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Abstract (poster session)

Efficacy of Candida albicans di- and tri-saccharide vaccine conjugates in an animal model and observation of complement binding to reduce bioburden

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Objective: This study was undertaken to determine if candidate Candida vaccine compounds would elicit an antibody response in a rabbit model of invasive candidiasis and to determine if opsonised yeasts would bind complement to support clearance of invasive infection in the model. Methods: Neutropenia was induced in New Zealand White rabbits with cyclophosphamide and triamcinolone. Candida beta-mannan antigens, conjugated with tetanus toxoid were administered twice (tri-saccharide) or four times (di-saccharide) prior to infection. C. albicans ATCC3153A (10^4CFU/ml) was inoculated intravenously. A control group immunized with tetanus toxoid was included. The animals were followed for 7 – 10 days and then were euthanized. Necropsy tissues were collected for colony counts from liver, spleen, kidney and lung. Complement fixation was performed by incubating diluted tri-saccharide rabbit serum from immunized animals with the appropriate yeast culture. Complement (1:100 dilution) was added; then polyclonal goat anti-complement C3 was added. Fixation was detected with rhodamine-labeled anti-goat antibody. Appropriate controls were included. Results: Control animals showed an increase in colony counts for all sites cultured from 10^6 to 10^9 CFU /g of tissue. The highest counts were in kidney. For the tri-saccharide vaccine, colony counts were reduced from control animals by approx. one-half log in lung and kidney, but were increased in liver and spleen. For the di-saccharide vaccine, colony counts were reduced by approx. 2 logs in liver and spleen, and by one-half to one log in kidney and lung compared to controls. No infection in brain was noted. Further, antibody opsonized C. albicans cells also induced the deposition of complement C3 component. This is consistent with the findings of others for protective monoclonal antibody C3.1 Conclusions: The efficacy of these synthetic Candida conjugate vaccines was observed to reduce the bioburden of invasive Candida in the neutropenic animal model. The model suggests that there are a few differences in efficacy between these di- and tri-saccharide vaccines. In these experiments, di-saccharide No. 2 reduced the expansion of organism loads by 2 logs in liver and spleen. Candida is often found in these two organs in serious infections in susceptible hosts. The observation of complement fixation by opsonised Candida albicans cells provides further evidence to support the protective effect of these vaccine candidates.