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Candida Vaccine Development and Protective Antibodies:

Proposed Minimum Criteria for Antibody Protection Against Fungal Disease

Yongmoon Han

College of Pharmacy, Dongduk Women's University, Seoul 136-714, Korea

Hyphothesis. The desirable vaccine formulation might result in reproducible and predictable fulfillment of each of the three criteria such as 1) specificity, 2) Ig isotype, and 3) titer. These criteria are unlikely to be met by a whole cell vaccine.

Summary. The third criterion should seem obvious, but the situation with experimental candidiasis may be more complex than merely a consideration of the minimum titer required for protection. In a preliminary study designed to obtain a dose-response curve relating the amount of MAb B6.1, we found that mice given very high amount of the antibody were less resistant against disseminated candidiasis than animals given less antibody.

Methods. In this experiment a single batch of MAb B6.1 was used and MAb B6 was used as a control. Mice were divided into groups and each received the appropriate antibody intraperitoneally (i.p.), and they were challenged four hours later with a lethal dose of *C. albicans* intravenously. Twenty-four hours later, they received an additional dose of the appropriate antibody i.p. Some groups of animals were sacrificed 44 h after infection and disease severity was measured by colony forming units (cfu) in kidney tissue, while other groups were observed for calculation of mean survival times (MST). The amounts of antibody were standardized as a function of agglutination activity and amounts given corresponded to agglutinin titers of 20, 80 and 320.

Results. The resultant cfu and MST were unaffected by MAb B6 at all concentration of antibody tested. This result was, of course, expected and was consistent with the lack of effect of MAb B6 as we previously reported. Mice that received MAb B6.1, however, produced few cfu's in kindney tissue and their MST were increased. Although MAb B6.1 caused enhanced resistance at all concentrations of antibody tested, those that received the highest amounts of antibody showed less protection than animals that received less antibody.

These results were instructive in that they showed that cfu measurements do not strictly correlate with MST and more antibody is not necessarily better for the animal.

Discussion. We have recently reported strong evidence that the mechanism of protection by MAb B6.1 is related to rapid complement activation on the surface of the fungal cell. These findings may offer an explanation for the above apparent conundrum. Kozel's group has studied the kinetics of C3 activation on the surface of *C. albicans* as a function of amount of MAb B6.1. At very high concentrations of antibody, the total amount of C3 deposited is less than at lower antibody concentrations. Presumably the decrease in C3 activation at very high concentrations of antibody is due to steric hindrance of complement binding by the high concentration of MAb B6.1 on the yeast cell surface. Nonetheless, we believe that the interesting finding will have minimal importance in a vaccine for human use.