Magnetic Resonance Assays for the Identification of Novel Lectin Inhibitors to Combat Antimicrobial Resistance

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Antimicrobial resistance is an emerging threat and requires the urgent identification of novel high affinity molecules as potential drugs. Within this project, the proteins of interest are key virulence factors of bacterial cell invasion, which is mediated by bacterial lectins that bind to glycans on host cells. To propose novel inhibitors for these lectins, based on modified glycans, we develop innovative NMR and MRI assays that simplify affinity determination and structure elucidation. So far, we successfully employed fluorinated glycans as reporters for the establishment of ^{19}F-based NMR assays for different target proteins to (i) determine the K_D of ligands (Cholera Toxin from *Vibrio Cholerae*), and to (ii) identify functional groups of the glycan that are essential for binding (LecB of *Pseudomonas aeruginosa*). In pursuit for a high affinity compound, we performed small molecule fragment screenings to explore second binding sites of the bacterial proteins, in which we validated the hits with competition assays. This information, together with the structural NMR-analysis of ^{13}C-^{15}N-isotopically labelled lectins in solution, provides a powerful combination for drug discovery.

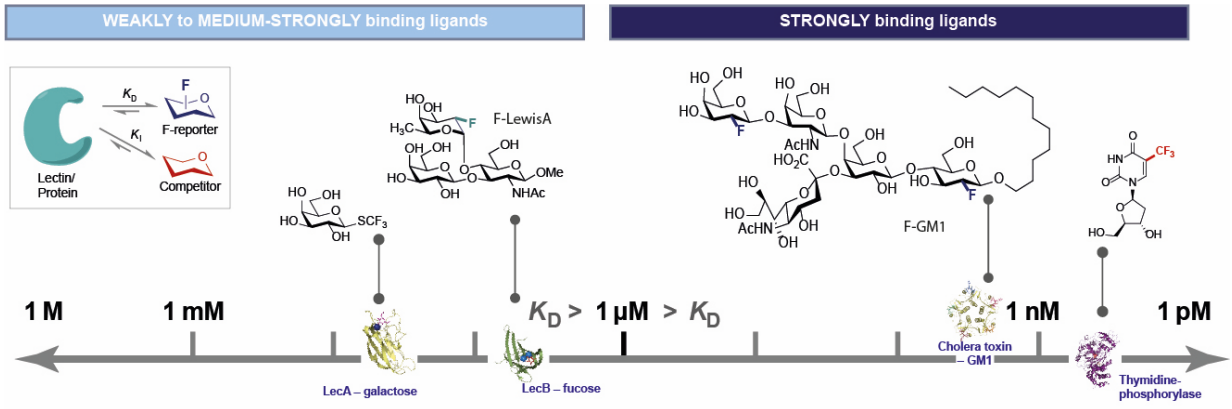

Figure 1. Overview of K_D ranges for NMR assay development.

The poster presented will include the chemical syntheses of the fluorinated carbohydrate ligands, NMR assay development and SAR studies of the carbohydrate and small molecule ligands.

[1] C. Jordan§, T. Hayashi§, A. Löbbert, J. Fan, C. S. Teschers, K. Siebold, M. Aufiero, F. Pape, E. Campbell, A. Axer, K. Bussmann, K. Bergander, J. Köhnke, A. D. Gossert, R. Gilmour *ACS Central Science*, **2024**, 10 (8), 1481-1489.

[2] K. Siebold, E. Chikunova, N. Lorz, C. Jordan, A. D. Gossert and R. Gilmour*, Angew. Chem. Int. Ed.* **2025**, e202423782.

[3] C. Jordan, M. Piotto, S. Loss, C. Dalvit & A. D. Gossert, *J. Anal. Chem., Manuscript submitted.*

[4] J. Suri, C. Jordan, C. S. Teschers, S. H. Rüdisser, A. D. Gossert, R. Gilmour, *Angew. Chem. Int. Ed., Manuscript submitted.*

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