Contribution ID: **24** Type: **oral (travel award)**

Whole-body irradiated Balb/c mice can be protected against experimental Francisella tularensis infection by passive transfer of immunity

Thursday, 18 October 2012 13:45 (15 minutes)

Francisella tularensis (F. tularensis) is a highly virulent, intracellular pathogen. An efficient immune response is dependent on T cell-mediated immune responses and IFN-gamma production during first days after F. tularensis LVS (LVS) infection. Nevertheless, there is also an evidence that B cells, as well as antibodies, are necessary for mice to develop a resistance against primary and secondary infection by LVS The understanding of the poorly described role of humoral immunity is more than important for the effort to develop effective prophylactic procedure against the infection with Francisella virulent strains. We utilized gamma-irradiated mice model for studies of the protective role of anti-F. tularensis antibodies in order to partially eliminate cellular responses and also address the responses in immunocompromised host. The gamma-irradiation by doses greater than 3 Gy completely impairs the resistance to infection and causes a disbalance of cytokine production in mice. Mice sublethally irradiated using a 60Co irradiation in the total dose of 4 Gy did not survive an intradermal infection with 10e2 CFU of F. tularensis LVS in comparison to their unirradiated counterparts. However, the passive transfer of immune sera from LVS immunized mice protected sublethally irradiated mice against the challenge with otherwise lethal LVS infection, led to the decrease of the IL-beta, IL-4, IL-6 or TNF-alpha serum levels, increased the level of IFN-gamma and conversely, had a minimal effect on the levels of these cytokines in organ homogenates when compared to the nonimmunized counterparts.
The necessity of cell-mediated immunity and cytokines for the protective effect of antibodies is still a controversial issue. Our results clearly demonstrate a significant effect of passive transfer of immunity performed by the transfer of specific anti-LVS antisera. Furthermore, our data conclude that in spite of changes in cytokine production after sublethal irradiation, specific antibodies are still able to protect the mice against lethal LVS infection. Moreover, the first evidence of combination of successful passive transfer of specific antisera and subsequent active immunization of immunocompromised animals is demonstrated. In summary, we demonstrate that B cell-mediated effector responses together with the induction of T cell-mediated immunity both play an important role and this should be taken into the account in the design of new vaccines.

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Session Classification: Awardees 2

Track Classification: Other