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The role of the CD32a in the physiopathology of cutaneous leishmaniasis

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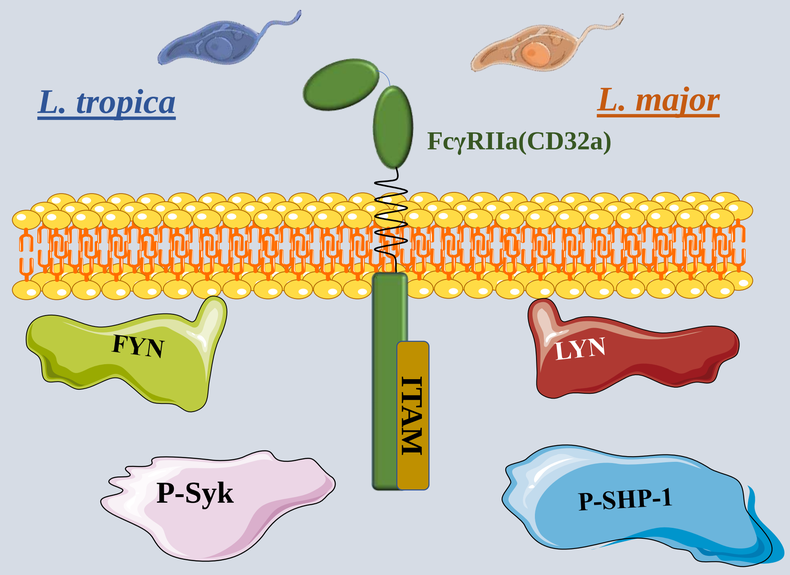
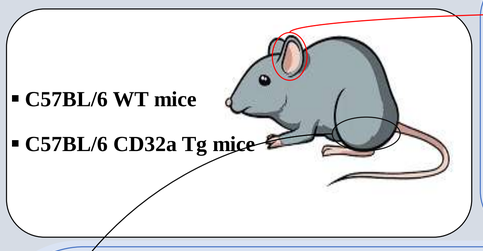
Introduction

Leishmaniases are complex parasitic diseases caused by obligate intracellular protozoa of the genus *Leishmania*. Cutaneous leishmaniasis (CL) is the most prevalent form globally, causing disfiguring lesions and disabilities. The immune system's initial response involves recognition by Fc Receptors, which can activate pathways aiding or hindering intruder invasion. This study aims to deeply investigate the interaction between the **CD32a** receptor (FcRIIa) and two *Leishmania* strains (***L. major*** and ***L. tropica***)

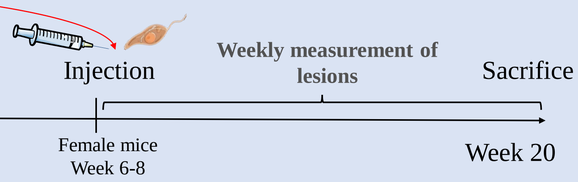


ITAM activator/inhibitor ??

Material & Methods

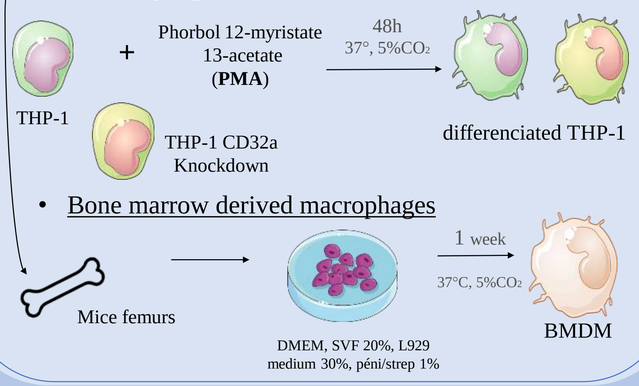


❑ ***In vivo* assays**



❑ ***In cellulo* assays**

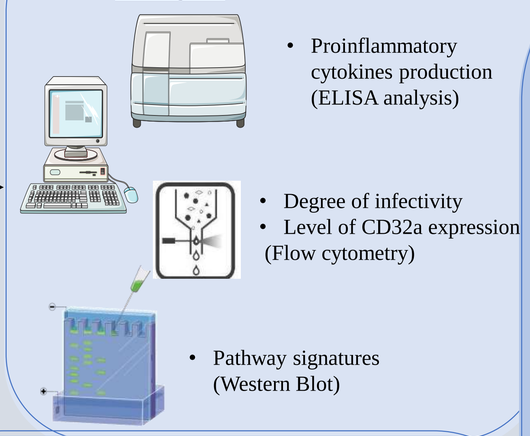
- Macrophage derived from THP-1 cell line



- Bone marrow derived macrophages

Infection

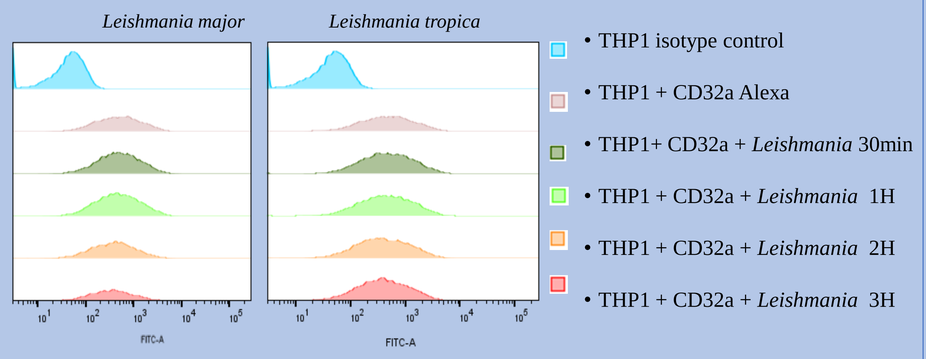
Analysis



- Proinflammatory cytokines production (ELISA analysis)
- Degree of infectivity
- Level of CD32a expression (Flow cytometry)
- Pathway signatures (Western Blot)

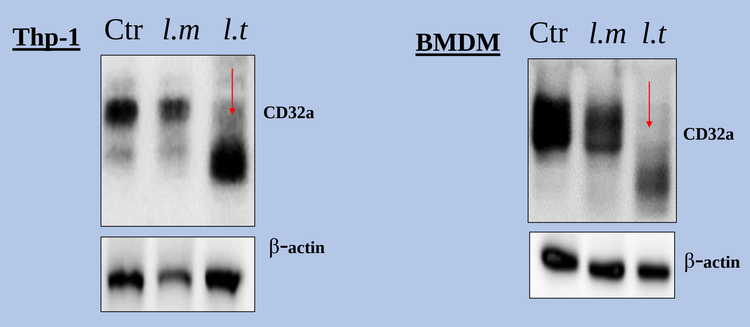
Results

❑ The surface cell expression of CD32a in THP-1 isn't affected after infection with *leishmania* (n=3)

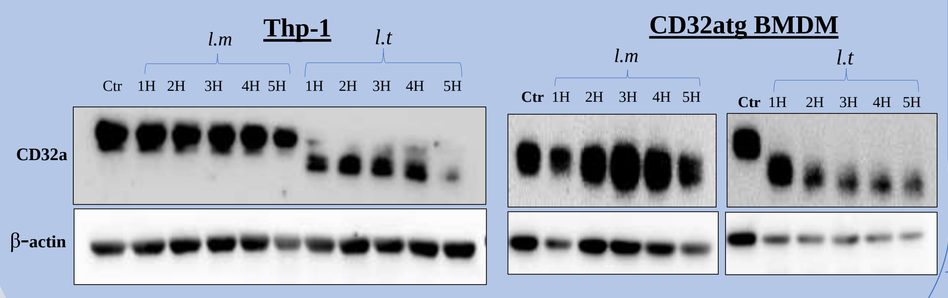


❑ CD32a Cleavage

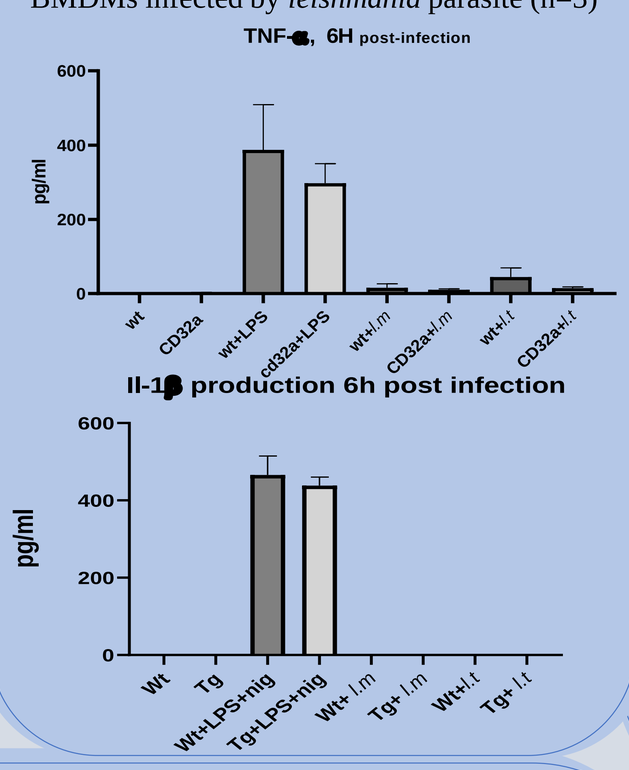
- Cleavage of CD32a after infection with *leishmania* in THP-1 and BMDMs (n=3)



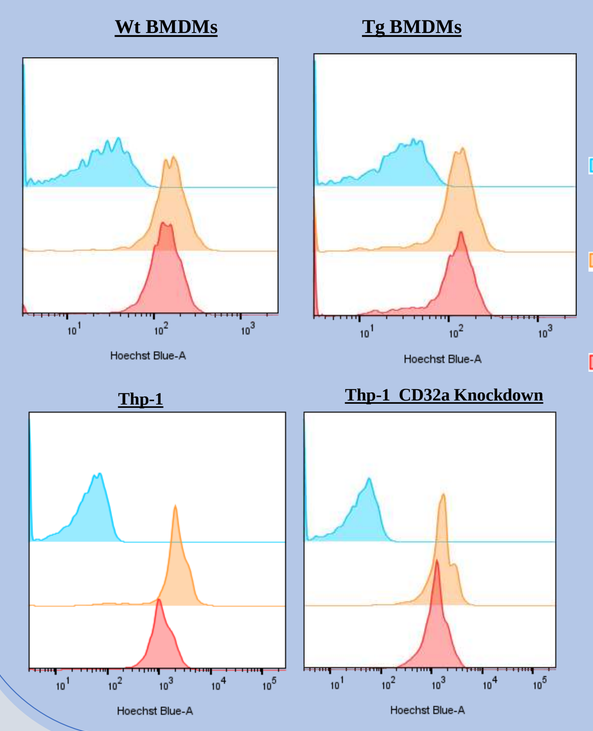
- Kinetic of CD32a cleavage after infection with *leishmania in* THP-1 and BMDM (n=3)



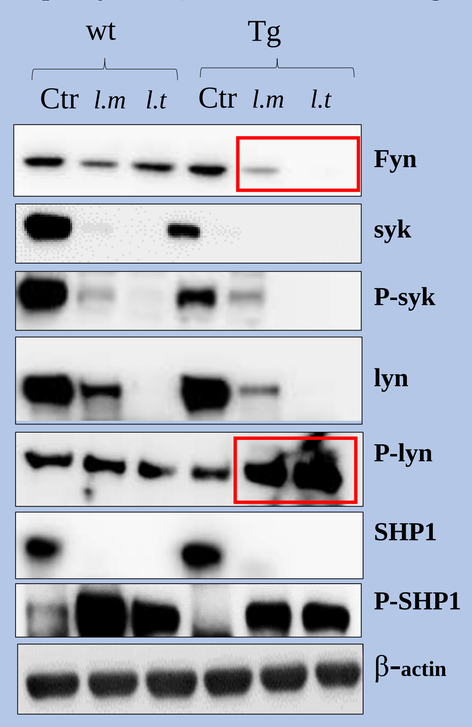
❑ No production of pro-inflammatory cytokines in BMDMs infected by *leishmania* parasite (n=3)



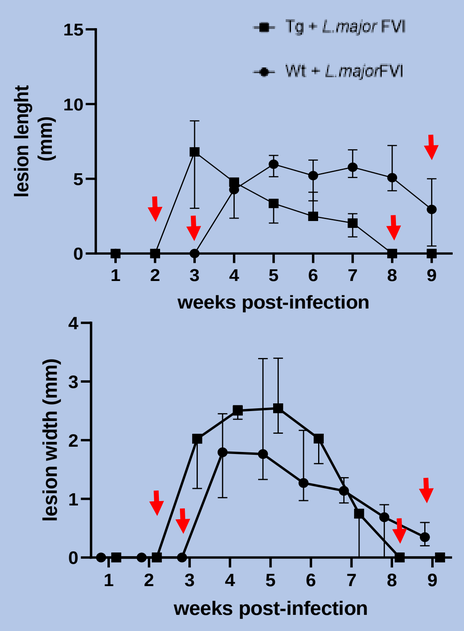
❑ *L. major* seems to infect cells more than *L. tropica* (n=3)



❑ Decrease in the expression of Fyn and an activation of Lyn (phosphorylation) in infected CD32atg BMDMs (n=3)



❑ Difference in the inflammation profile between the two genetic backgrounds



Conclusion and perspectives

CD32a may play a role in shifting the balance ITAMi/a in leishmanaisis

❑ ***In cellulo:***

- CD32a is cleaved by *Leishmania tropica* but not *leishmania major*
- The cleavage seems to be intracellular
- CD32a may play a role in shifting the balance into an inhibitory pathway the infection by the:
  - Downregulation of FYN
  - Activation of Lyn
- CD32a doesn't seem to affect the production of pro-inflammatory cytokines
- CD32a doesn't seem to affect the infectivity of BMDMs or THP-1

❑ ***In vivo:***

- It seems that the inflammation is limited in ears of Tg mice
- The inflammation in Wt mice seems to propagate in all the ear

○ Perspective

➢ Study the consequence of CD32a cleavage.