eP137
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Vaccine development

TH CYTOKINE PATTERN INDUCED BY SYNTHETIC MANNO-AND GLUCOOLIGOSACCHARIDE CONJUGATES

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Objectives: Candidiasis are infections caused by a dimorphic fungus *Candida spp*. (*C. albicans, C. glabrata* etc.). It can infect e.g. the bucal and vaginal mucosa, skin, gastrointestinal, respiratory, and urinary tract. About 75 % of women will get a vaginal *Candida spp*. infection during their fertile lifetime. The other groups at risk are immunocompromised patients and those with predisposition (e.g. bone marrow transplantation, malignancies, long-term treatment with antibiotics, chemotherapeutics, glucocorticoids or other immunosuppressive agents). The aim of this study was to evaluate the immunobiological efficacy of synthetically prepared mannan- and glucan-derived oligosaccharidic BSA-conjugates.

Methods: Balb/c mice were immunized (10 mice per group, prime, 1st, 2nd intraperitoneal (i.p) and / or subcutaneous (s.c) boost, 7 weeks (wks) after 2nd boost, 3- wks boost´s intervals) by immunization formulas: mannan and glucan-derived synthetic oligosaccharidic i.e heptamannoside (M7) and nonaglucoside (G9) BSA conjugates and *Candida albicans* CCY 29-3-32 whole cell formula (WC).

Cytokines: mouse IL-4, mouse IL-10, mouse IL-17, mouse IFN-g, mouse TNF-a, mouse IL-1a, mouse IL-1b, mouse IL-6 were detected by the ELISpot method (e-Bioscience). Quantitative evaluation of spots were visualised and quantified by Axio Imager.A1, KS ELISPOT 4.10 (C. Zeiss).

Results: Prime- boost vaccination of Balb/c mice with synthetic-BSA conjugated heptamannoside and nonaglucoside revealed pro-T_H1 over T_H2 immune responses based on increasing frequency of IFN-g and decreasing frequency of IL-4 producing splenocytes throughout the i.p and/or s.c immunisation routes. Acceleration of T_H17 and depression of T_r responses were generated predominantly by immunisation with nonaglucoside conjugate. Immunomodulation of specific T_H1, T_H2, T_H17 and T_r cytokine release by both conjugated oligosaccharides throughout the vaccination demonstrated on activated mice splenocytes, allows to detect immunobiological diversity of such oligosaccharidic constructs suitable for *Candida* vaccine.

Conclusion: The novel synthetized glycooligosacccharidic conjugates, which mimicking the structure of native *Candida* mannooligosaccharide and glucooligosaccharide epitopes demonstrate immunobiological efficacy *in vivo*. These model structures offer oppportunity to follow up the relationships between structure and immunobiological effectivity.