Macrophages and interferon gamma in host defense against disseminated candidiasis
by Qinfang Qian

A thesis submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Microbiology
Montana State University

Abstract:
To evaluate the role of macrophages in experimental disseminated candidiasis, mouse splenic macrophages were eliminated by intravenous delivery of liposome-entrapped dichloromethylene diphosphonate (L-Cl2MDP). Splenic tissue sections immunoperoxidase stained with monoclonal antibodies against marginal zone macrophages, red pulp macrophages and neutrophils showed that 3 days after L-Cl2MDP treatment, macrophages but not neutrophils were depleted, and circulating neutrophils responded normally to an irritated peritoneum and showed normal phagocytic and killing ability to C. albicans. The spleens from L-Cl2MDP-treated mice lost their ability to bind yeasts, which agrees with our previous findings that yeast cells bind specifically to marginal zone macrophages. When macrophage-depleted mice were given intravenously with C. albicans, the clearance of Candida from blood in these mice was slower, their kidneys had higher recoverable CFU, and they did not survive as long as control mice. These results indicate that macrophages play an important role in host resistance to experimental disseminated candidiasis, but the mechanism does not appear to involve thymus derived T-cell functions.

IFN-γ gene knock-out (GKO) mice were used to evaluate the role of interferon gamma (IFN-γ) in host defense against disseminated candidiasis. Genotypes of mice were determined by PCR, and were confirmed by ELISA, which showed no detectable IFN-γ produced by their splenocytes. GKO mice infected intravenously with C. albicans survived as long as wild type (WT) mice did and showed no difference in Candida CPU from different organs as compared to controls. When animals were given Candida intragastrically, there was no fungal dissemination to different organs from GKO or WT mice. Candida CPU recovered from the stomach or intestines of GKO and WT mice did not differ. GKO mice did not show evidence of more tissue damage or fungal invasion in the stomach cardial-atrium fold, where the fungus was located, than WT mice. Finally, the jejunum of both types of mice showed no evidence of fungal invasion. Although, IFN-γ is critical for Candida induced LA antigen expression by peritoneal macrophages, IFN-γ is not essential in host defense against disseminated candidiasis in mice.

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APPROVAL

of a thesis submitted by

Qinfang Qian

This thesis has been read by each member of the thesis committee and has been found to be satisfactory regarding content, English usage, format, citations, bibliographic style, and consistency, and is ready for submission to the College of Graduate Studies.

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Date 4/23/97

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