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

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Background

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

http://www.msgoe.co.at
Background

Multiple Sclerosis

– Autoimmune disease

– Initiating factors largely unknown
  • Genetic polymorphisms
  • Infections
  • Smoking

– Progressive loss of myelinsheaths followed by astrocytic scars

– Relative preservation of Axons

Background

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

http://theassassinbug.com/category/chagas-disease/page/2/
http://www.chagasdisease.org/?p=53
Hypothesis

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$_2$ 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
Results

![Graph showing stimulation index (SI) 21 days after immunization for different groups: Control, IMM, IMM/INF, and INF. The graph compares LNC (Lymph Node Cells) and SC (Somatic Cells).]
Results

SN of spleen cells after stimulation with MOG

Results

Spleen cells of infected animals induce apoptosis

<table>
<thead>
<tr>
<th></th>
<th>PKH-26⁺/Annexin V⁺</th>
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<tbody>
<tr>
<td>SC Normal + SC IMM</td>
<td>4.8 ± 0.2</td>
</tr>
<tr>
<td>SC INF 7 + SC IMM</td>
<td>2.9 ± 0.1</td>
</tr>
<tr>
<td>SC INF 12 + SC IMM</td>
<td>8.9 ± 0.2</td>
</tr>
<tr>
<td>SC INF 12 + SC IMM + NMMA</td>
<td>3.8 ± 0.3</td>
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</tbody>
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Results

Results

Infec@on 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!