Genetic susceptibility to Aspergillosis in allogeneic stem cell transplantation

Agostinho Carvalho, PhD

Dep. Experimental Medicine and Biochemical Sciences

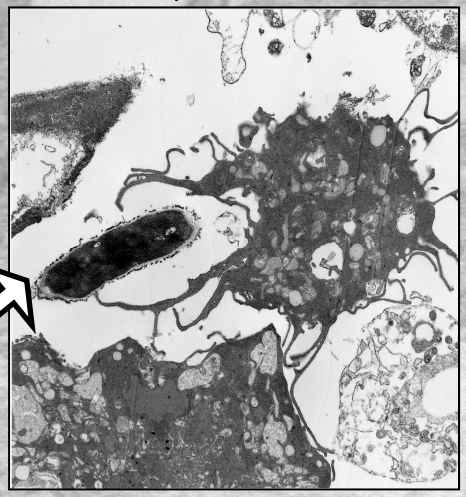
Microbiology Section

University of Perugia, Italy

A saprophitic lifestyle

The surface

The resistance to oxidative stress



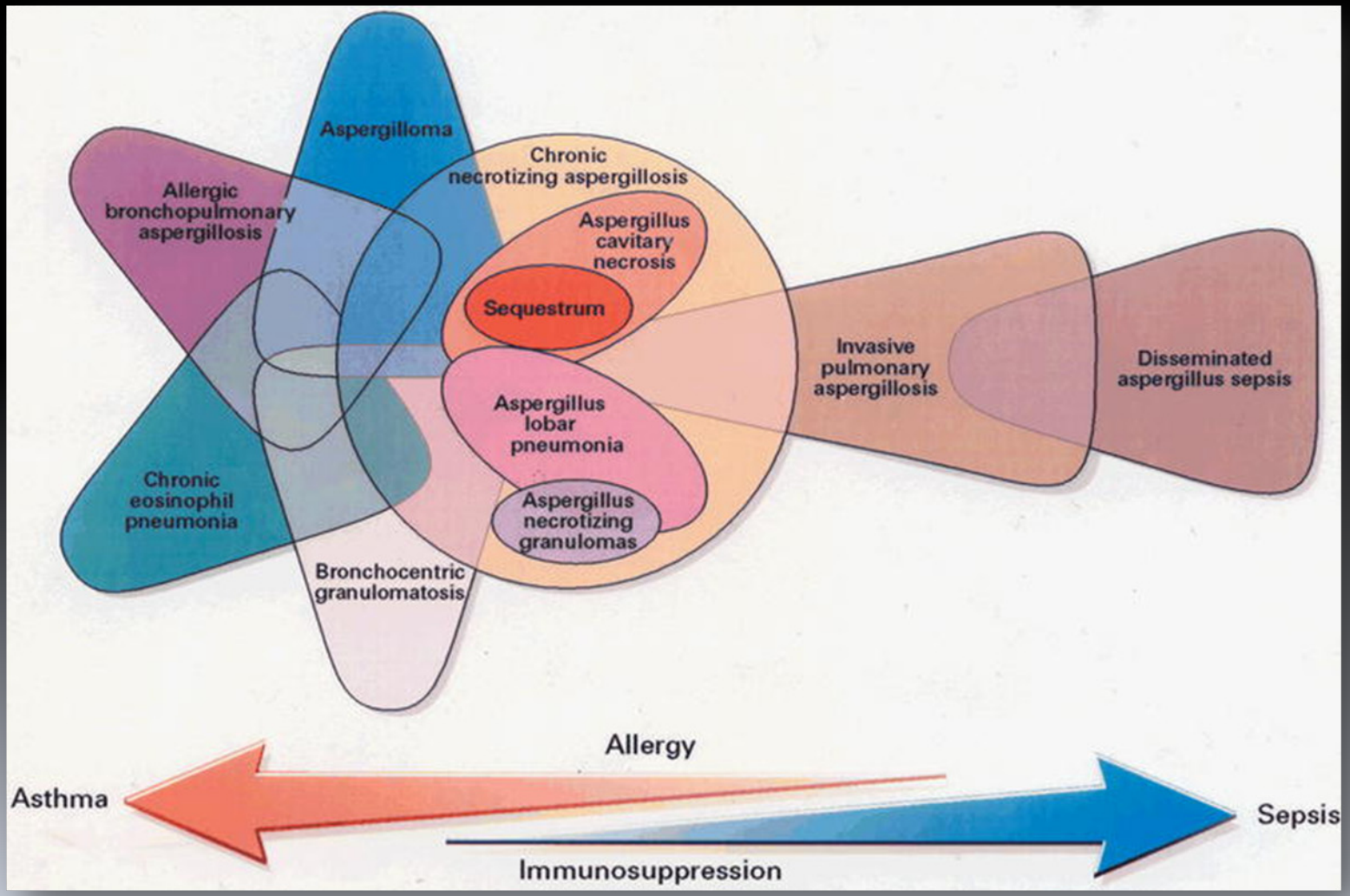
The cell wall

The fungal growth

…However, virulence is secondary to the immune status of the host

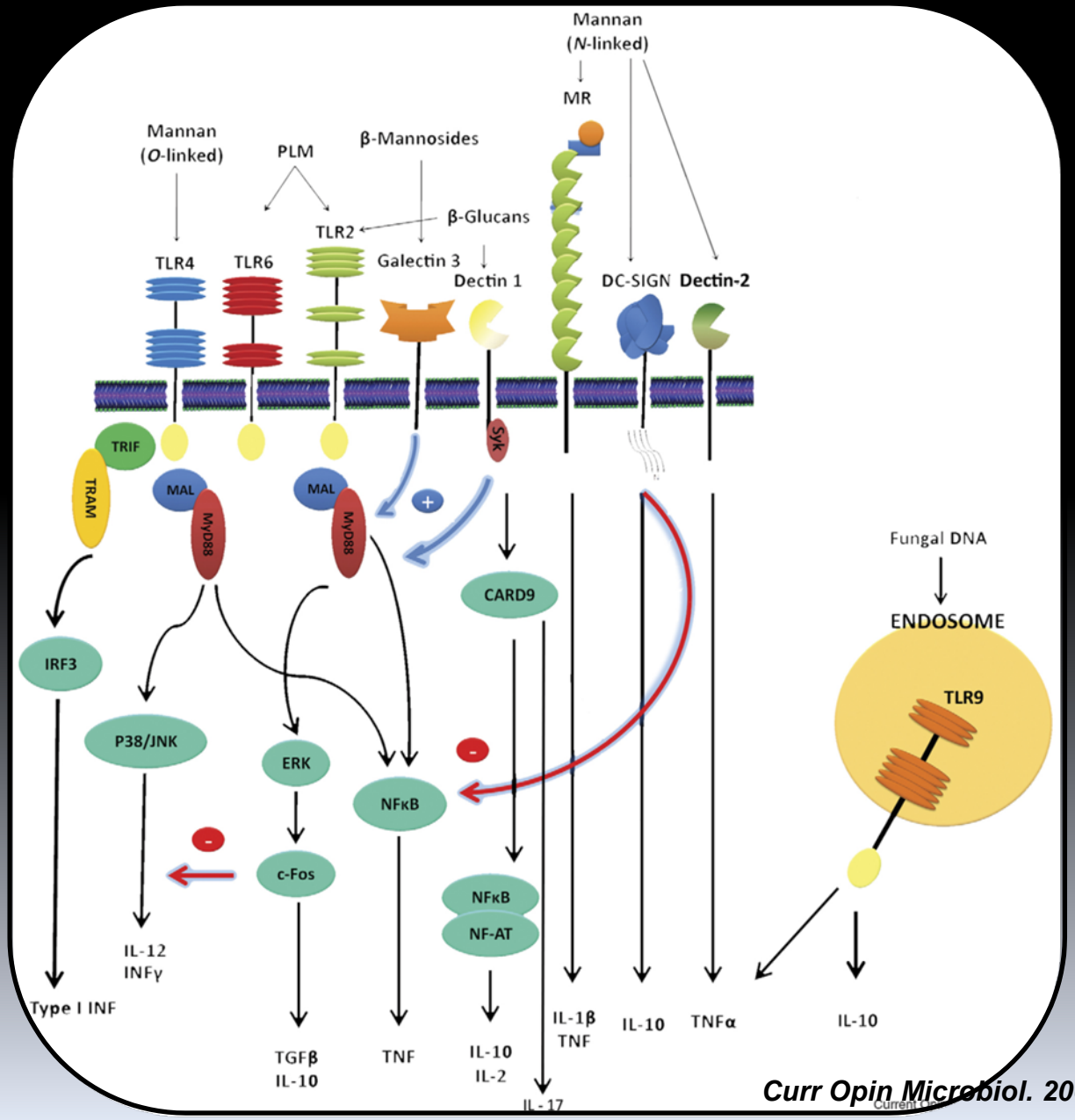
Eukaryot Cell. 2007; 6(11):1953-63

Diagram of a spectrum of disorders of lung caused by Aspergillus spp



Arch Pathol Lab Med. 2008 ;132:606

PRRs in the innate and adaptive immunity



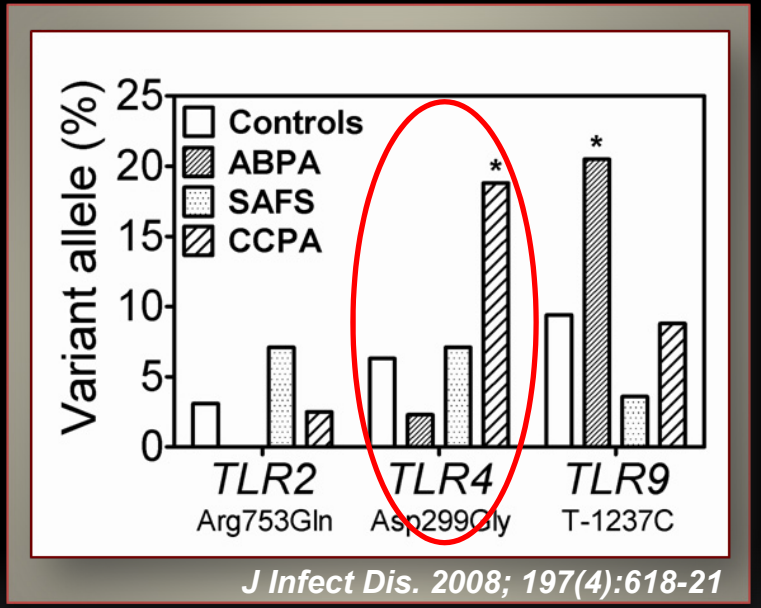
Curr Opin Microbiol. 2008;11(4):305-12

Genetic susceptibility to pulmonary Aspergillosis

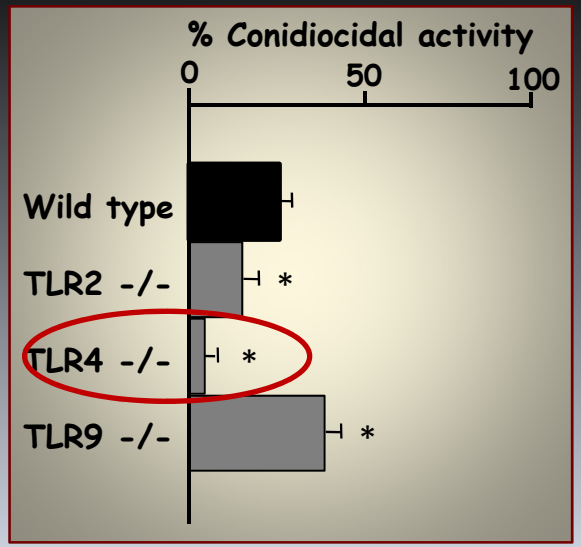
Polymorphisms in Toll-Like Receptor Genes and Susceptibility to Pulmonary Aspergillosis

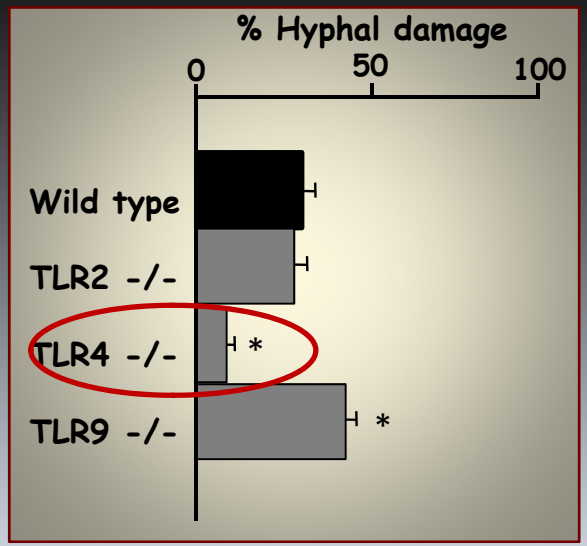
A. Carvalho,[1] A. C. Pasqualotto,[2] L. Pitzurra,[3] L. Romani,[3] D. W. Denning,[2] and F. Rodrigues[1]

[1]Life and Health Sciences Research Institute (ICVS), School of Health Sciences, University of Minho, Braga, Portugal; [2] School of Medicine, University of Manchester and Wythenshawe Hospital, Manchester, United Kingdom; and [3] Department of Experimental Medicine and Biochemical Sciences, University of Perugia, Perugia, Italy



J Infect Dis. 2008; 197(4):618-21





J Immunol. 2004; 173(12):7406-15

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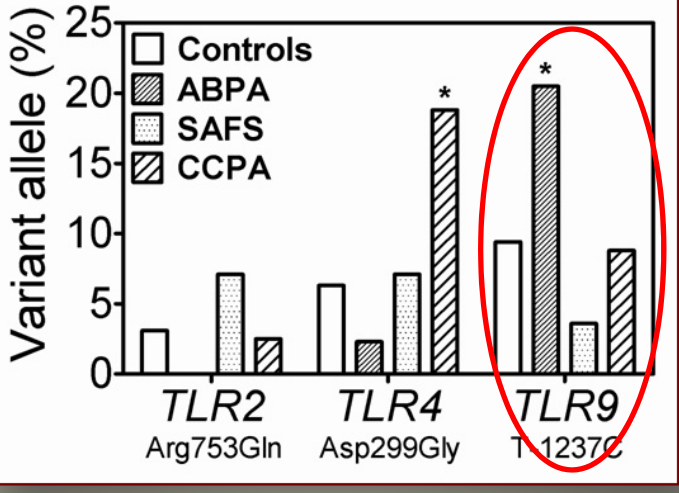

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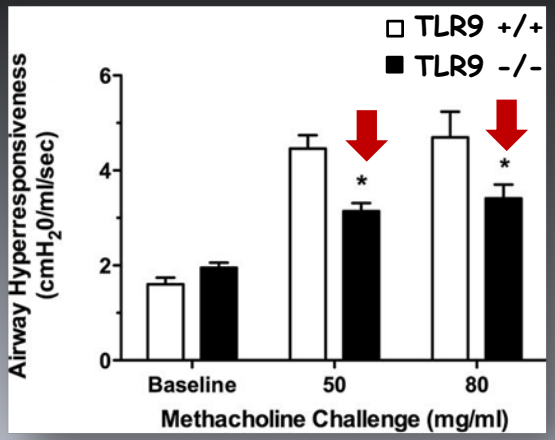
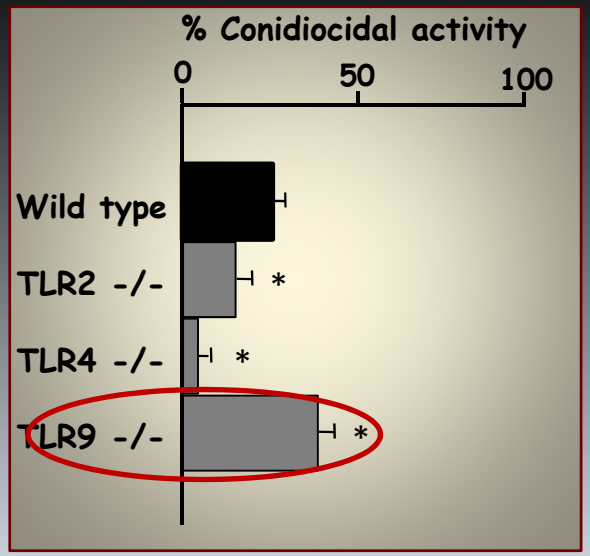
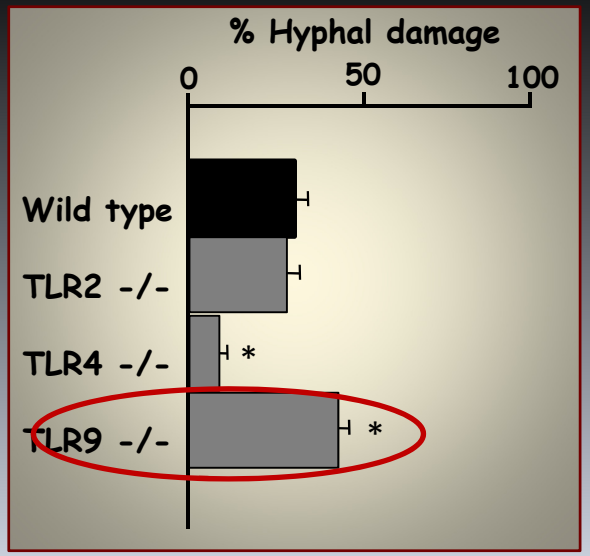


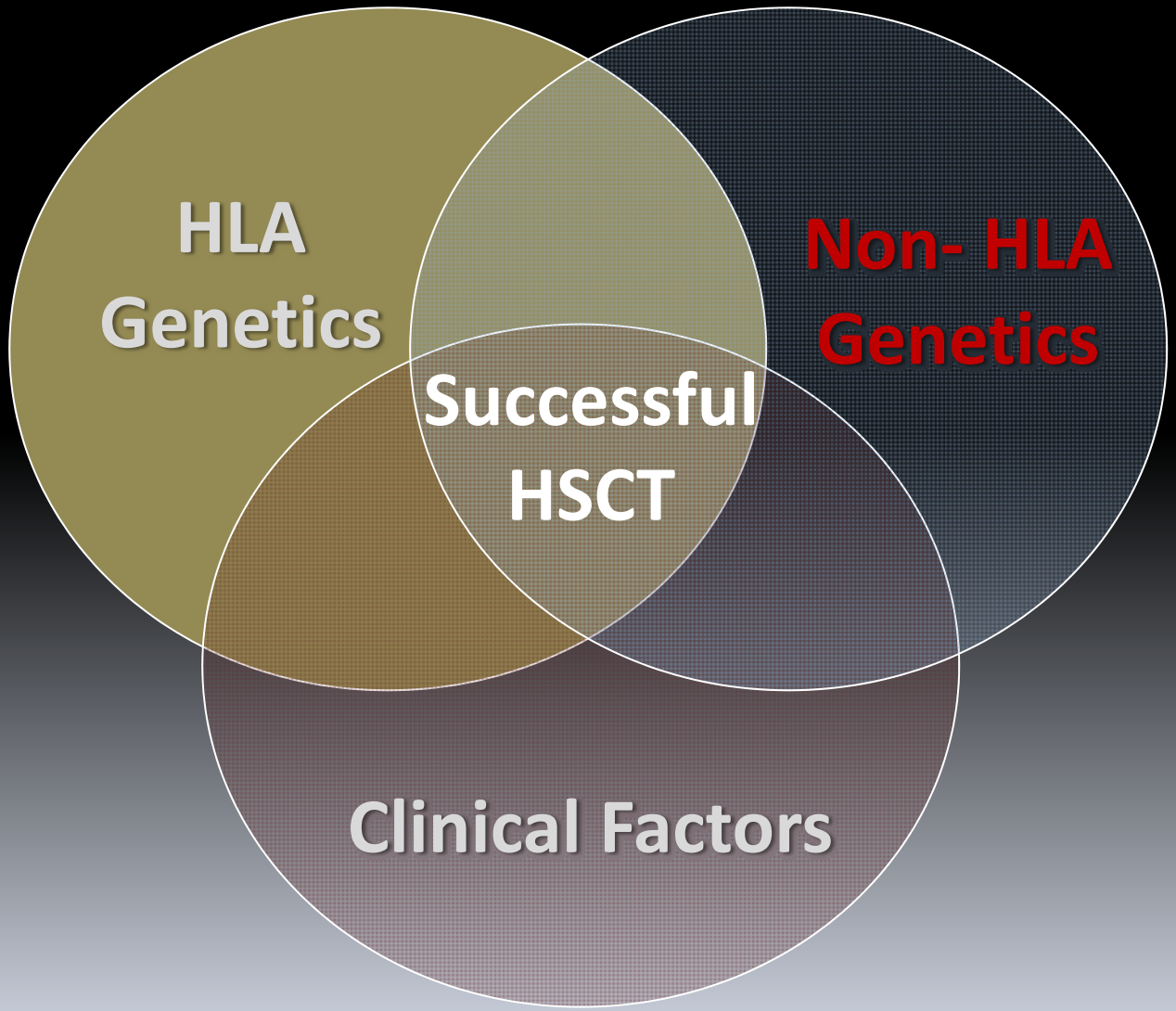
Infect Immun. 2009; 77(1):108-19





J Immunol. 2004; 173(12):7406-15

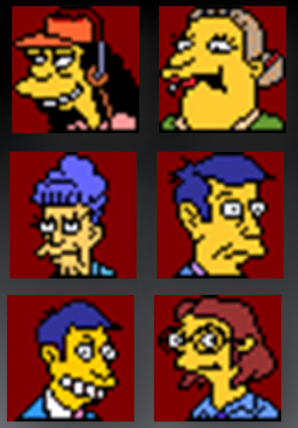
Factors affecting clinical outcome post-HSCT



Genetic susceptibility to Aspergillosis in the HSCT setting

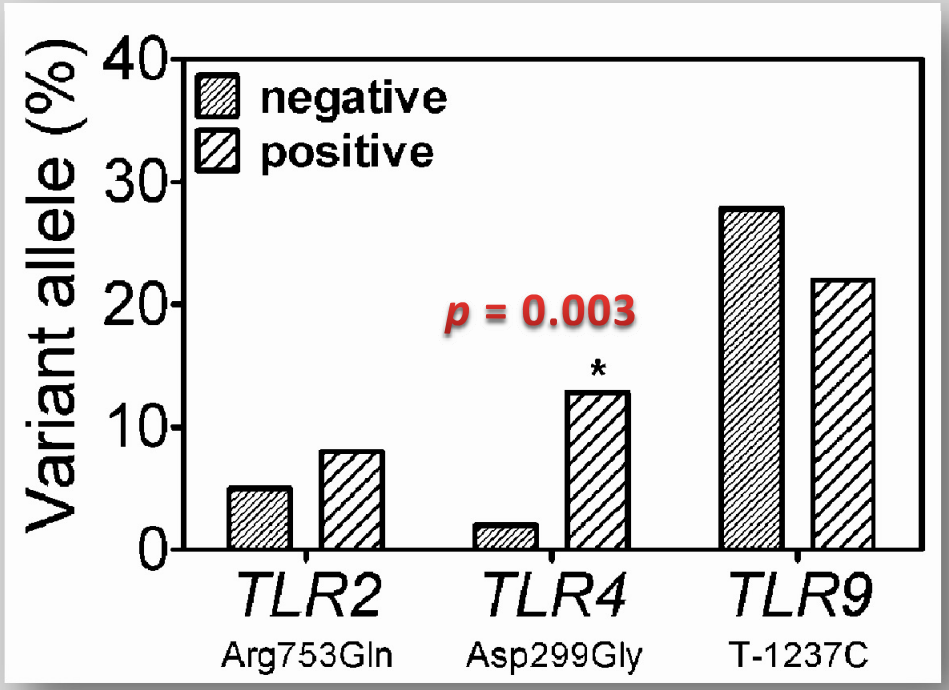
Why does only a fraction of patients with similar degrees of immunosuppression develop infection ?

Aspergillus spp.-resistant HSCT population



Aspergillus spp.-susceptible HSCT population

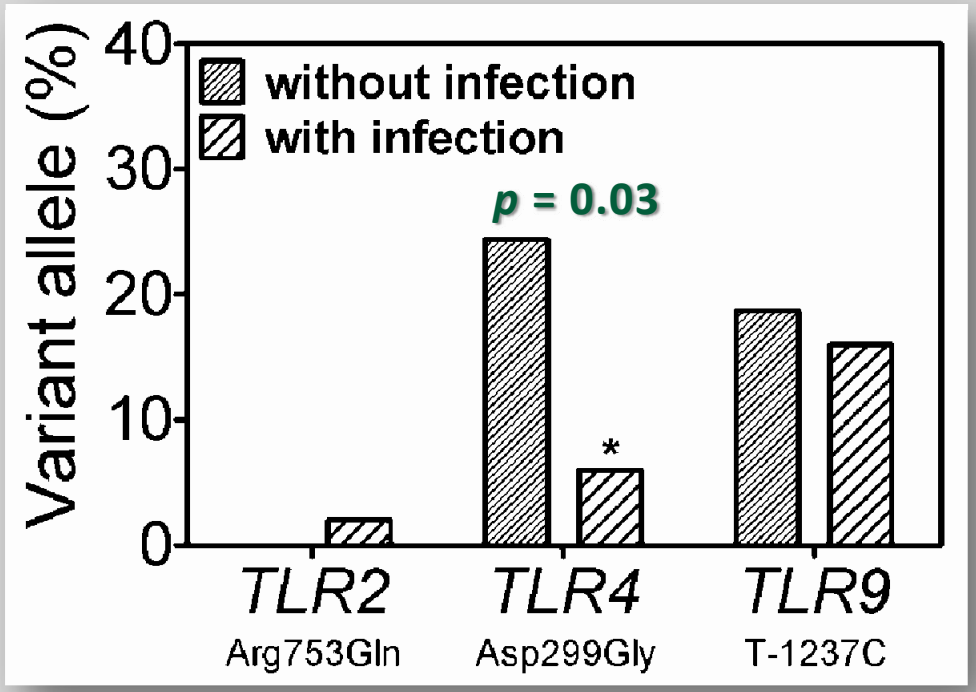
Genetic susceptibility to Aspergillosis in the HSCT setting



Exp Hematol. 2009; 37(9):1022-9

Increased risk of Aspergillus spp. colonization

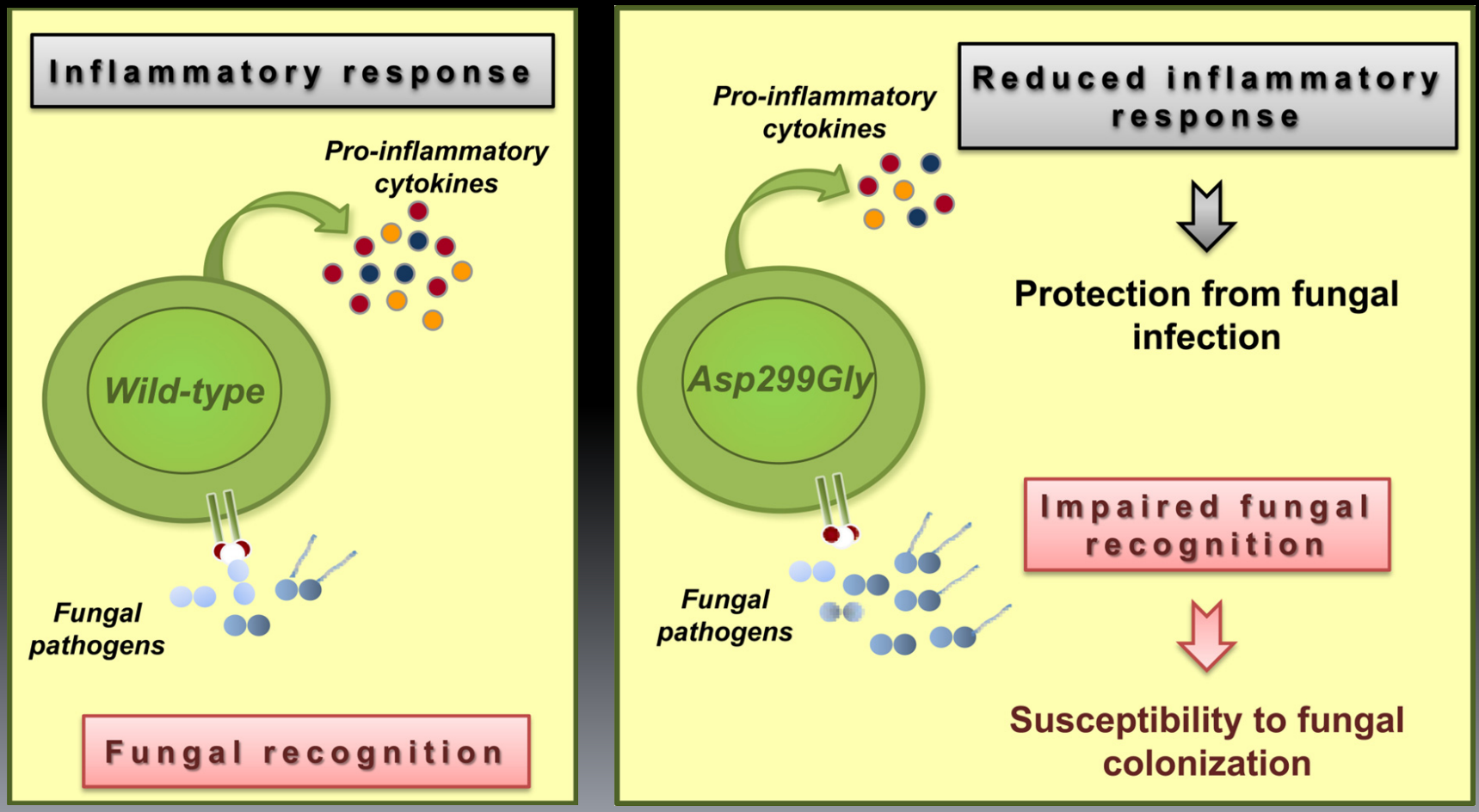
Genetic susceptibility to Aspergillosis in the HSCT setting



Exp Hematol. 2009; 37(9):1022-9

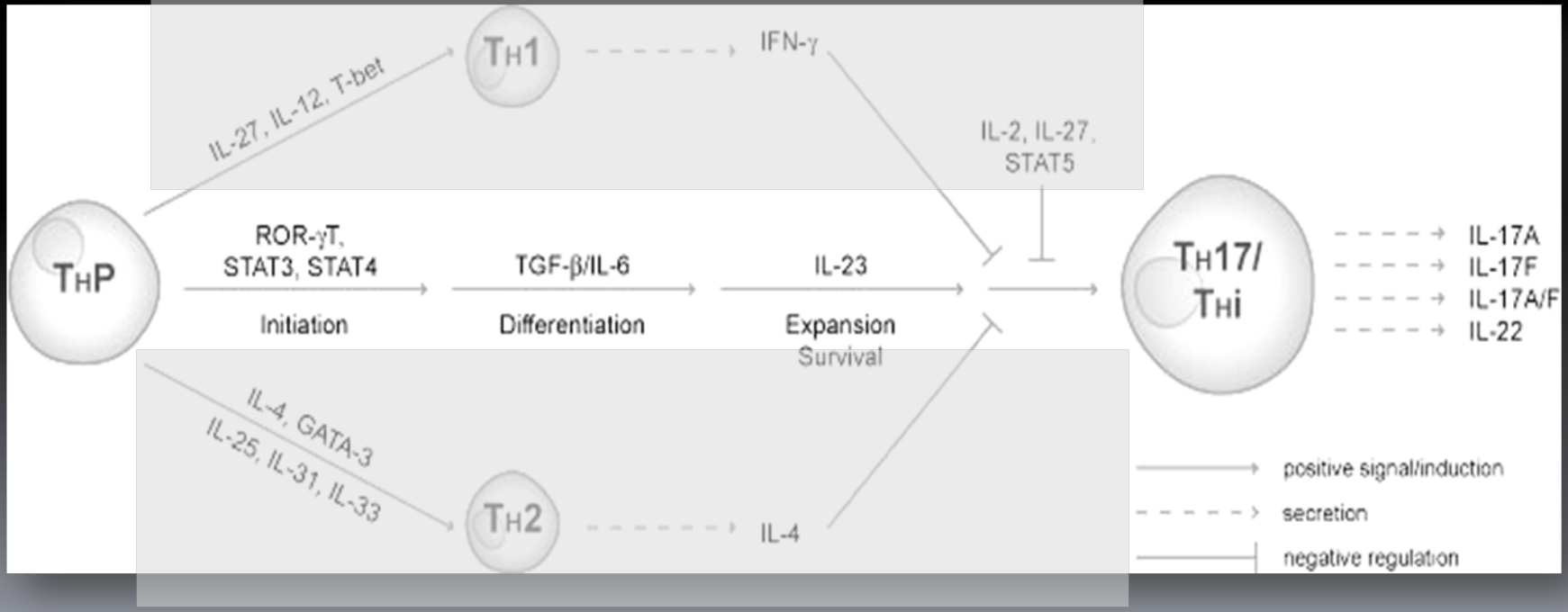
Protection from Aspergillosis

Genetic susceptibility to Aspergillosis

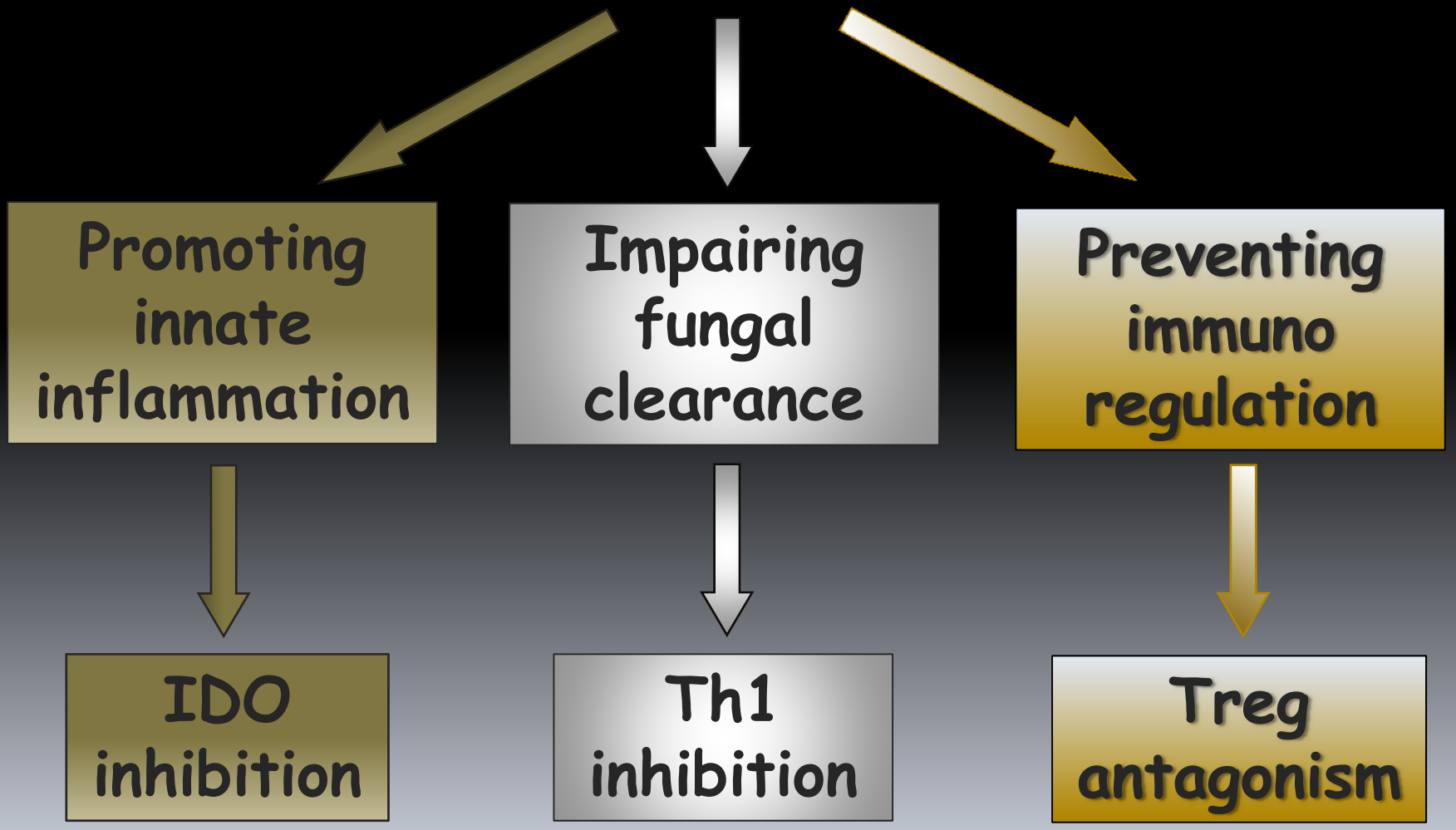


Int J Infect Dis. 2009; [Epub ahead of print]

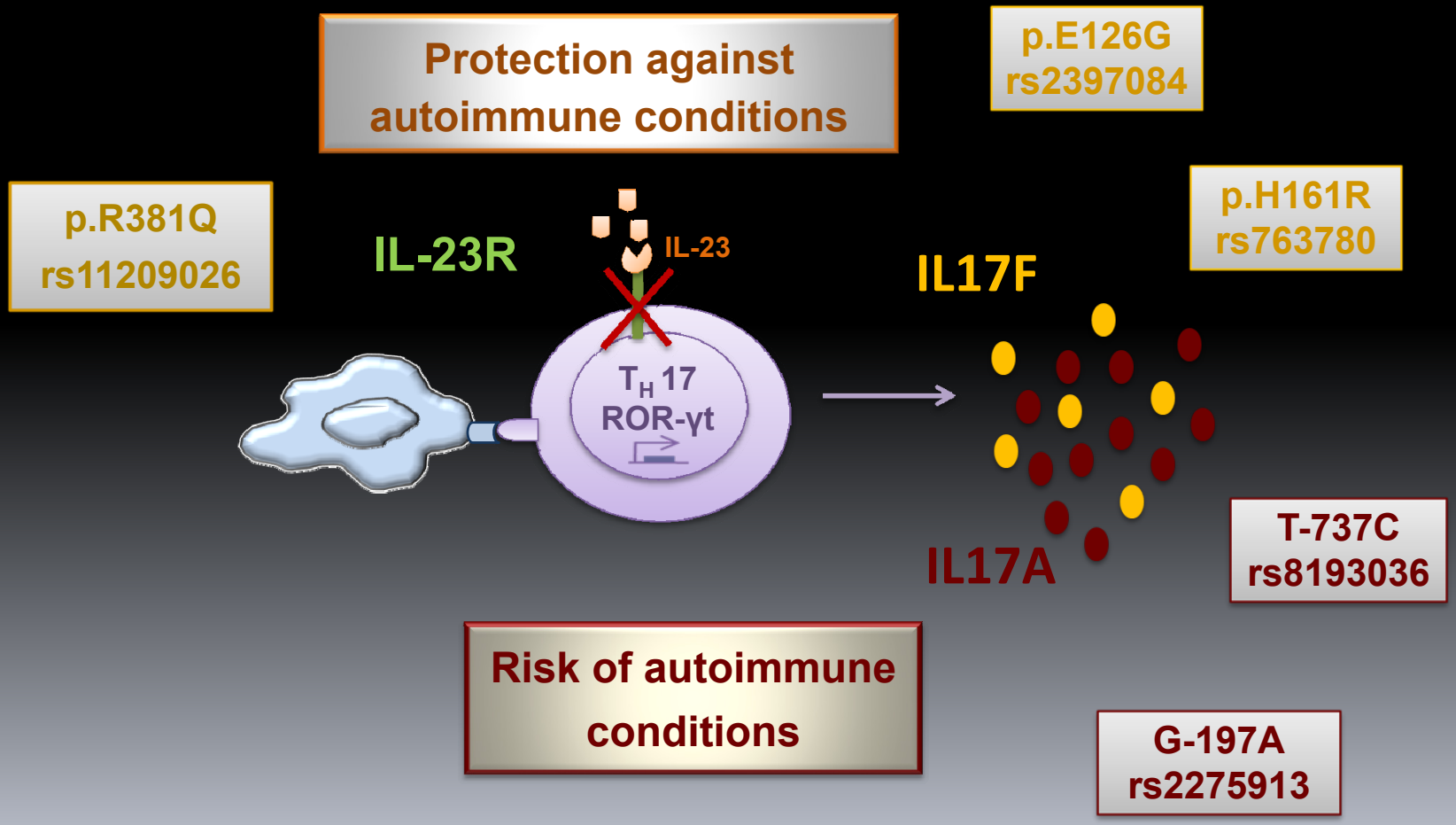
The Th17 pathway: *An emerging subset*



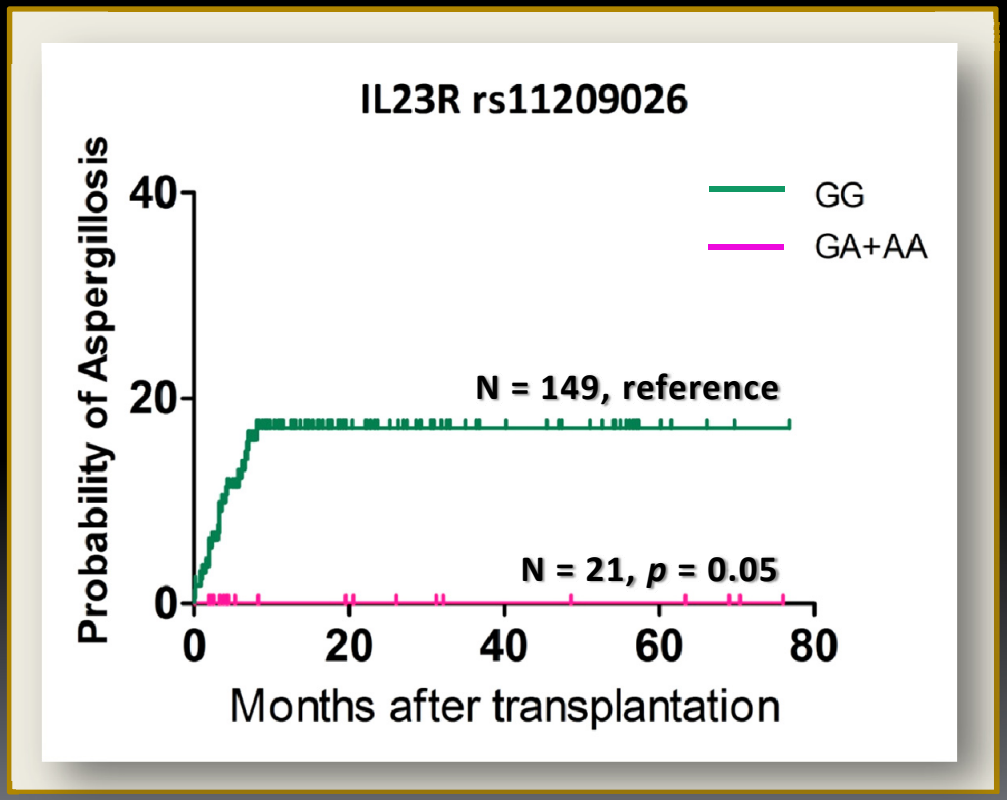
Th17 in action



The impact of genetic variants in the IL23/Th17 pathway on disease susceptibility



Genetic susceptibility to Aspergillosis in the HSCT setting



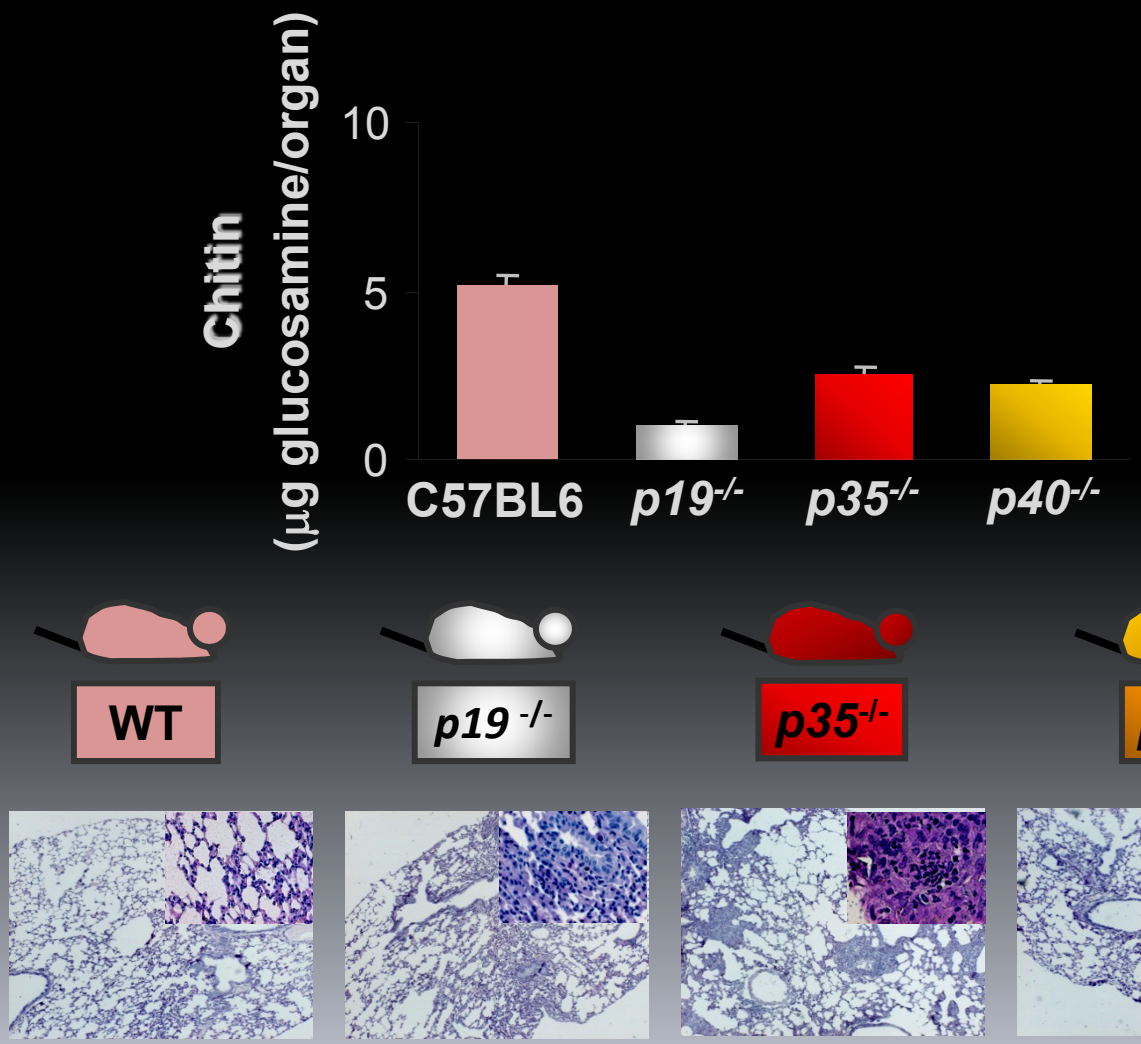
R381Q decreased the risk of Aspergillosis

Bone Marrow Transplant. 2010; (in press)

Consistent with the protective effects of IL-23 signaling attenuation in experimental aspergillosis

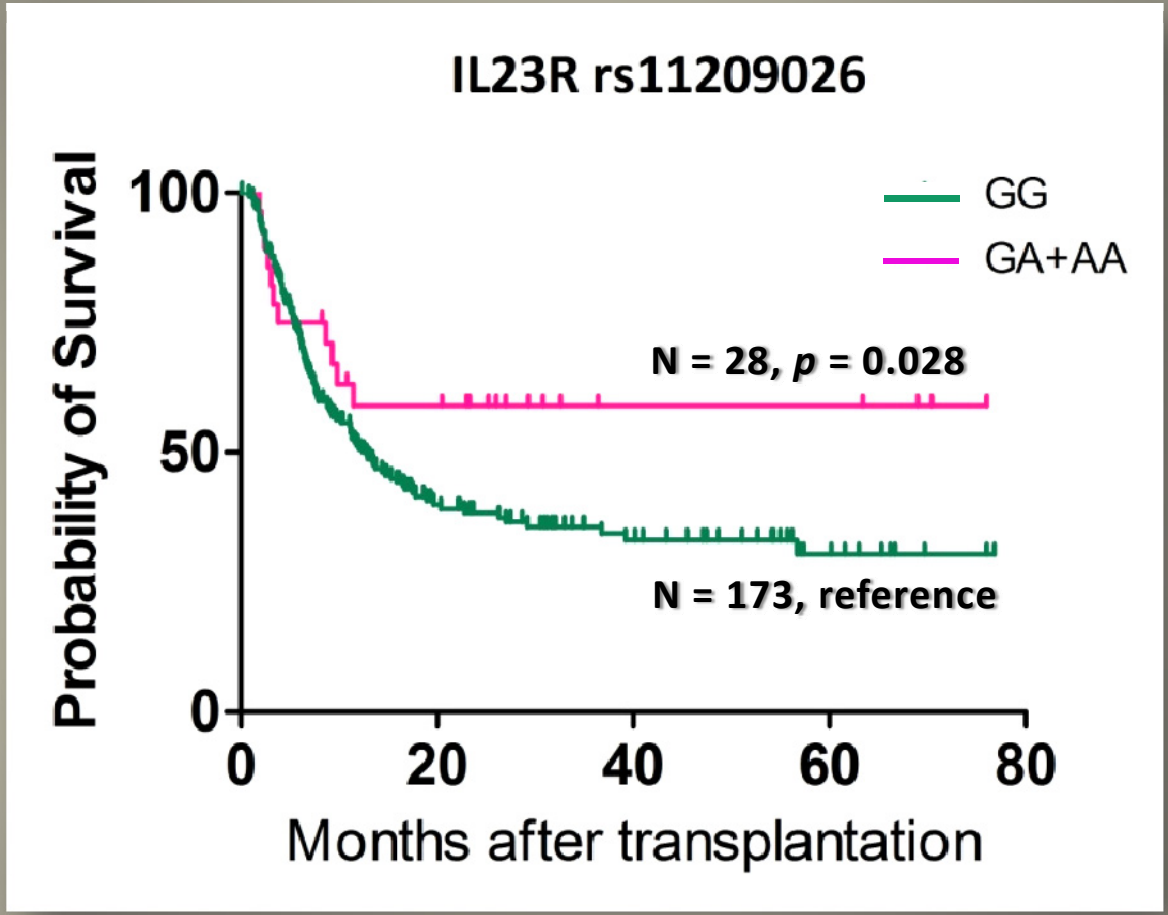
Eur J Immunol. 2007; 37(10): 2695-706

Th17 pathway correlates with susceptibility to aspergillosis



Eur J Immunol. 2007; 37(10): 2695-706

Overall Survival

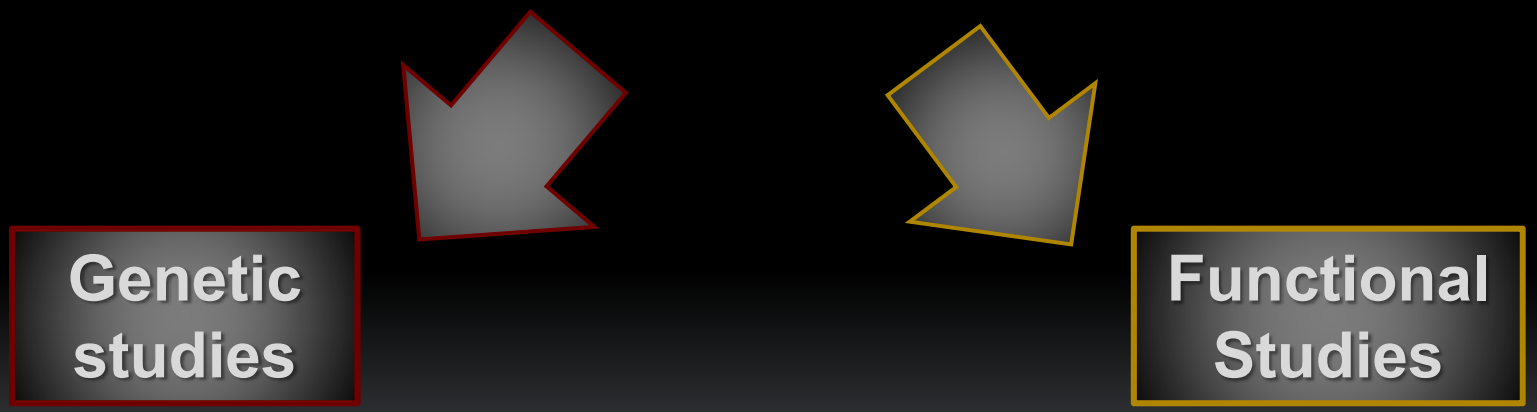


GG – 38% long-term survivors

GA+AA – 63% long-term survivors

Bone Marrow Transplant. 2010; (in press)

From Bench to Bedside:
A translational approach

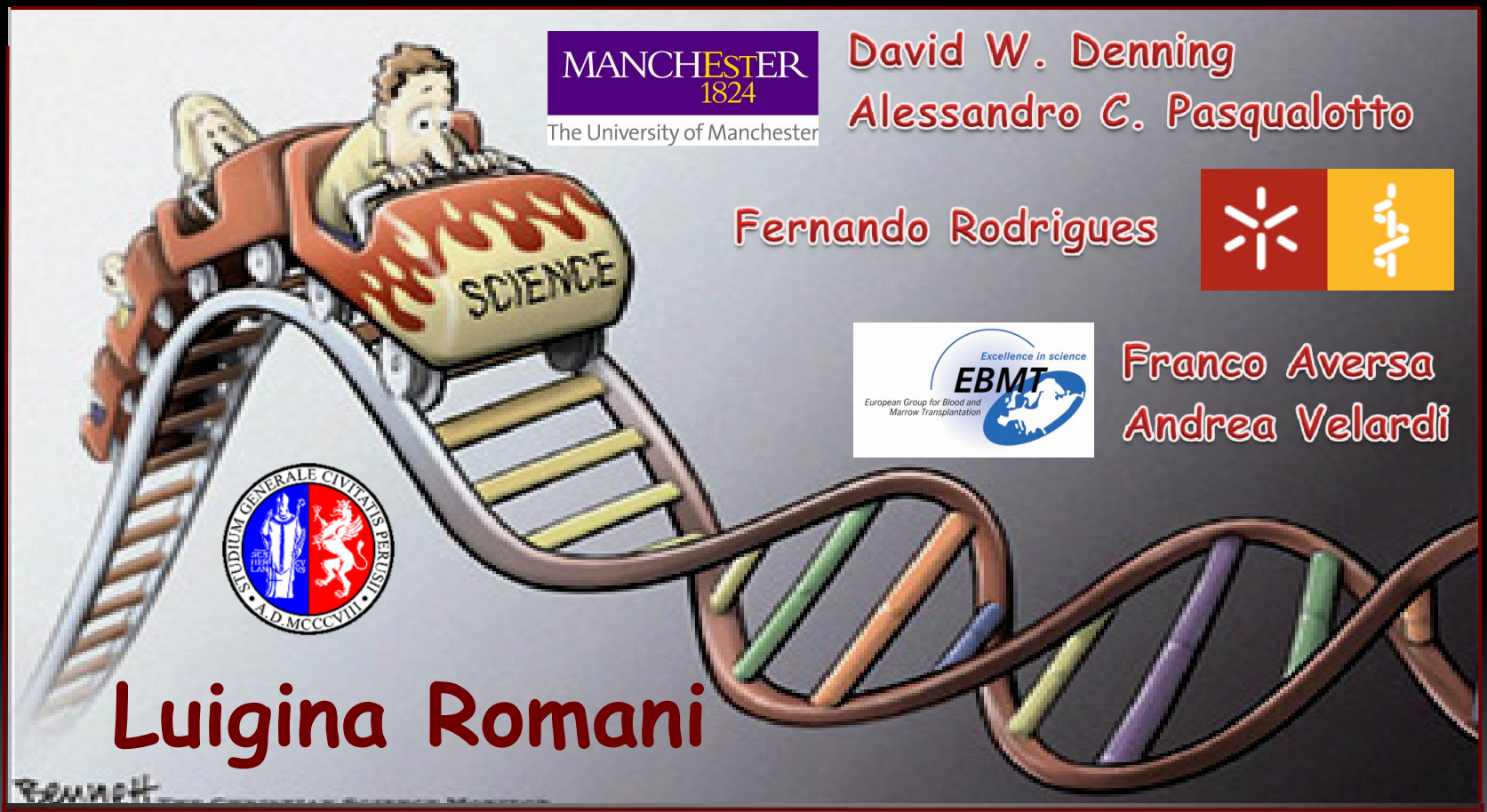


Donor selection

Patient evaluation

Identification of therapeutic targets

Design of prophylactic strategies



MANCHESTER 1824
The University of Manchester

David W. Denning
Alessandro C. Pasqualotto

Fernando Rodrigues

Excellence in science
EBMT
European Group for Blood and Marrow Transplantation

Franco Aversa
Andrea Velardi

STUDIUM GENERALE CIVITATIS PERUSII · A.D. MCCCVIII ·

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