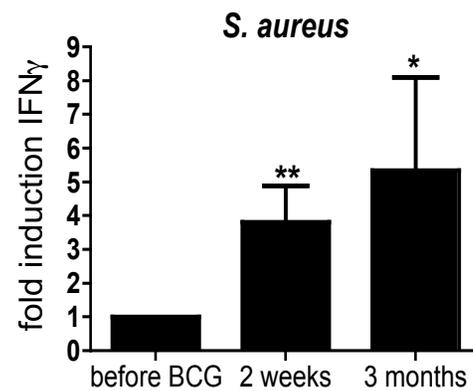
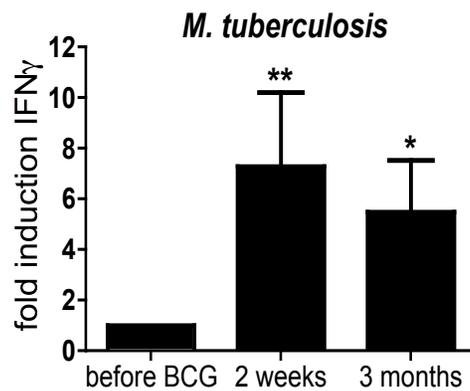
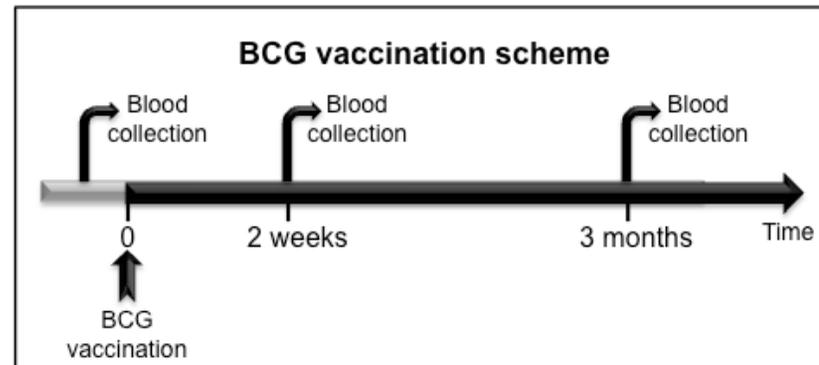
Some vaccines seem to provide us with a host of extra
benefits. **Michael Brooks** sees the cornerstone of
modern medicine in a new light

UMC  St Radboud



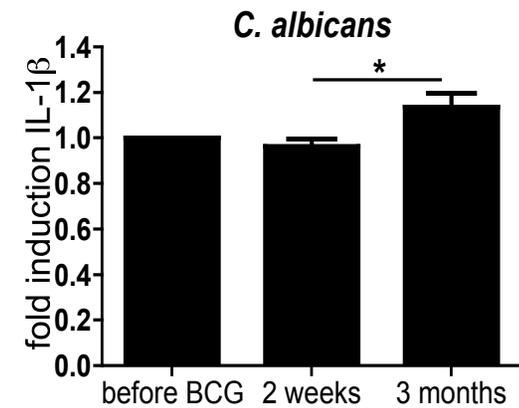
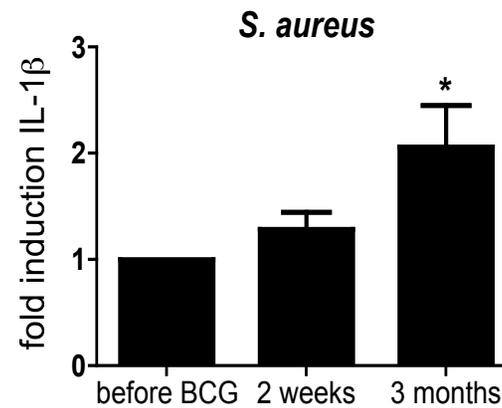
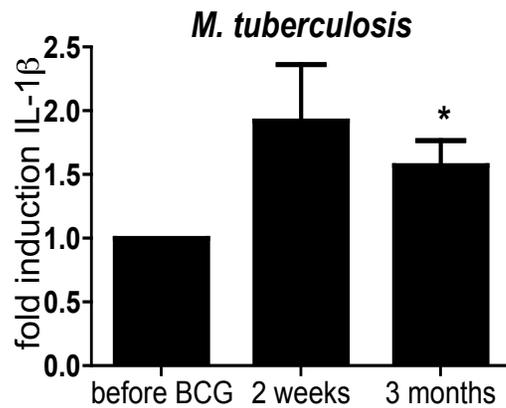
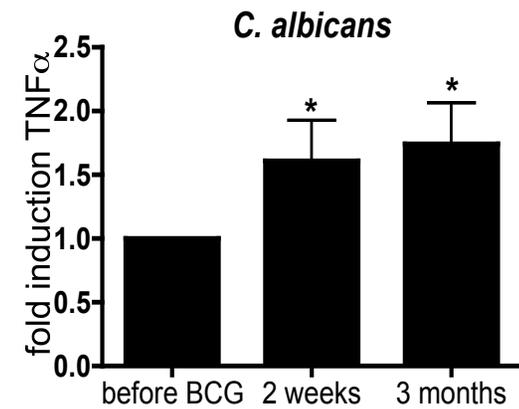
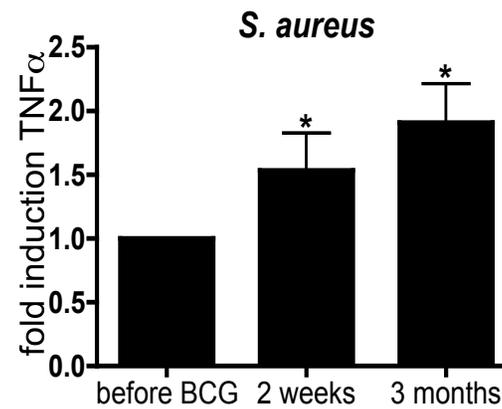
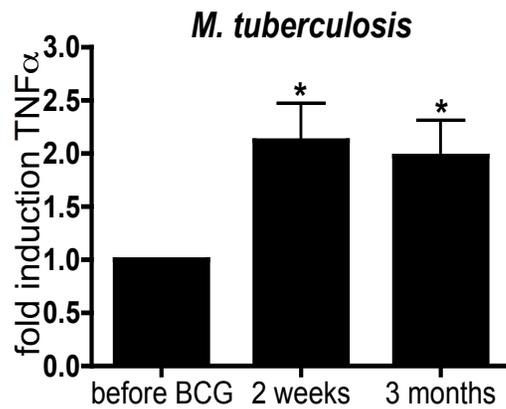
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Does this happen in vivo in humans?



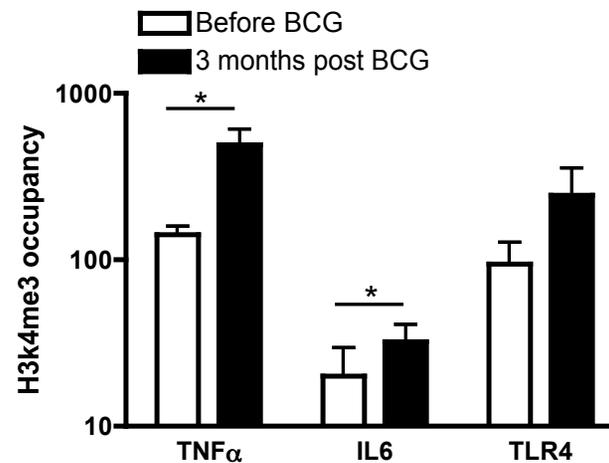
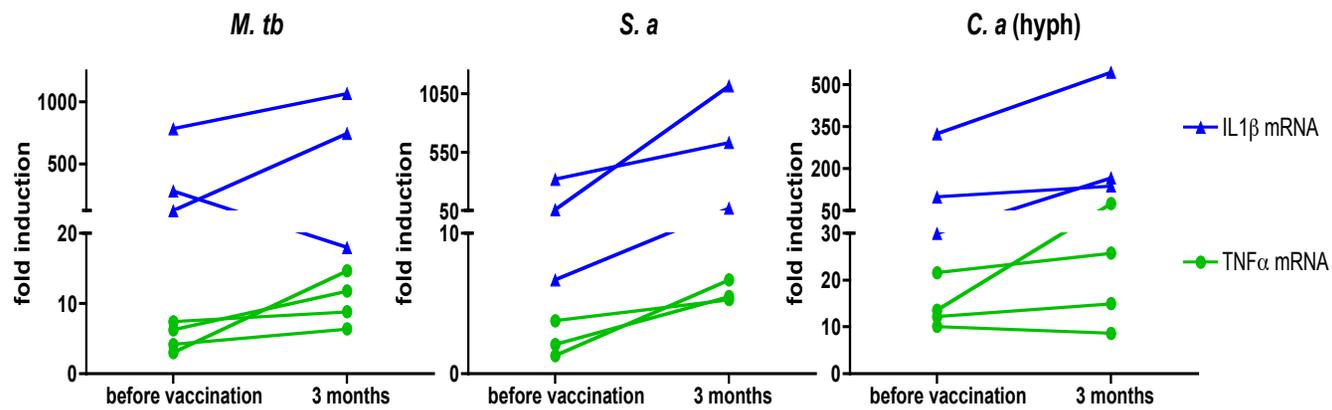


BCG enhances monocyte-derived cytokines





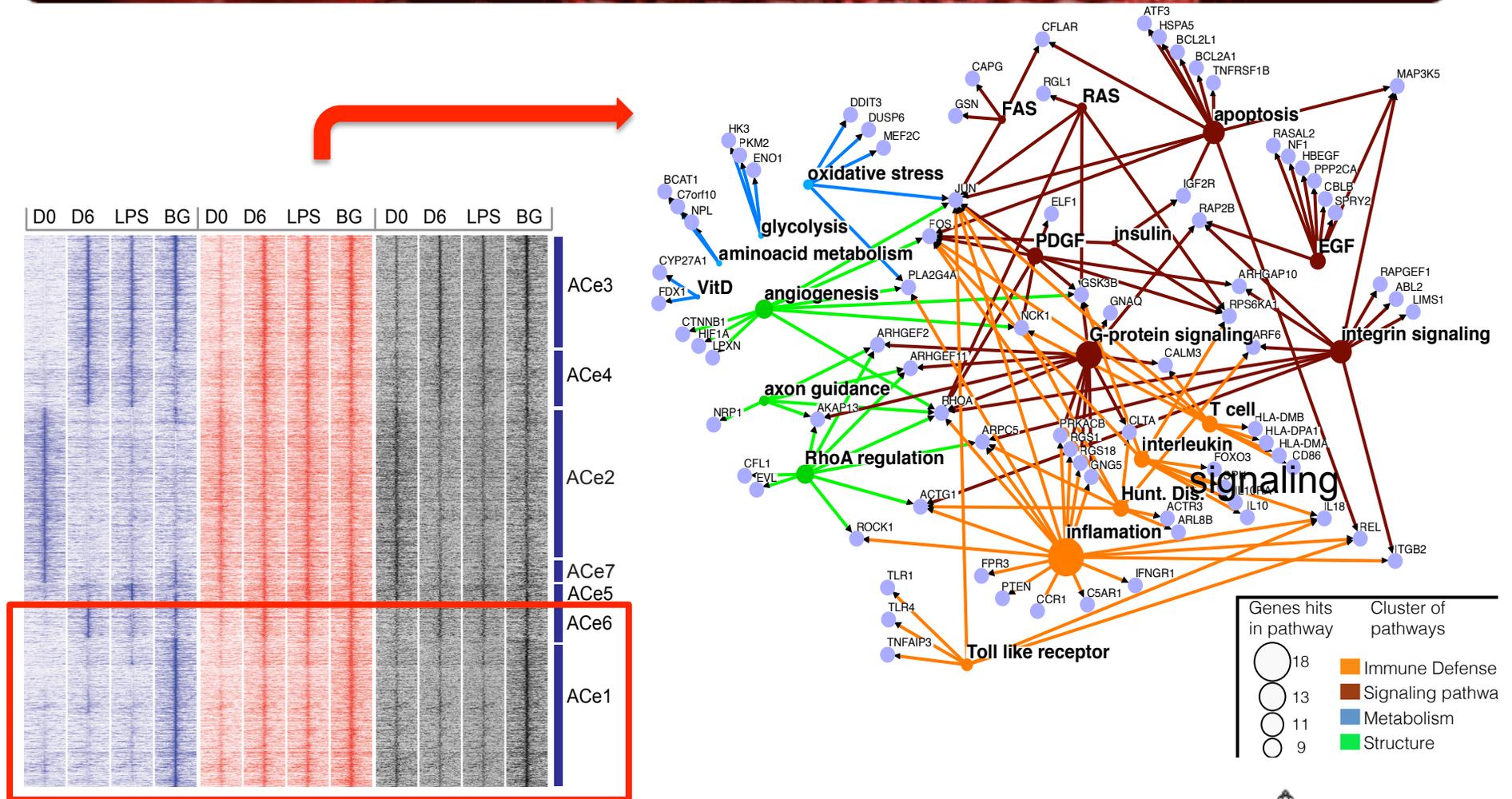
BCG effects on epigenetics and transcription





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What are the pathways distinguishing Training vs Tolerance?



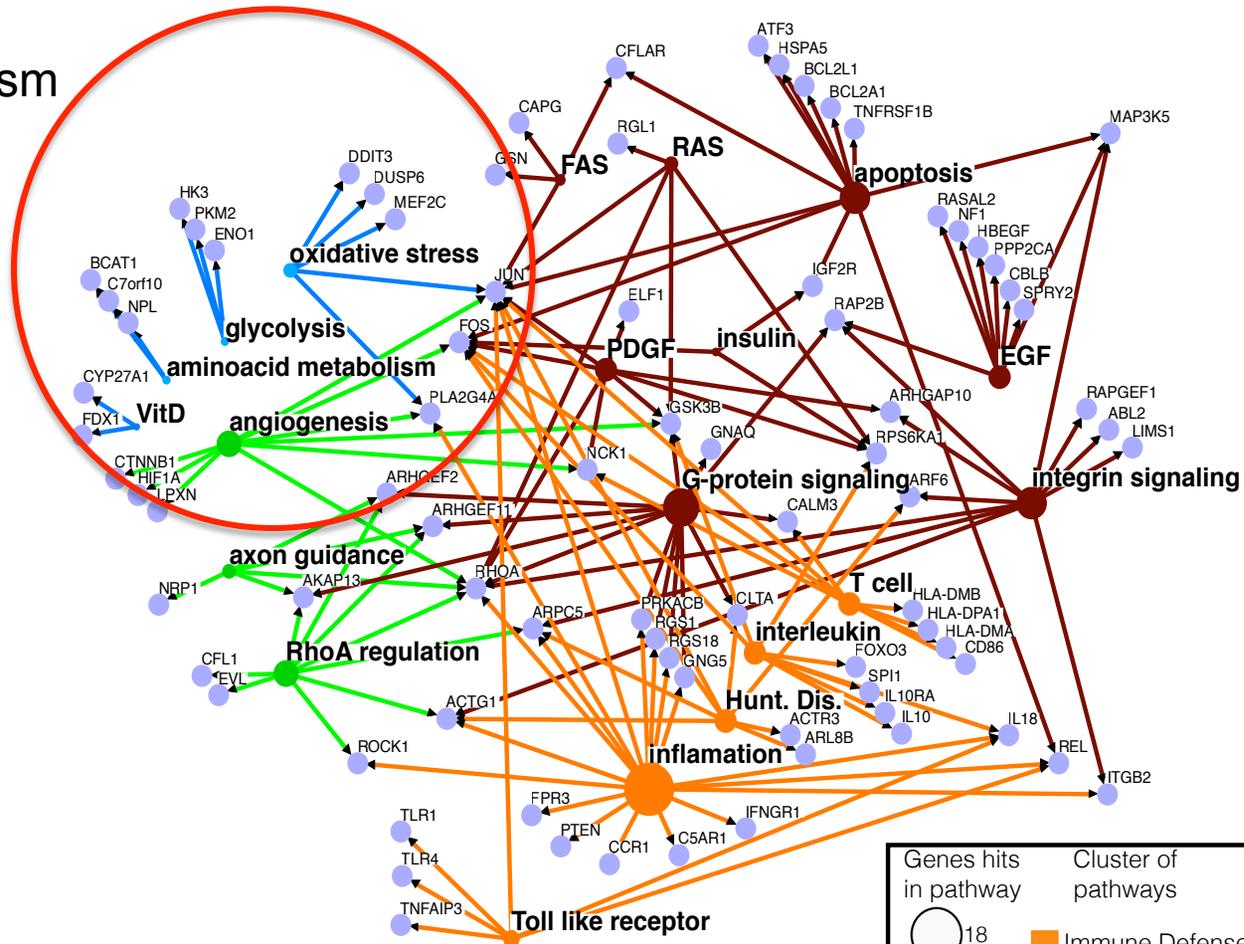
Saeed, Quintin et al, Science, 2014



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What are the pathways distinguishing Training vs Tolerance?

metabolism



signaling

Genes hits in pathway	Cluster of pathways
18	Immune Defense
13	Signaling pathway
11	Metabolism
9	Structure

Saeed, Quintin et al, Science, 2014



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Glucose metabolism and host defense

- The metabolic pathways through which immune cells metabolize glucose are crucial for immune activation
- Cellular metabolism has a signaling function linking immune signals and long-term epigenetic reprogramming of cell function
- Understanding cellular metabolism of immune cells during infection (TB) is crucial to fully describe the cell function
- Modulation of cell metabolism may represent a novel therapeutic target in improving host defense in tuberculosis



Nijmegen Institute for
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Thank you !

Our lab

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Trinity College

Luke O'Neill

Athens University

Evangelos Giamarellos



Summer Frontiers of Science
Systems Biology of Innate Immunity
Sept 7-9th, 2016
Nijmegen, The Netherlands

Functional genomics

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Mihai Netea
Norman Pavelka

Microbiome

Ramnik Xavier
Cisca Wijmenga
Eran Elinav

Epigenomics

Ido Amit
Giacchino Natoli
Joachim Schulze
Brian Brown

Immunometabolism

Luke O'Neill
Edward Pearce
Lionel Ivashkiv
Tom van der Poll

Innate immune memory

Reinout van Crevel
Eicke Latz
Bali Pulendran

Systems biology of disease

Adrian Hill
Leo Joosten
Eoin Mckinney

Organizers: Mihai Netea (Radboud UMC), Leo Joosten (Radboud UMC), Zoltan Fehervari (Nature Immunology)



www.humanfunctionalgenomics.org