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**Depletion of dendritic cells impairs the innate response to *Francisella tularensis* LVS**S. A. Roberts<sup>1</sup>, K. L. Elkins<sup>1</sup><sup>1</sup>FDA, Center for Biologics Evaluation and Research, Bethesda, United States

**Aims:** Relatively little is known about the *in vivo* role of dendritic cells (DCs) during *Francisella tularensis* infection. Our goal is to determine whether DCs are required for the initial innate immune response to *F. tularensis* and for the subsequent development of an adaptive response.

**Methods:** We have used a transgenic mouse model in which DCs can be transiently depleted. In this model, mice express the simian receptor for diphtheria toxin (DT) under the control of the CD11c promoter. Because CD11c is a cell-surface marker expressed primarily on DCs, administration of DT to these mice results in specific and transient depletion of DCs, allowing infection with the live vaccine strain of *F. tularensis* (LVS) to be studied in their absence. Wild-type (WT) and DC-depleted mice were infected with LVS via the intradermal (i.d.) route and observed for survival, bacterial burden, and antibody responses. Some survivors of this primary infection were assayed for the development of a memory response by a secondary intraperitoneal (i.p.) challenge. Others were sacrificed for use in an *in vitro* co-culture assay in which the ability of splenocytes to control intramacrophage LVS growth is measured.

**Results:** DC-depleted mice are very susceptible to LVS. While the LD<sub>50</sub> of LVS i.d. infection is on the order of 10<sup>5</sup> colony forming units (CFU) for WT mice, DC-depleted mice succumb to i.d. infection with an LVS dose as low as 10<sup>1</sup> CFU. DC-depleted mice infected with 10<sup>2</sup> LVS i.d. have ten-fold greater bacterial burden in the spleen before dying than do WT mice given the same dose. DC-depleted mice typically die from LVS i.d. infection within about five days, indicating a deficiency in the innate immune response. However, those mice that do survive a primary LVS infection while depleted of DCs develop a memory response. These mice survive a secondary LVS i.p. infection dose of 10<sup>4</sup> CFU, which is 1000 LD<sub>50</sub>s for naïve mice. DC-depleted mice that are primed with LVS develop substantial LVS-specific antibodies, as well as memory T-cells that are capable of controlling intramacrophage LVS growth.

**Conclusion:** We have found that dendritic cells are necessary for the innate immune response to i.d. LVS but that their reduction does not lead to an absolute deficiency in the adaptive immune response. This suggests that other cells may compensate for the lack of DCs or that small numbers of DCs are sufficient to prime adaptive responses.