

HIGH-AFFINITY LECTIN LIGANDS ENABLE THE DETECTION OF PATHOGENIC *PSEUDOMONAS AERUGINOSA* BIOFILMS: IMPLICATIONS FOR DIAGNOSTICS AND THERAPY

Alexander Titz^{a-c}, Eva Zahorska^{a-c}, Lisa Marie Denig^{a-c}, Stefan Lienenklaus^d, Sakonwan Kuhaudomlarp^{e,f,g}, Thomas Tschernig^h, Peter Lippⁱ, Antje Munder^{j,k}, Emilie Gillon^e, Saverio Minervini^a, Varvara Verkhova^{a-c}, Anne Imberty^e, Stefanie Wagner^{a-c}

^a Chemical Biology of Carbohydrates (CBCH), Helmholtz Institute for Pharmaceutical Research Saarland (HIPS), Helmholtz Centre for Infection Research, 66123 Saarbrücken, Germany

^b Deutsches Zentrum für Infektionsforschung (DZIF), Standort Hannover-Braunschweig

^c Department of Chemistry, Saarland University, 66123 Saarbrücken, Germany
alexander.titz@helmholtz-hzi.de

^d Hannover Medical School, Institute of Laboratory Animal Science, 30625 Hannover, Germany

^e Université Grenoble Alpes, CNRS, CERMAV, 38000 Grenoble, France

^f Department of Biochemistry, Faculty of Science, Mahidol University, Bangkok 10400, Thailand

^g Center for Excellence in Protein and Enzyme Technology, Faculty of Science, Mahidol University, Bangkok 10400, Thailand

^h Institute of Anatomy and Cell Biology, Medical Faculty of Saarland University, 66421 Homburg/Saar, Germany

ⁱ Center for Molecular Signaling (PZMS), Medical Faculty of Saarland University, 66421 Homburg/Saar, Germany

^j Department of Pediatric Pneumology, Allergology and Neonatology, Hannover Medical School, 30625 Hannover, Germany

^k Biomedical Research in Endstage and Obstructive Lung Disease Hannover (BREATH), Member of the German Center for Lung Research (DZL), 30625 Hannover, Germany

Pseudomonas aeruginosa is a critical priority I pathogen and causes life-threatening acute and biofilm-associated chronic infections. The choice of a suitable treatment for complicated infections requires lengthy culturing for species identification after swabs or invasive biopsy. To date, no fast and pathogen-specific diagnostic tools for *P. aeruginosa* infections are available. Here, we present the non-invasive pathogen-specific detection of *P. aeruginosa* using novel fluorescent probes that target the bacterial biofilm-associated lectins LecA and LecB. Several glycomimetic probes were developed to target these extracellular lectins and demonstrated to stain *P. aeruginosa* biofilms in vitro. Importantly, for the targeting of LecA an activity boost to low-nanomolar affinity could be achieved which is essential for in vivo application. In vitro, the nanomolar divalent LecA-targeted imaging probe accumulated effectively in biofilms under flow conditions, independent of the identity of the fluorophore. Investigation of these glycomimetic imaging probes in a murine lung infection model and fluorescence imaging revealed accumulation at the infection site. These findings demonstrate the use of LecA- and LecB-targeting probes for the imaging of *P. aeruginosa* infections and suggest their potential as pathogen-specific diagnostics to accelerate the start of the appropriate treatment [1].

Acknowledgements: We acknowledge an ERC Starting Grant to A.T., Sweetbullets grant no 716311 and an ERASMUS fellowship (to S.M.). A.I. and S.K. thank the French National Research Agency (ANR-17-CE11-0048) for support and A.I. further acknowledges Glyco@Alps (ANR-15-IDEX-0002) and Labex Arcane/CBH-EUR-GS (ANR-17-EURE-0003).

References:

1. Zahorska, E.; Denig, L. M.; Lienenklaus, S.; Kuhaudomlarp, S.; Tschernig, T.; Lipp, P.; Munder, A.; Gillon, E.; Minervini, S.; Verkhova, V.; Imberty, A.; Wagner, S.; Titz, JACS Au, **2024**, *4*, 4715–4728.