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Protection from Disseminated Cryptococcus Infection in Mice by Anti-CD40 and IL-2

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Cryptococcus neoformans is a ubiquitous fungus that causes life-threatening infections in 6-8% of AIDS patients. The immunological mechanisms underlying Cryptococcus resistance are poorly understood. In this study, we investigated the effects of an agonist antibody to CD40, anti-CD40, in combination with interleukin 2 (IL-2) in promoting host immunity against disseminated Cryptococcus infections. Previous data have shown that anti-CD40 and IL-2 synergistically promoted anti-tumor responses in advanced metastatic cancer by increasing dendritic cell and CD8 T cell responses. In a murine model, only the combination of anti-CD40 and IL-2 was shown to prolong the survival of mice previously infected with Cryptococcus neoformans. The protection is correlated with decreased yeast burdens in the organs of mice. Increased immune cell populations in the spleens, as well as increases in serum interferon-gamma (IFN-gamma) levels were observed in infected mice treated with anti-CD40 and IL-2. Further experiments with IFN-gamma knockout (GKO) mice demonstrated that untreated GKO mice were more susceptible to Cryptococcus and the protection induced by anti-CD40 and IL-2 treatment was completely abrogated. These studies indicate that anti-CD40 and IL-2 has significant therapeutic potential in augmenting host immunity against disseminated Cryptococcus infections and that IFN-gamma is essential for this protection.