The evaluation of synthetically prepared β-(1→3)-nonaglucoside as an anti-Candida immune response modifier

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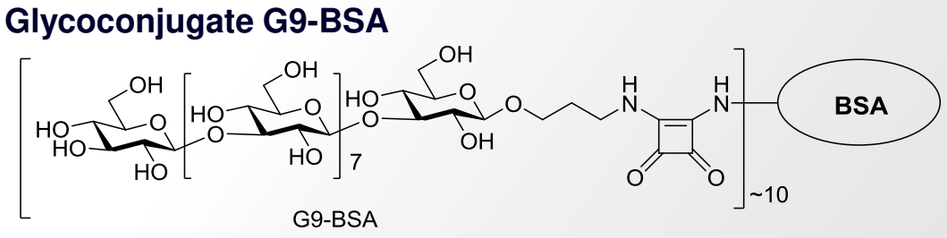
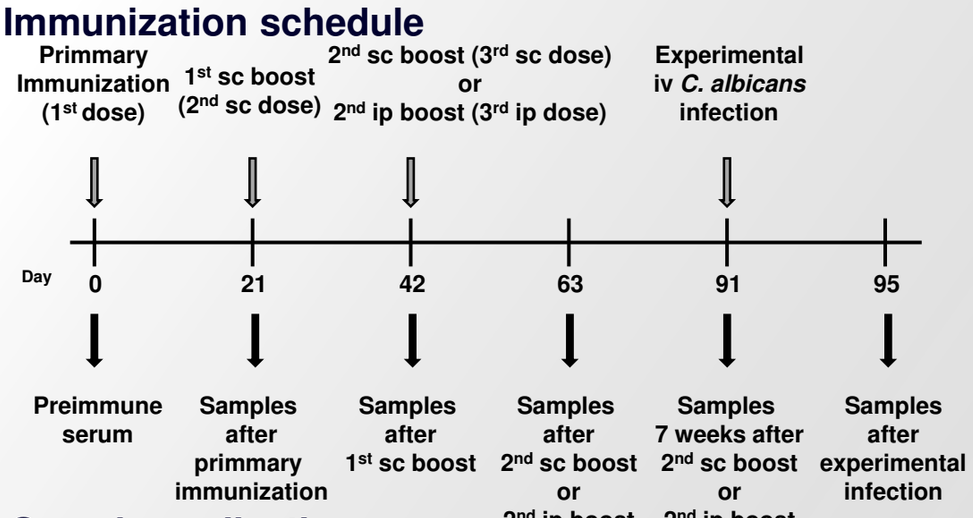
Candida albicans forms part of the commensal microbial flora of mucosal surfaces and alimentary tract in humans. This fungus is able to cause severe mucosal and life - threatening systemic infections in immunocompromised patients. *C. albicans* cell wall represents the important host-pathogen interface. Immunologically most active cell wall polysaccharides, β-D-glucans and mannans, represent pathogen-associated molecular patterns. We analysed immunomodulatory properties of synthetically prepared linear β-(1→3)-nonaglucoside ligand (G9) bovine serum albumin (BSA) conjugate (G9-BSA).

Glycoconjugate G9-BSA



G9-BSA

Immunization schedule



Samples collection

Preimmune sera | Control | 1st | 2nd | 3rd sc | 3rd sc 7w | 3rd ip | 3rd ip 7w | 3rd sc inf | 3rd ip inf | Control inf.

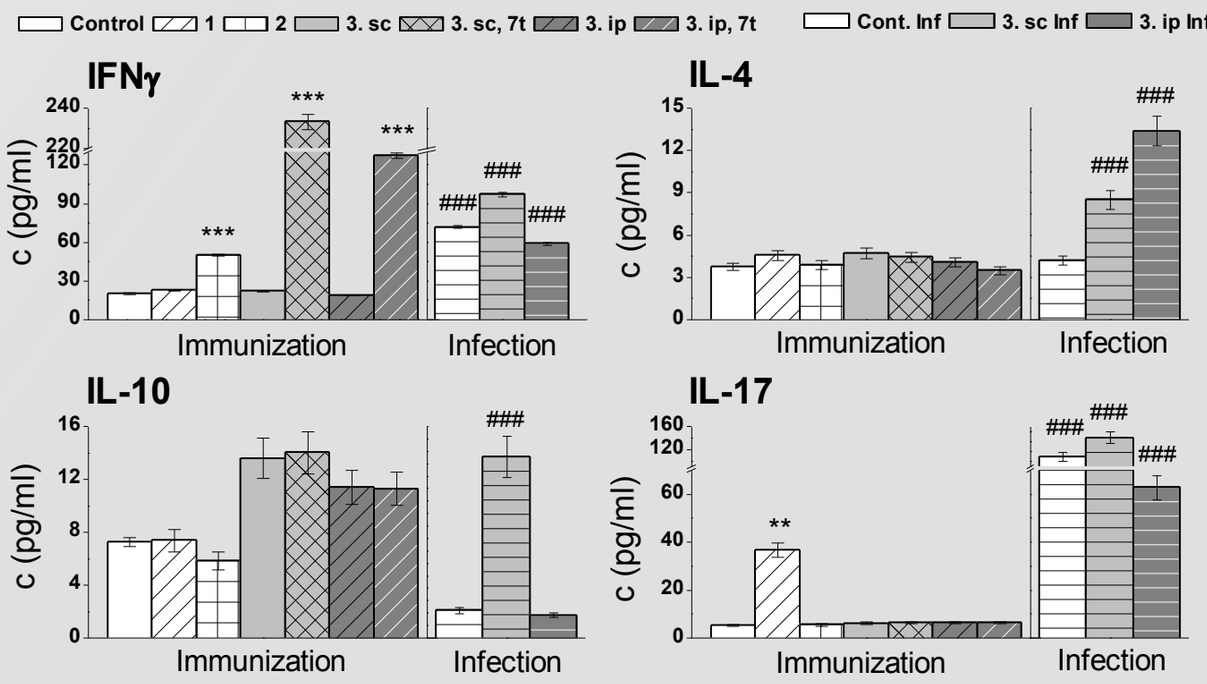
Methods

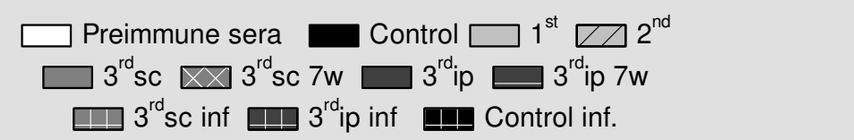
Balb/c mice (6 – 8 weeks old) were used for sequential immunizations with synthetically prepared G9–BSA conjugate (100 µl per dose, 6 µg of β-(1→3)-nonaglucoside ligand). ELISA and ELISPOT were used to follow up specific humoral response and Th1/Th2/Th17 polarization. Experimental infection was induced with azole-resistant clinical *C. albicans* strain (CCY 29-3-164, CCY, IC SAS, Slovakia).

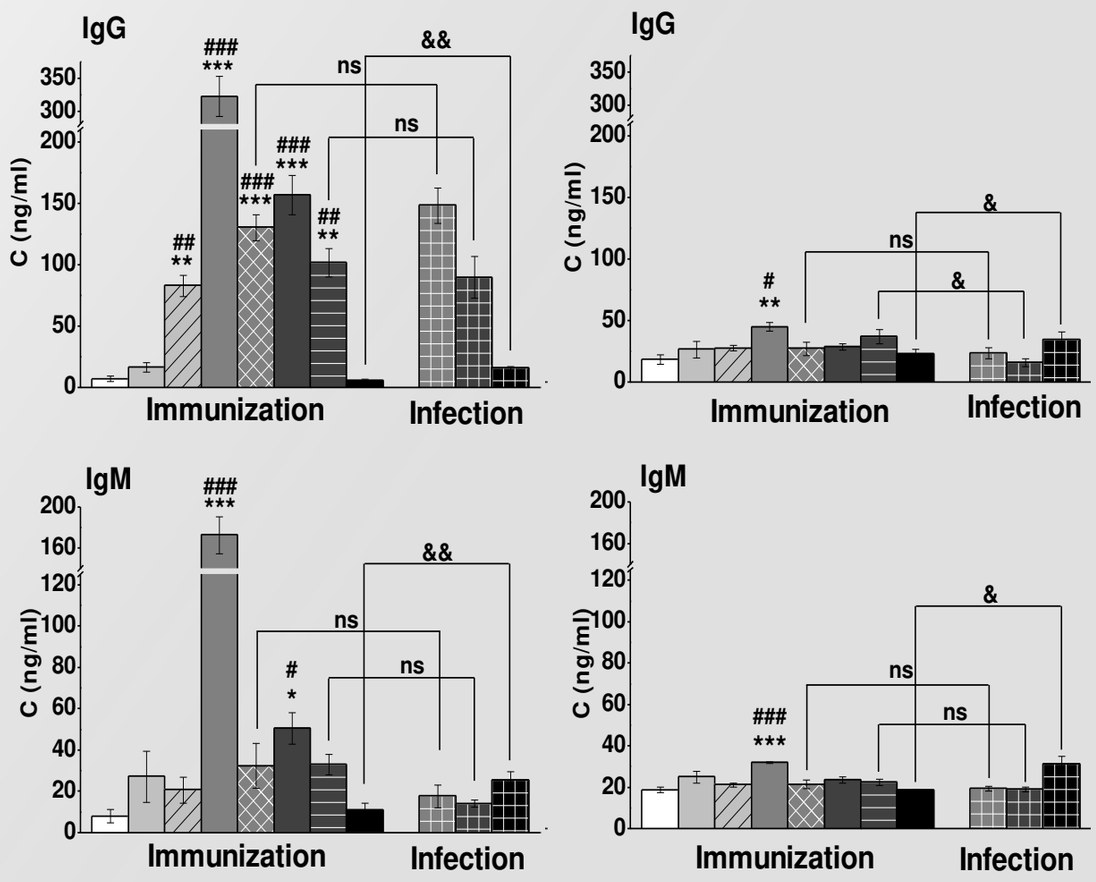
Results

Specific IgG response following 2nd s.c. boost immunisation was dominant (45-times increase vs pre-immune) and persisted post-immunisation. Contrary to the slight increase of *C. albicans* yeast form - specific antibody levels, G9–BSA immunization significantly increased hyphae - specific IgG levels. IFNµ (Th1 cytokine) production overcame IL-4 (Th2 cytokine). In G9-BSA immunized mice *C. albicans* organs dissemination was reduced compared to the control and experimental infection reveals differences based on the route of vaccine administration.

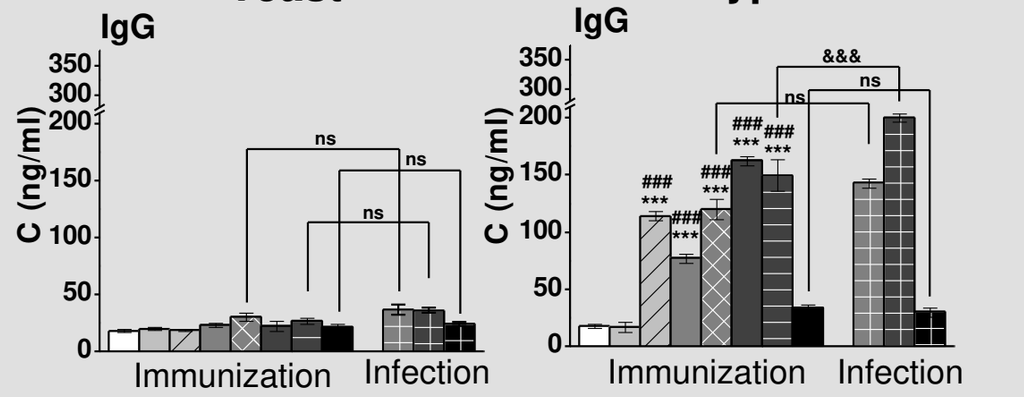
Levels of cytokines induced by immunization and subsequent *C. albicans* infection







Linear G9 and β-D-glucan-specific antibody levels.



C. albicans serotype A yeast- and hyphae-specific antibody responses.

Fungal burden in kidney, spleen, liver and lymph nodes tissues after intravenous *C. albicans* infection in G9-BSA immunized mice

	Control	Infection 7w post 2nd sc boost		Infection 7w post 2nd ip boost	
Organ	Log CFU.g^{-1}	Log CFU.g^{-1}	% Reduction	Log CFU.g^{-1}	% Reduction
Kidney	6.82 ± 0.02	6.37 ± 0.02	65.0 ± 0.5	5.95 ± 0.11	86.3 ± 3.1
Spleen	6.73 ± 0.02	6.32 ± 0.05	61.6 ± 2.7	5.96 ± 0.06	83.1 ± 1.4
Liver	6.71 ± 0.02	6.02 ± 0.02	79.5 ± 0.2	5.98 ± 0.03	81.2 ± 0.3
Lymph nodes	6.62 ± 0.04	6.18 ± 0.03	64.0 ± 0.2	5.98 ± 0.08	77.1 ± 2.3

The data are expressed as the mean Log of colony forming units per gram of tissue (LogCFU.g^{-1}) ± SD

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