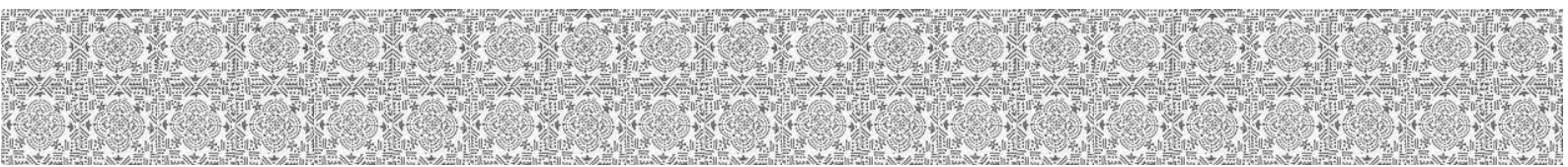


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**Book of Abstracts**





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ICS 2018

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## MUC1 GLYCOPEPTIDES RECOGNITION PROFILING BY MACROPHAGE GALACTOSE LECTIN TO TARGET DENDRITIC CELLS

Fayna Garcia-Martin,<sup>[a],\*</sup> Gerard Artigas,<sup>[a]</sup> João T. Monteiro,<sup>[b]</sup> Bernd Lepenies,<sup>[b]</sup>  
Hiroshi Hinou,<sup>[a]</sup> and Shin-Ichiro Nishimura<sup>[a]</sup>

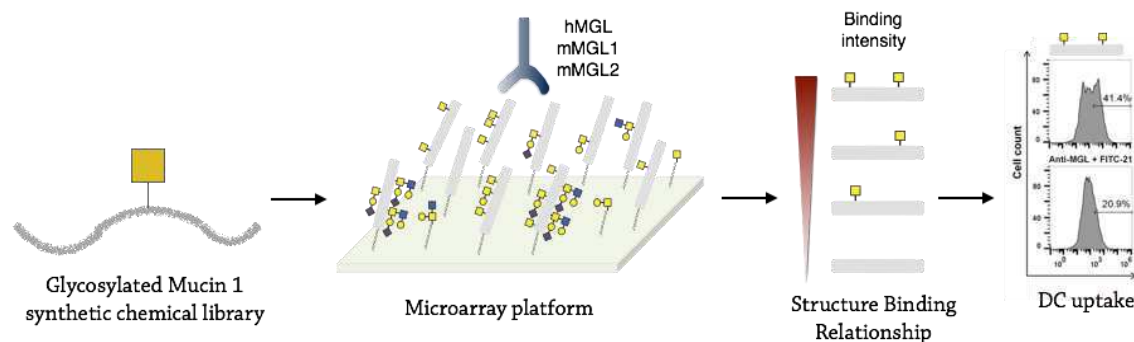
- [a] Faculty of Advanced Life Science and Graduate School of Life Science, Hokkaido University, N21, W11, Kita-ku, 001-0021 Sapporo, Japan, faynagm@sci.hokudai.ac.jp  
[b] Immunology Unit & Research Center for Emerging Infections and Zoonoses (RIZ), University of Veterinary Medicine Hannover, Bünteweg 17, 30559 Hannover, Germany

Lectin–carbohydrate interactions have essential roles on the modulation of the immune system. In literature, many examples focused on how single carbohydrate moieties bind to the immune system receptors. However, in the surface of cells many glycans are linked to proteins. In here, we hypothesize the contribution of both glycan and protein backbone on the binding to lectins. In this regard, here we confined our attention on macrophage galactose lectin (MGL), present on dendritic cells (DCs) and macrophages, and it can bind to galactose (Gal) and *N*-acetylgalactosamine (GalNAc). As potential ligand, we chose mucin 1 (MUC1) glycoprotein as it expresses altered truncated glycans as terminal Gal and GalNAc during malignant processes. These structural differences have placed MUC1 as a prioritized objective of study to create an efficient cancer vaccine.

In the present study, we employ a MUC1-based glycopeptide microarray to characterize the specificities of three MGL (Clec10a) orthologs: human MGL (hMGL), murine MGL1 (mMGL1) and MGL2 (mMGL2). This research work covers (i) synthetic chemical library of 35 compounds, (ii) evanescent-field fluorescence microarrays as a high-throughput screening approach to detect lectin ligands with high reproducibility<sup>1</sup> and (iii) internalization assays on DCs.

As result, by using our microarray platform we were able to monitor, under equilibrium conditions, the similar recognition profile of hMGL and mMGL2 with natural mimetic MUC1 glycoforms. Herein, we have shown the so far unprecedented role of mucin-based peptides on the recognition by lectins of GalNAc moieties expressed in tumour-altered mucins. On this account, we have demonstrated the relevance of the sugar site in the MUC1-mMGL1 binding. In addition, for three orthologs, we have also proved a positive direct correlation the bivalency effect and the binding affinity. To assess the utility of the glycopeptide binders of the MGL orthologs for MGL targeting, we performed uptake assays with fluorescein-MUC1 using murine DCs. The diglycosylated MUC1 peptide was highly internalized in an MGL-dependent fashion, thus showing the utility for bivalent GalNAc to target MGL.<sup>2</sup>

In conclusion, the MGL-dependent uptake of MUC1-derived glycopeptides into murine DCs highlights the potential of MGL-based DC targeting which may be used to design novel anticancer vaccines with an enhanced effectiveness.



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