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MUC1 glycopeptide based anti-cancer vaccines

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MUC1 variable number tandem repeats (VNTRs) conjugated to tumor-associated carbohydrate antigens (TACAs) have been shown to break self-tolerance in humanized MUC1 transgenic mice. Therefore, we hypothesized that a MUC1 VNTR TACA-conjugate can be successfully formulated into a liposome-based anti-cancer vaccine. The immunogenicity of the vaccine should be further augmented by incorporating surface displayed L-rhamnose (Rha) epitopes onto the liposomes to take advantage of a natural antibody-dependent antigen uptake mechanism. To validate our hypothesis we synthesized a 20-amino acid MUC1 glycopeptide containing a GalNAc-O-Thr (Tn) TACA by SPPS and conjugated it to a functionalized Toll-like receptor ligand (TLRL). An L-Rha-cholesterol conjugate was prepared using Tetra Ethylene Glycol (TEG) as a linker. The liposome-based anti-cancer vaccine was formulated by the extrusion method using TLRL-MUC1-Tn conjugate; Rha-TEG-cholesterol and 1, 2-dipalmitoyl-sn-glycero-3-phosphocholine (DPPC) in a total lipid concentration of 30 mM. Groups of female BALB/c mice were immunized and boosted with a rhamnose-Ficoll (Rha-Ficoll) conjugate formulated with alum as adjuvant to generate the appropriate concentration of anti-Rha antibodies in the mice. The mice were then immunized with the TLRL-MUC1-Tn liposomal vaccine formulated either with or without the surface displaying Rha epitopes. Sera collected from the groups of mice initially immunized with Rha-Ficoll and later vaccinated with the Rha-displaying TLRL-MUC1-Tn liposomes showed a >8-fold increase in both anti-MUC1-Tn and anti-Tn antibody titers in comparison to the groups of mice that did not receive Rha-Ficoll. The anti-MUC1-Tn antibodies in the vaccinated mice serum also recognized MUC1 on human leukemia U266 cells.

Biography

Sourav Sarkar has completed his PhD from University of Toledo and Postdoctoral studies from Complex Carbohydrate Research Center, University of Georgia. Presently he is working as a Research Scientist III in the Department of Chemistry at Lehigh University. He has published numerous papers in reputed journals and is an inventor of the patent "Xeno-antigenic anti-tumor vaccines". He is a member of the American Chemical Society and has served as a peer reviewer for *Elsevier, Royal Society of Chemistry, Springer* and many more journals.

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Page 44