Role of the CD47-SIRPα axis in the clearance of *Babesia microti* in vivo

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BACKGROUND

Human babesiosis is an emerging tickborne disease in the US caused by the RBC infecting parasite *Babesia microti.* Infection is primarily transmitted by *Ixodes* ticks, and less frequently by pregnancy or transfusion. Infections are usually asymptomatic or mild among healthy individuals but potentially severe in immunocompromised patients (1).

The mechanisms underlying pathogenesis and immune response remain unresolved. In addition, novel therapeutic approaches are needed given the risk for relapsing babesiosis with immunodeficiency (2, 3).

Fig. 1. Life Cycle of *Babesia microti*

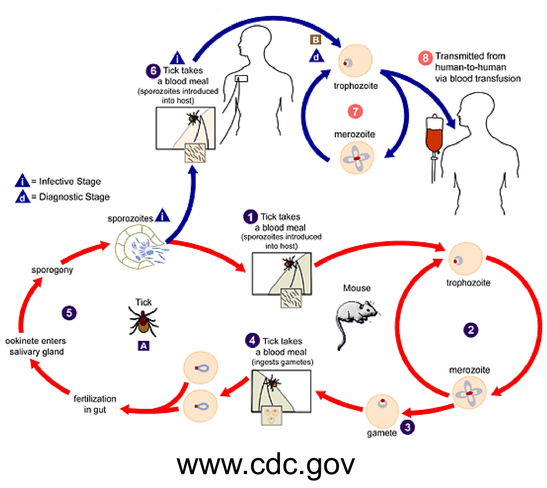

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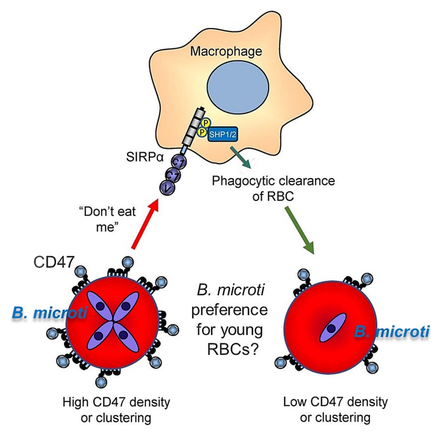
Fig. 2. A Role for CD47 in Babesiosis



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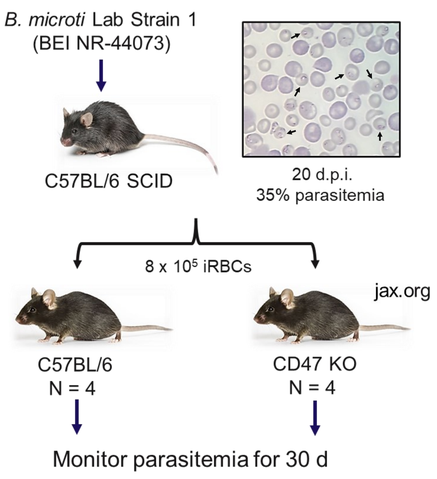
EXPERIMENTAL APPROACH

Fig. 3. Infection of CD47 KO Mice

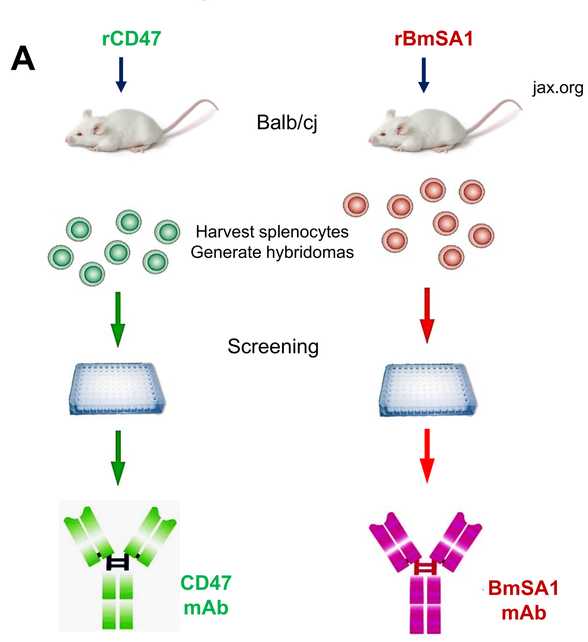


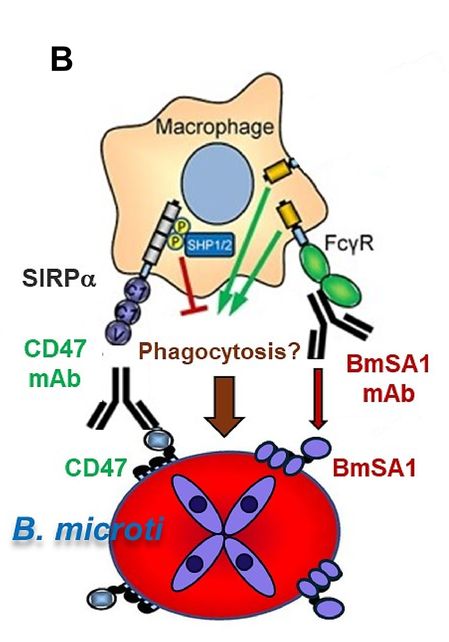
Objective. To investigate the role of CD47 on the growth of *Babesia microti* in mice.

- *B. microti* Lab Strain 1 (BEI NR-44073) was propagated in C57BL/6 SCID mice.
- Eight-week-old female C57BL/6 and CD47 KO (B6.129S7-Cd47^{tm1Fpl}) mice were injected i.p. with 8 x 10^5 infected red blood cells (iRBCs).
- Blood samples were collected from the tail veins and parasitemia was monitored over a 30-d period of infection by microscopic examination.

- **A.** In separate experiments, monoclonal antibodies (mAbs) to recombinant CD47 and *B. microti* surface antigen BmSA1 were generated in Balb/c mice.
- **B.** The utility of these mAbs to block CD47 signaling and promote parasite clearance in susceptible mouse strains is the subject of current research in our laboratory.

Fig. 4. Generation of mAbs to study the role of CD47 in babesiosis





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RESULTS

Fig. 5. Susceptibility of CD47 KO mice to *B. microti*

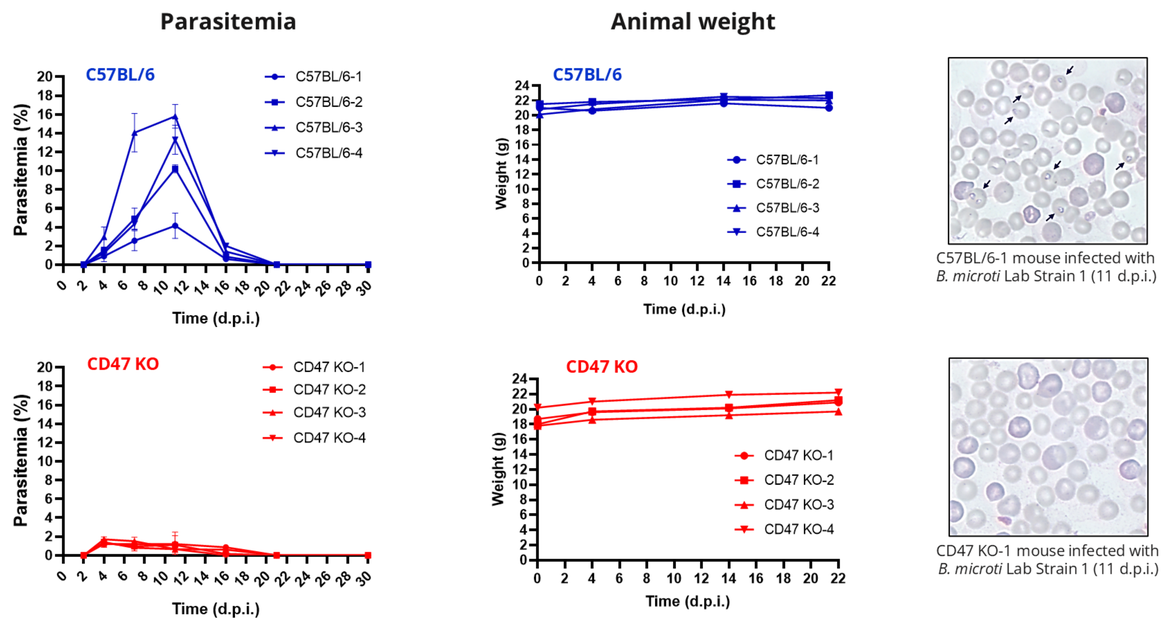
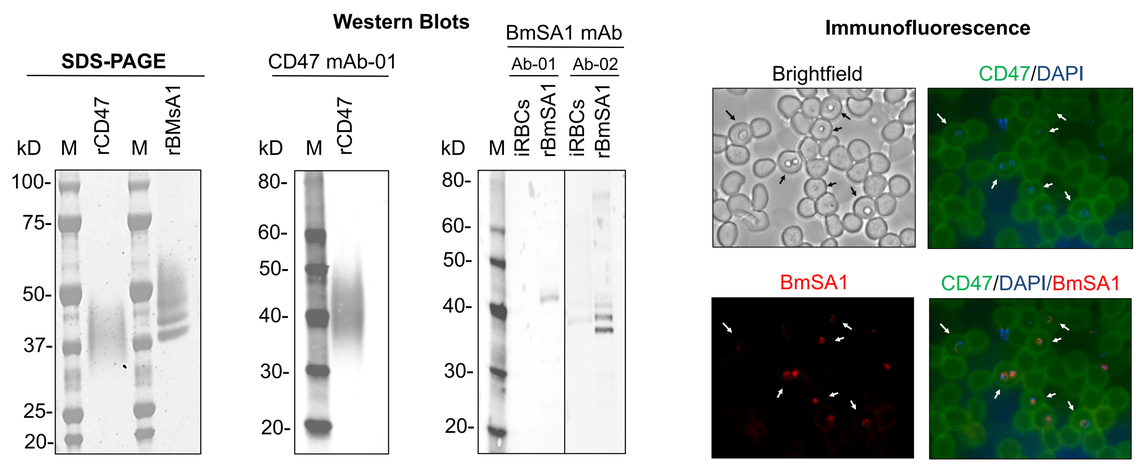


Fig. 6. Characterization of CD47 and BmSA1 mAbs



M: Protein marker

iRBCs: *B. microti*-infected RBCs

SUMMARY

- The present study determined the effect of CD47 loss on *B. microti* growth by comparing parasitemia in wild-type C57BL/6 and CD47 KO mice.
- On average, C57BL/6 mice developed 6% parasitemia by day 7 and reached peak parasitemia of 11% by day 11, with infection self-resolving by day 21.
- In contrast, CD47 KO mice developed markedly low parasitemia that on average did not reach >1.5% throughout infection and resolved by day 16.
- We generated and characterized mAbs to CD47 and the *B. microti* antigen BmSA1 for use in subsequent studies in infected SCID mice.
- Future studies will examine the correlation between CD47 level on RBCs and parasite burden, the capacity of *B. microti* to invade CD47 KO RBCs, and the immunological basis underlying the observed CD47-mediated resistance in babesiosis.

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