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Synergistic ablation of TNF in myeloid and lymphoid T cell subsets is a signature of CNS *M.tuberculosis* infection

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Background: Central nervous system tuberculosis is the most severe form of extra-pulmonary tuberculosis, characterized by the formation of rich foci, a brain form of granulomas and tuberculous meningitis. Granulomas contain mycobacteria by recruitment of immune cells that surround the bacteria. the cytokine tumor necrosis factor (TNF) has been found to be involved in the recruitment of the immune cells and the structure maintenance of granulomas. During central nervous system tuberculosis, excess of TNF has been implicated in persisting hyperinflammation, however deficiency of TNF leads to uncontrolled bacterial growth; both phenomena causing necrotic lysis. The aim of this study was to investigate the contribution of TNF by specific immune cell types in the control of cerebral *Mtb* infection.

Methods & Materials: We investigated the role of TNF derived from microglia/macrophages, neutrophils, $CD4^+$ and $CD8^+$ T cells in host immunity against *Mtb;* using an experimental murine model with cell type-specific gene targeting.

Results: We found that mice deficient for TNF in microglia/macrophages and neutrophils are not susceptible to *Mtb* infection, with a phenotype similar to wild type mice. Surprisingly, mice with ablation of TNF in microglia/macrophages, neutrophils, $CD4^+$ and $CD8^+$ T cells were highly susceptible to cerebral *Mtb* infection with a phenotype similar to that of complete deficient TNF mice, which succumbed by 21 days post-infection.

Conclusion: Our data suggest that microglia/macrophages and neutrophils derived TNF are not required for effective cerebral immune response. These findings also add knowledge in development of immunomodulatory therapy strategies of central nervous system tuberculosis.

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Efficacy of early treatment of acute hepatitis C infection with pegylated interferon

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Background: Treatment of acute hepatitis C (HCV) in HIV-infected patients has been poorly addressed.

Objective: To evaluate the efficacy and tolerability of a 24 week course of pegylated interferon alfa 2a (PeglFNa2a) and ribavirin for the treatment of acute HCV infection in HIV-infected patients.

Methods & Materials: This was a prospective pilot study of 25 consecutive HIV-infected men with acute HCV infection defined by documented HCV seroconversion to anti-HCV positive antibody and positive qualitative HCV RNA measurement. Patients with delectable HCV RNA (>50IU/ml) 12 weeks after diagnosis were offered treatment with PeglFNa2a (ISO jjigAveek) and ribavirin (800 mg/day) for24 weeks. Sustained virolog-ical response was defined by a negative qualitative HCV RNA measurement 24 weeks after the end of treatment.

Results: At baseline, 23 patients were taking HAART, 23 patients had HIV RNA < 200 copies/ml and a median CD4 count of 345 cells/|J. Only one patient, with genotype 3 HCV, had a spontaneous clearance of HCV RNA. Of the remaining 24 patients, four refused anti-HCV therapy, ribavirin was contraindicated in one and 19 initiated anti-HCV therapy. Median time between acute HCV diagnosis and initiation of study treatment was 14 weeks. Of the 14 patients who have achieved the post-treatment follow-up at 24 weeks, 10 had a sustained virological response (71%). Study treatment was well tolerated, with no change in CD4 cell count.

Conclusion: Early treatment of acute HCV infection with PeglFNa2a and ribavirin for 24 weeks yields a high sustained virological response rate in HIV-infected patients.

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