TIFR Centre for Interdisciplinary Sciences
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Internal Seminar

Inhibition of Lymphotoxin-a protects C57BL/6 mice from Experimental Cerebral malaria and neuronal cell death during Plasmodium berghei ANKA infection

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Background: Cerebral malaria pathogenesis is poorly understood and the patients survived from the disease suffer from permanent cognitive impairment. Therefore, the aim of the study was to understand basis of pathogenesis and mechanism of neuronal cell death during ECM.

Methods: C57BL/6 mice was infected with Plasmodium berghei ANKA and the control groups were injected with same amount of PBS intraperitoneally. Severe anemia mice were taken as ECM negative group. In vivo effect of Lymphotoxin-α was studied by injecting 100 ng of recombinant Lymphotoxin-α and injection of serum from ECM mice (SE) to naïve mice. Lymphotoxin-α was inhibited in vivo by intravenous injection of antibody against it and the consequences to brain pathology was studied.

Results: PbA infection caused elevated expression of Lymphotoxin-α in brain and protein levels in serum and brain of ECM mice samples. Treatment of mice with recombinant Lymphotoxin-α, administrating the naïve mice with serum from experimental cerebral malaria mice is lethal and cause neuronal cell death. Lymphotoxin-α inhibition protected the mice from ECM and increased the survival till 30 days p.i. without effecting the parasite life cycle. Inhibition also mitigated the levels of Lymphotoxin-α, decreased ICAM-1, VCAM-1 and CXCR-4, T cell infiltration, pRBCs sequestration, Granzyme-b levels and active caspase-3 and calpain1 associated neuronal cell death in the brain of PbA infected mice.

Conclusion: These findings demonstrate that Lymphotoxin-α plays a central role in ECM pathogenesis and integrates the immune component and hypoxia that culminates in neuronal killing and making chronic pathology into an acute cerebral malaria.

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11:30 AM (Tea/Coffee at 11:15 AM)

Seminar Hall, TCIS