

## **Research group Yvette van Kooyk**

### **Understanding cellular encounters of DCs**

C-type lectins are cell membrane receptors on dendritic cells that contribute in the recognition of glycosylated ligands expressed on immune cells that mediate DC-cellular interactions. We have explored the biology of various DC-specific C-type lectins, such as DC-SIGN and MGL, that interact with endogenous ligands. DC-SIGN binding to ICAM-2 and ICAM-3 has shown to mediate DC mediated endothelial migration and T cell interactions. Also DC-SIGN mediated binding to Neutrophils has been demonstrated to potentiate innate immune responses. C-type lectins such as MGL have reported regulatory cellular interactions with effector T cells through CD45. Our interest is focused on understanding how DC expressed C-type lectins regulate their cellular encounters through modified glycosylation. We furthermore explore how the glycosylation of DC during their differentiation and maturation process can modify cellular adhesion and migratory capacity during homeostatic control and inflammatory responses.

### **C-type lectin recognition of glycosylated antigens homeostatic control versus immune activation**

Glycan binding receptors such as the C-type lectins MGL and DC-SIGN have shown to regulate recognition of a large variety of pathogens (viruses, bacteria, parasites and fungi) that modify DC responses on the basis of the presence of a specific glycan structure. Also in specific tissue micro-environments secreted self antigens from tumor cells such as MUC1 and CEA have shown to bind to DC specific C-type lectin receptors. Glycan modification of the metastatic behavior of tumor cells correlates with C-type lectin binding. Also in fluids like human milk, various glycosylated antigens have shown to interact with C-type lectins, and potentially may contribute to homeostatic control.

Current studies are focused on unraveling whether these alterations in glycosylation have consequence for the DC function and its immune potential to modify immune responses, or to inhibit pathogen interactions.

### **DC-antigen recognition and presentation “from basics to application”**

Dendritic cells are professional antigen presenting cells, that capture antigen in the periphery and take up antigen and migrate to the draining lymph node to present antigen to T cells to induce a T cell mediated immune response. Targeting antigen to C-type lectins have been shown to improve antigen presentation to induce antigen specific CD4 and CD8 T cells. Depending on the receptors involved in antigen capture recognition receptors (C-type lectins and Toll like receptors (TLR)) either immunity or tolerance can be induced. We have demonstrated that modification of antigens by glycans can differentially direct antigens into distinct intracellular compartments. Our aim is to identify the routing of glycosylated antigen to enhance MHC class I and II loading, in vitro and in-vivo.

Furthermore our research is aimed to construct specific glycosylated antigen formulation that will induce potent anti-tumor CD8 and CD4 T cell responses. On the other hand we will evaluate strategies that use specific glycans structures to inhibit auto-immune diseases such as Multiple Sclerosis.

Our aim is to develop in-vivo vaccination strategies to improve anti-tumor responses and auto-immune diseases, using glycans to target DC in-vivo and use them as enhancers or inhibitors for antigen presentation.

## Highlights

VENI grant accepted in 2008 by Juan Garcia Vallejo “Glycosylation controls immune homeostasis”

### Reviews of interest:

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