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# The Role of Igf-1 In Murine Macrophages against Mycobacterium Tuberculosis

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**Background:**

The ability of macrophages to modulate their phenotype in response to environmental signals from local tissues make them a crucial mediator of immune response, *Mtb* has several ways of subverting host immune responses; understanding the mechanisms and the genes involved is required for the development of novel strategies to combat the disease. Insulin-like growth factor 1(IGF-1) is one of the genes identified to be upregulated during alternative activation of macrophages in deepCAGE transcriptomics atlas on murine macrophages. IGF-1 in macrophages is downregulated upon infection with *Mtb* clinical and H37Rv strains. Lentivirus-mediated knockdown of IL-4 regulated IGF1 results in decrease in bacterial burden in bone marrow derived macrophages, and decrease pro-inflammatory cytokines. Chemical blocking of IGF-1 also led to decrease in bacteria growth, overall these results suggest that IGF-1 may play a role in the control of *Mtb* in vitro.

**Methods:**

Primary macrophages, Bone marrow derived macrophages(BMDMs) were derived from 8-12week old BALB/C male mice, cultured for 10 days at 37°C in M-CSF supplemented medium for macrophage differentiation. BMDMs were harvested and plated overnight in the presence or absence of activators (100U/ml IL-4, IL-13 and IFNy) after 24hours of stimulation, the BMDMswere either left uninfected or infected with live logarithmic phase hyper virulent Mtb HN878 strain or H37Rv strain at a MOI 5:1 (bacilli: macrophage).Cells were transduced with shRNA containing lentivirus against IGF-1 gene for 10days, stimulated with Il-4 to induce expression of IGF-1, after 24hours cells were replenished with medium containing gentamicin.Following 4 hours, 3 days and 6 days infection, macrophages were lysed to determine bacterial growth, CFUs and cytokines were measuredusing ELISA. BMDMs IGF-1 receptor were chemically blocked with tyrophostin and CFUs evaluated.

**Results:**

We validated the Deep CAGE by RTqPCR. We observed an increase expression of IGF-1 expression upon alternative activation with no change in the classicallyactivated BMDMs. Upon infection with both strains there was a down regulated expression of IFG-1. Knockdown of IFG-1 was confirmed with targeted shRNA containing lentivirus against IgF-1 with a corresponding reduction in CFUs at day 3 relative to the vector. IGF-1 chemical blocking resulted in reduction in CFU also. There was also a reduction in pro-inflammatory cytokines in the IGF-1 knockdown and blocked BMDMs.

**Conclusion:**

We have shown that IGF-1 plays a role in the control of *Mtb* growth in primary macrophages. Further investigation on the mechanisms involved would suggest new strategies that can be used to design more effective drugs against Tuberculosis.