A106 TARGETING SIGLEC-E ON MURINE DENDRITIC CELLS INHIBITS ANTIGEN PRESENTATION AND CD4 AND CD8 T CELL RESPONSES

M Bax, W Unger, S Kaur Singh, E J McKenzie, M Litjens, J J Garcia-Vallejo, E Saeland, S J van Vliet, P R Crocker, Y van Kooyk *Department of Molecular Cell Biology and Immunology, VUMC, Amsterdam, The Netherlands*

10.1136/ard.2010.129627s

Dendritic cells (DCs) are the most potent antigen presenting cells of the immune system. They are important regulators of immune responses by their capacity to induce tolerance or immunity, depending on the type of antigen they encounter with their cell surface receptors. An important group of cell surface receptors expressed by DCs are lectins which specifically recognise carbohydrate structures. Siglecs are sialic acid-recognising lectins expressed on the cell surface of immune cells that regulate cellular adhesion, antigen uptake and signalling. Siglec-E is predominantly expressed on DCs and bears a tyrosine-based inhibitory signalling motif, which makes it an interesting targeting candidate to prevent undesirable immune responses. However, there is little information available on the precise role of Siglec-E in antigen uptake and antigen presentation to T cells.

The authors studied the effect of targeting DC-expressed Siglec-E for antigen presenting capacity with its natural ligand α 2,8-linked disialic acid. α 2,8-linked disialic acid is an unusual glycan structure which, under steady state conditions, is expressed on gangliosides in the brain. The authors found that Siglec-E expressed on murine BM-DCs strongly binds to α 2,8-linked disialic acids. They established that α 2,8-linked disialylated OVA is rapidly and specifically taken up by BM-DC-expressed Siglec-E and transported to early endosomes and lysosomes, unlike unmodified OVA. Intriguingly, although α 2,8-linked disialylated OVA was rapidly internalised in BM-DCs compared with unmodified OVA, antigen presentation was diminished, leading to inhibited OVA-specific CD4 T cell and CD8 T cell proliferation. Together, these data show that Siglec-E is a promising target on DCs to dampen unwanted CD4 T cell and CD8 T cell responses which occur in autoimmune diseases.