A181 CRITICAL ROLE OF PROTEIN GLYCOSYLATION IN T CELL IMMUNITY/AUTOIMMUNITY

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10.1136/ard.2010.129668r

Background Glycosylation is the most frequent post-translational protein modification and N-glycosylation is the most abundant form of glycosylation in humans. Many of the known autoantigens, including those found in hyaline cartilage, are heavily glycosylated. There is a relative backlog in the understanding of glycoimmunology (compared with anti-protein immunology) which might be explained, at least partially, by the substantial technical difficulties of carbohydrate synthesis and sequencing. Until glycopeptides are available on a large scale for cellular immunology studies, our present combined in silico approach may enable us to gain the first biological system insight into the largely unknown role of antigen glycosylation in T cell immunity and autoimmunity. The present analysis was made possible by currently available

databases (representing full proteomes, known human T cell epitopes and autoantigens) as well as glycosylation prediction tools. Although there are several experimental data related to T cell autoepitope recognition, surprisingly few biology systems approaches have investigated the structural features of human T cell epitopes/autoepitopes.

Results First the authors analysed the probable glycosylation of human T cell epitope sequences extracted from the ImmuneEpitope database. Our analysis suggests that, in contrast to full length SwissProt entries, only a minimal portion of experimentally verified T cell epitopes is potentially N- or O-glycosylated (2.26% and 1.22%, respectively). Bayesian analysis of entries extracted from the Autoantigen database suggests a correlation between N- but not O-glycosylation and autoantigenicity. Autoantigens were found to contain significantly more N-glycosylation sites ($+1.74 \pm 0.32$) than normal proteins ($+0.91 \pm 0.04$). According to our data, most HLA DP and DQ alleles tolerate N-glycosylation much less than HLA DR, with the exception of DQA1*0501 – DQB1*0301. The analysis of random generated sequences shows that glycosylation probability is also affected by peptide length. Our data suggest that the lack of peptide glycosylation, a feature that probably favours effective recognition by T cells, might have resulted in a selective advantage for short peptides to become T cell epitopes. The length of T cell epitopes is at the intersection of curves determining specificity and glycosylation probability. Thus, the range of length of naturally occurring T cell epitopes may ensure the maximum specificity with the minimal glycosylation probability.

Conclusions The findings of this bioinformatical approach shed light on fundamental factors that might have shaped adaptive immunity during evolution. Our data suggest that amino acid sequence-based hypo/non-glycosylation of certain segments of proteins might be significant for determining T cell immunity/autoimmunity.