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CD2 biased immune response skews the SAG mediated therapy for a predominant Th1 response to treat kidney infection in experimental infection

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Objectives: We have evaluated the effect of combining CD2 with conventional antimonial (sb) therapy in protection in BALB/c mice infected with either drug sensitive or resistant strain of *Leishmania donovani* with 3×10^7 parasites via-intra-cardiac route

Methods: Mice were treated with anti CD2 adjunct SAG sub-cutaneously twice a week for 4 weeks. Assessment for measurement of weight, spleen size, anti-*Leishmania* antibody titer, T cell and anti-leishmanial macrophage function was carried out day 0, 10, 22 and 34 post treatments.

Results: The combination therapy was shown boosting significant proportion of T cells to express CD25 compared to SAG monotherapy. Although, the level of IFN- γ was not statistically different between combination vs monotherapy ($p=0.298$) but CD2 treatment even alone significantly influenced IFN- γ production than either SAG treatment ($p=0.045$) or with CD2 adjunct SAG treatment ($p=0.005$) in Ld-S strain as well as in Ld-R strain. The influence of CD2 adjunct treatment was also documented in anti-leishmanial functions in macrophages. As shown, the super-oxide generation began enhancing very early on day 10 after SAG treatment with CD2 during which SAG action was at minimum. Interestingly, the super-oxide generation ability remained intact in macrophage after treatment with immuno-chemotherapy even in mice infected with *Leishmania* resistant strain. Unlike SAG treatment, treatment of SAG with CD2 also led to production of nitric oxide and TNF- α , resulting in resulting in most effective clearance of *L. donovani* from infected macrophages. Our results indicate that CD2, which can boost up a protective Th1 response, might also be beneficial to enable SAG to induce Macrophages to produce Leishmanicidal molecules and hence control the infection in clinical situation like Kala-azar.

Conclusions: Drug resistance is the major impedance for disease control but the encouraging results obtained after infecting mice with resistant strain of the parasite strongly imply that this drug can be effective even in treating resistant cases