Recognition of Dimeric Lewis X by Anti-Dimeric Le^x Antibody SH2

Publons ID	(not set)
Wos ID	WOS:000581728700001
Doi	10.3390/vaccines8030538
Title	Recognition of Dimeric Lewis X by Anti-Dimeric Le^x Antibody SH2
First Author	
Last Author	
Authors	Jegatheeswaran, S; Asnani, A; Forman, A; Hendel, JL; Moore, CJ; Nejatie, A; Wang, A; Wang, JW; Auzanneau, FI;
Publish Date	SEP 2020
Journal Name	VACCINES
Citation	4
Abstract	The carbohydrate antigen dimeric Lewis X (DimLe(x)), which accumulates in colonic and liver adenocarcinomas, is a valuable target to develop anti-cancer therapeutics. Using the native DimLe(x) antigen as a vaccine would elicit an autoimmune response against the Le(x) antigen found on normal, healthy cells. Thus, we aim to study the immunogenic potential of DimLe(x) and search internal epitopes displayed by DimLe(x) that remain to be recognized by anti-DimLe(x) monoclonal antibodies (mAbs) but no longer possess epitopes recognized by anti-Le(x) mAbs. In this context, we attempted to map the epitope recognized by anti-DimLe(x) mAb SH2 by titrations and competitive inhibition experiments using oligosaccharide fragments of DimLe(x) as well as Le(x) analogues. We compare our results with that reported for anti-Le(x) mAb SH1 and anti-polymeric Le(x) mAbs 1G5F6 and 291-2G3-A. While SH1 recognizes an epitope localized to the non-reducing end Le(x) trisaccharide, SH2, 1G5F6, and 291-2G3-A have greater affinity for DimLe(x) conjugates than for Le(x) conjugates. We show, however, that the Le(x) trisaccharide is still an important recognition element for SH2, which (like 1G5F6 and 291-2G3-A) makes contacts with all three sugar units of Le(x). In contrast to mAb SH1, anti-polymeric Le(x) mAbs make contact with the GlcNAc acetamido group, suggesting that epitopes extend further from the non-reducing end Le(x). Results with SH2 show that this epitope is only recognized when DimLe(x) is presented by glycoconjugates. We have reported that DimLe(x) adopts two conformations around the beta-d-GlcNAc-(1 -> 3)-d-Gal bond connecting the Le(x) trisaccharides. We propose that only one of these conformations is recognized by SH2 and that this conformation is favored when the hexasaccharide is presented as part of a glycoconjugate such as DimLe(x)-bovine serum albumin (DimLe(x)-BSA). Proper presentation of the oligosaccharide candidate via conjugation to a protein or lipid is essential for the design of an anti-cancer vaccine or immunotherapeutic based on DimLe(x).
Publish Type	Journal
Publish Year	2020
Page Begin	(not set)
Page End	(not set)
Issn	
Eissn	2076-393X
Url	https://www.webofscience.com/wos/woscc/full-record/WOS:000581728700001
Author	ARI ASNANI, S.Si, M.Sc., Ph.D