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Poster Session V
Immunology, vaccination and host defences

PROPHYLAXIS WITH POLY(I:C) PROTECTS NEUTROPENIC MICE AGAINST ESCHERICHIA COLI MENINGOENCEPHALITIS

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Objectives: *Escherichia coli* K1 meningitis is associated with a high rate of mortality and long-term sequelae despite antimicrobial therapy, especially in pediatric and immunocompromised patients. Polyinosine–polycytidylic acid [poly(I:C)] is a mimetic of viral RNA that stimulates Toll-like receptor (TLR)3. TLR3 induces immune responses via the TLR/IL-1 receptor (TIR)-domain containing adaptor protein inducing IFN-β (TRIF). *In vitro*, poly(I:C) increased phagocytosis and intracellular killing of *E. coli* K1 by primary cultures of microglial cells. Here, we assessed the protective effect of poly(I:C) pre-treatment in wild-type (wt) and TRIF-deficient ($trif^{lps2}$) mice (n=14-26/group) against *E. coli* K1 meningoencephalitis. **Methods:** Wt mice were rendered neutropenic by daily administration of an anti-Ly-6G monoclonal antibody starting 4 days before infection with a total of 7 injections. Three days prior to intracerebral infection, wt and $TRIF^{-/-}$ mice received an intraperitoneal injection of 200 µg poly(I:C) or vehicle. Kaplan-Meier survival curves were constructed and and compared by log-rank test. In bacteriological studies, mice were sacrificed 30 h after infection. Then, bacterial titers of blood, cerebellum and spleen homogenates were determined. Also, FACs analysis of the right brain hemisphere containing the site of inoculation was performed. Differences between vehicle and poly(I:C)-treated groups were analysed by Mann-Whitney U-test. $P < 0.05$ was considered statistically significant. **Results**: Pre-treatment with 200 µg poly(I:C) significantly improved survival of neutropenic wt mice ($P = 0.001$) and reduced bacterial concentrations in blood, cerebellum and spleen 30 h after infection ($P <= 0.04$). The protective effect of poly(I:C) correlated with an increase of the number of NK cells ($CD45^{+}NK1.1^{+}CD3^{-}$) in the central nervous system (CNS) 30 h after infection. $TRIF^{-/-}$ mice were not protected by prophylaxis with poly(I:C) ($P = 0.70$). **Conclusions:** Pre-conditioning with poly(I:C) strengthened the resistance of neutropenic mice against E. coli K1 meningoencephalitis in a TRIF-dependent manner. Administration of poly(I:C) decreased bacterial burdens in the cerebellum and spleen, reduced the degree of bacteremia and increased the amount of NK cells in the CNS. Systemic administration of poly(I:C) may help to prevent CNS infections in immunocompromised individuals even after direct inoculation of bacteria into the intracranial compartments, which can occur with open head trauma and after surgery, including placement of an external ventricular drain.