

*Experimental autoimmune encephalomyelitis  
can be prevented and cured by infection with  
*Trypanosoma cruzi**

Carlos E Tadokoro et al.

*Journal of Autoimmunity 23 (2004) 103-115*

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## Multiple Sclerosis

- Incidence: 149/100,000
  - Worldwide: 2.5 million patients
  - AUT: 8.000 patients
- F:M = 2:1
- 50 % need walking assistance within 15 years

*N Engl J Med* **343**, 938-952 (2000)

<http://www.msgoe.co.at>

## Multiple Sclerosis

- Autoimmune disease
- Initiating factors largely unknown
  - Genetic polymorphisms
  - Infections
  - Smoking
- Progressive loss of myelin sheaths followed by astrocytic scars
- Relative preservation of Axons

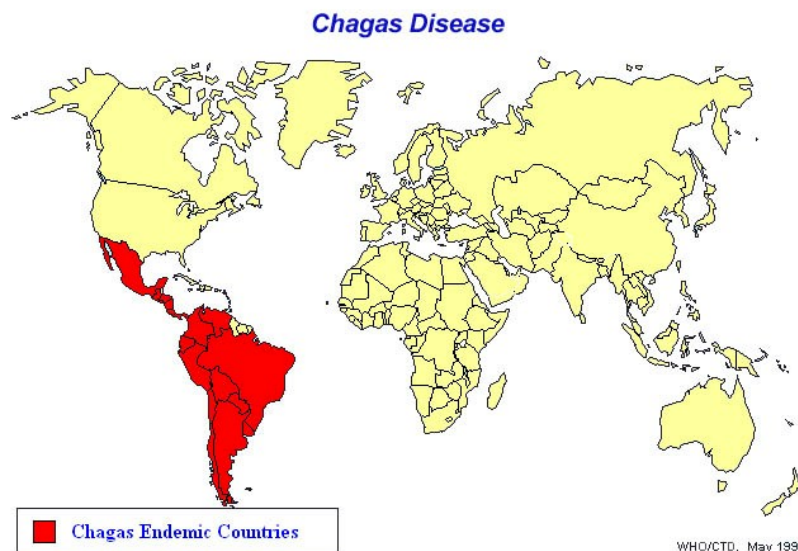
## Experimental Autoimmune Encephalitis (EAE)

- Common animal model for studying MS
- CD 4+ T-cell mediated disease (TH1 and TH17)

# Background

## Trypanosoma cruzi

- Intracellular parasite
- Chagas' Disease
- Kissing bug



Mem Inst Oswaldo Cruz. 1999; **94** Suppl 1: 71-80.  
<http://theassassinbug.com/category/chagas-disease/page/2/>  
<http://www.chagasdisease.org/?p=53>

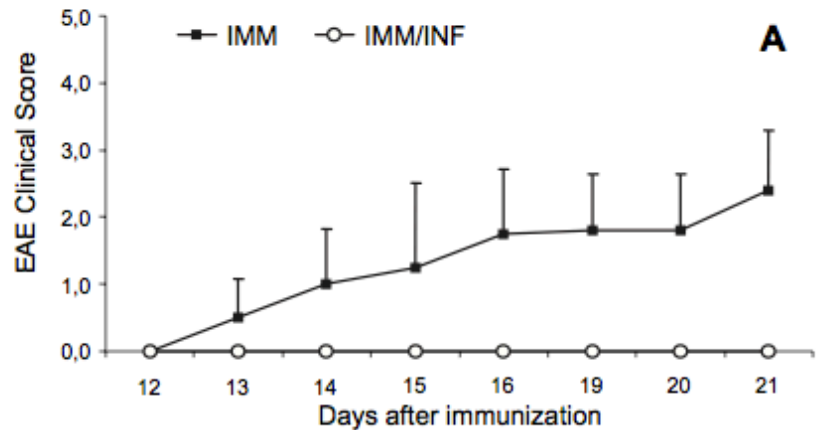
## Parasitic infection ameliorates course of EAE

- MS prevalence in tropical regions lower
- Acute phase of parasitic infection -> immunosuppression
  - Decreased IL-2 production
  - Increased NO-production
  - Increased PGE<sub>2</sub> synthesis
  - Increased CD95 (Fas) expression

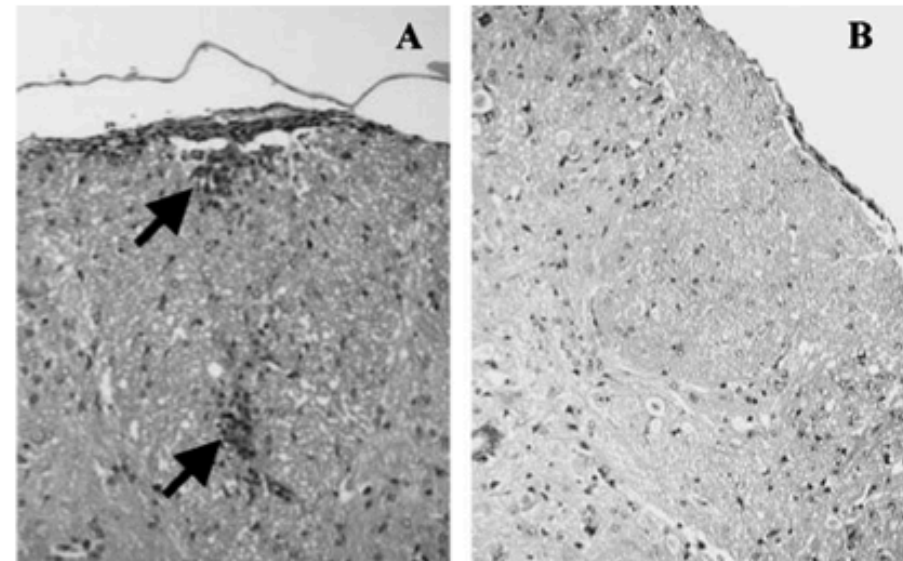
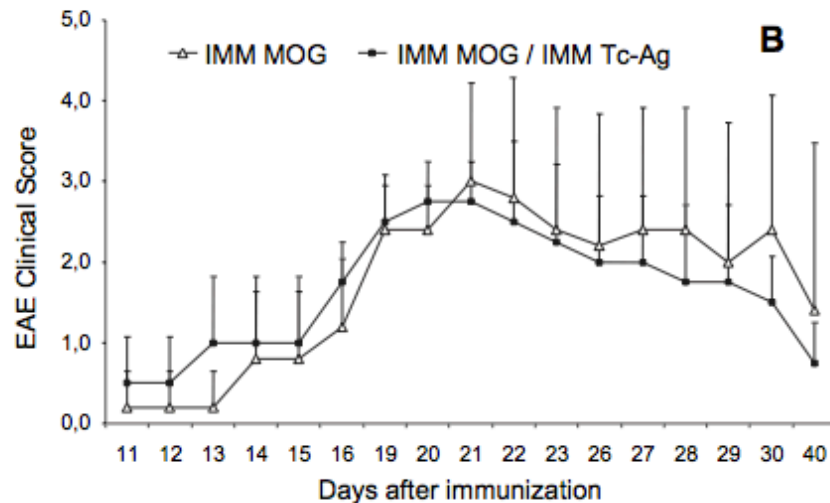
# Methods

- C57Bl/6, C57Bl/6 IL-10-KO, C57Bl/6 iNOS-KO
- Active EAE with MOG immunization
- T. cruzi infection or T. cruzi Ag-administration
- Histology, Cytokine assays, FACS analysis

# Results



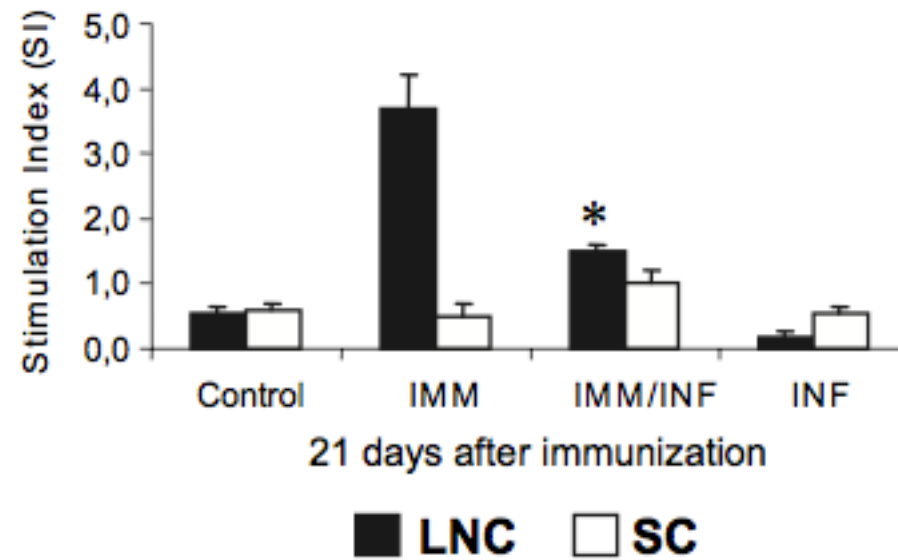
T. cruzi infection prevents development of EAE  
 T. cruzi Ag alone -> no effect



J Autoimmun. 2004; **23**(2): 103-15.

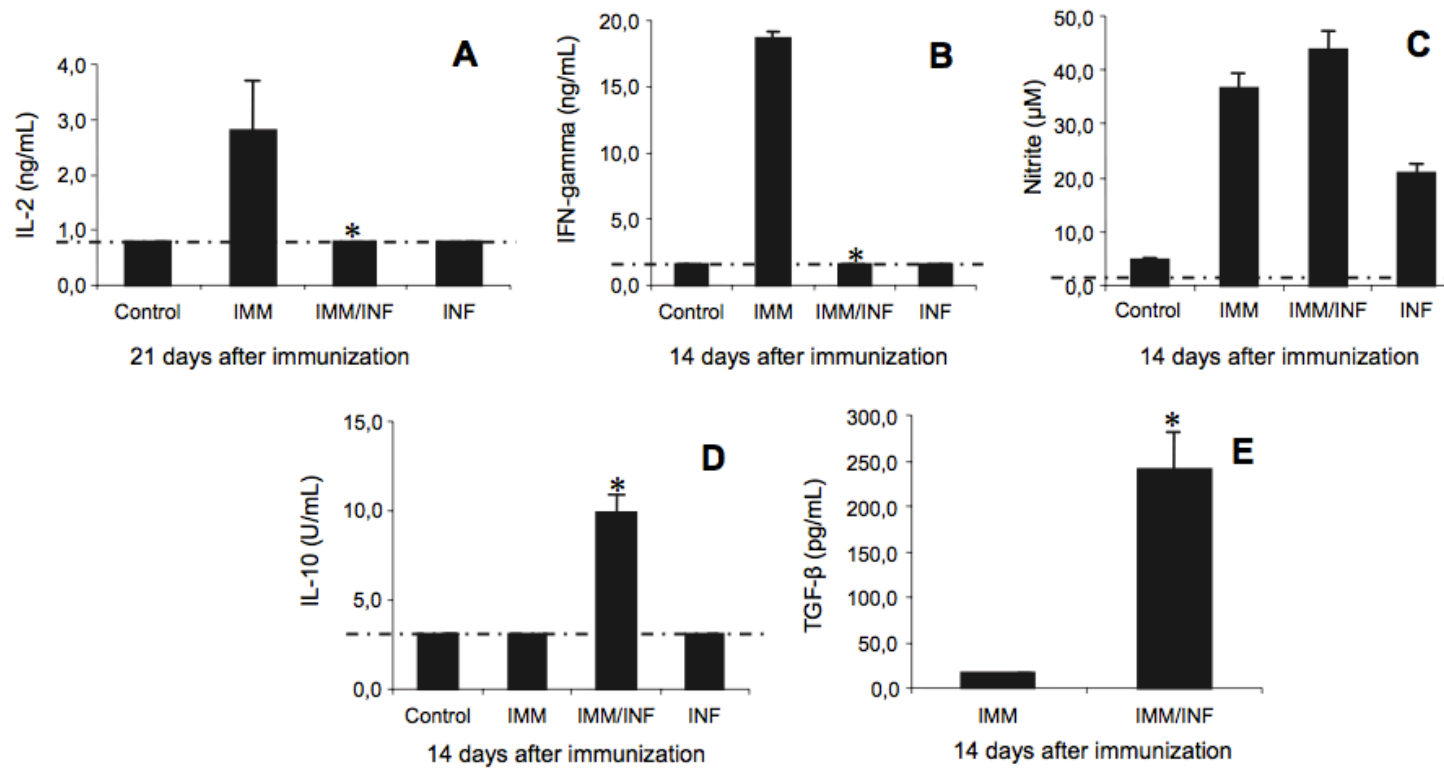


# Results



# Results

## SN of spleen cells after stimulation with MOG



J Autoimmun. 2004; 23(2): 103-15.

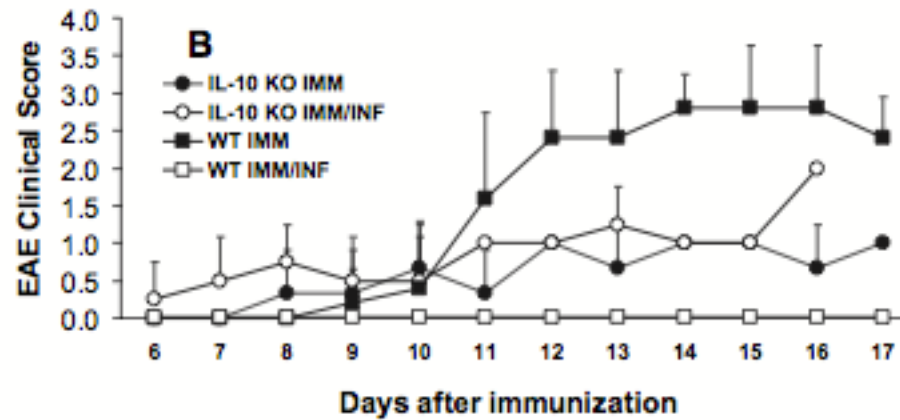
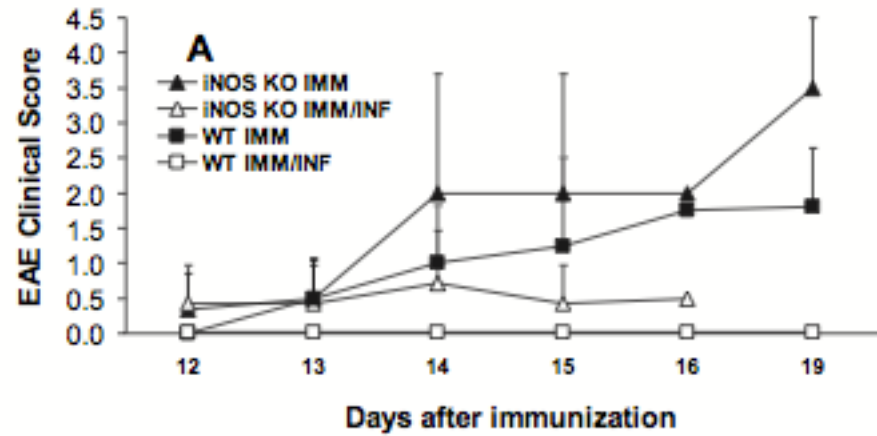
# Results

Spleen cells of infected animals induce apoptosis

	PKH-26 <sup>+</sup> /Annexin V <sup>+</sup>
SC Normal + SC IMM	4.8 ± 0.2
SC INF 7 + SC IMM	2.9 ± 0.1
SC INF 12 + SC IMM	8.9 ± 0.2
SC INF 12 + SC IMM + NMMA	3.8 ± 0.3

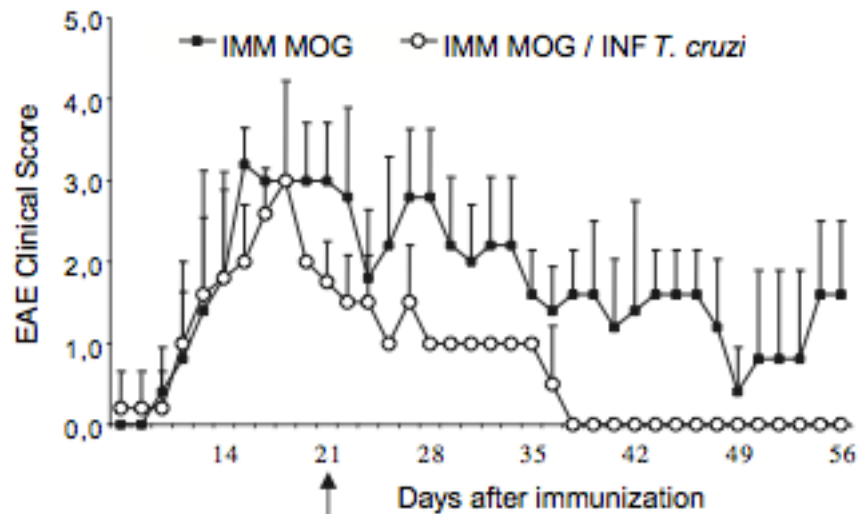


# Results

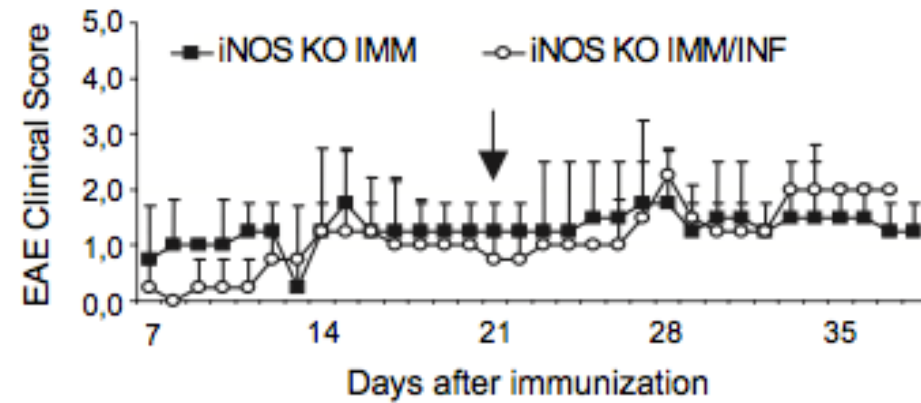


# Results

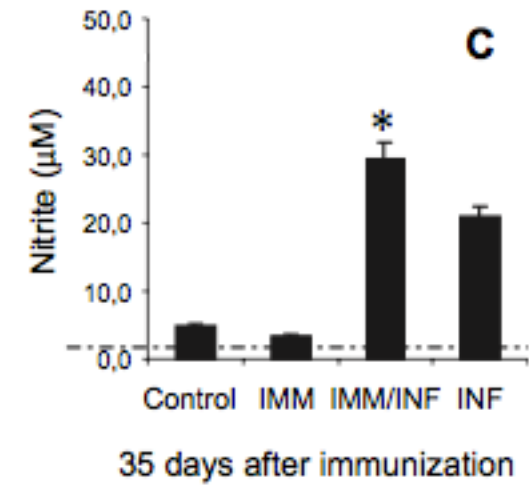
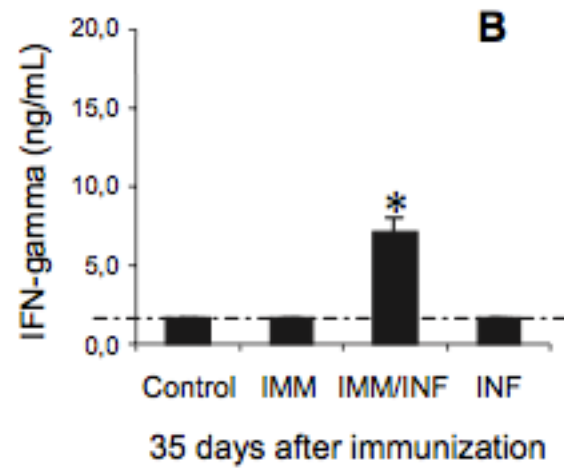
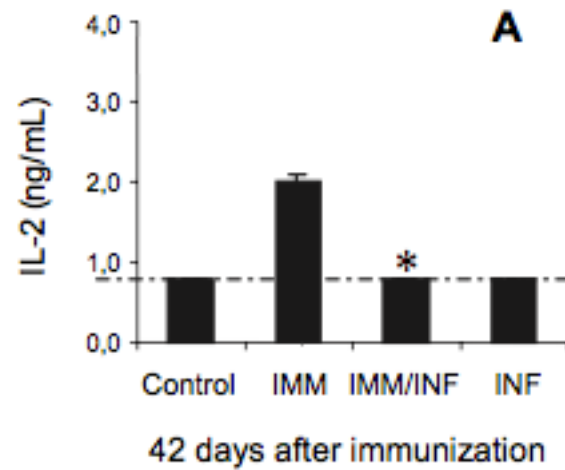
Infection on d21 leads to remission of EAE



... But not in iNOS KO mice



# Results



# Discussion

- Simultaneous *T. cruzi* infection seems to be beneficial for the course of EAE in mice
- NO/IL-10 dependent mechanism of immunosuppression

# Limitations

- T. cruzi preparation/administration ? (Balb/c)
- High dose of T. cruzi (50 times higher)
- Clinical score in WT mice varies
- Scoring of sick animals?
- IL-10KO mice - recovery from EAE after infection on d21?



Thank you for your attention!