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NOVEL LECTIN-TARGETING THERAPEUTICS AND DIAGNOSTICS FOR *Pseudomonas aeruginosa* INFECTIONS

Keywords: *P. aeruginosa*, biofilms, LecA inhibitors, LecB inhibitors, prodrug antibiotic conjugates, cystic fibrosis

INVENTION NOVELTY

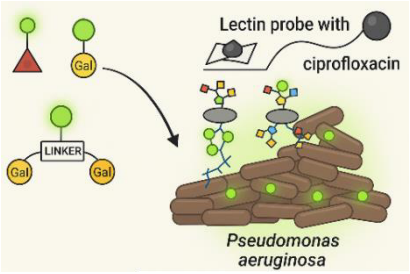
Three distinct approaches targeting bacterial lectins LecA and LecB, critical components in the biofilm formation of *Pseudomonas aeruginosa,* to prevent nosocomial and chronic infections, in cystic fibrosis and immunocompromised patients:

- **Lectin-targeting conjugates:** Prodrug antibiotic and imaging agent conjugates designed to bind bacterial lectins, utilizing bacterial proteases for selective drug release at infection sites
- **Bivalent LecA inhibitors:** Glycomimetic inhibitors that prevent bacterial virulence and biofilm formation by blocking LecA, enhancing bacterial vulnerability to antibiotic treatment and the immune system
- **LecB inhibitors:** Small molecules that disrupt biofilms and sensitize bacteria to antibiotics

VALUE PROPOSITION

- **Targeted therapy:** Direct drugs to infection sites, reducing systemic side effects
- **Enhanced antibiotic efficacy:** Disrupts biofilm integrity, making bacteria more susceptible to treatment
- **Improved pharmacokinetics:** Increased stability, solubility, and targeted action
- **Versatile application:** Potential as a stand-alone or adjunctive therapeutic and as a diagnostic probe

These features highlight the potential to meet an unmet medical need in *P.* aeruginosa treatment.



Diagnostic approach using the antibiotic prodrug (modified from Zahorska et al. and Meiers et al.)

TECHNOLOGY DESCRIPTION

- ***In vitro* activity***:* Nanomolar binding affinity, inhibition of bacterial virulence and biofilm formation
- ***In vitro* ADME/T:** Excellent profile with low cytotoxicity
- ***In vivo* target engagement:** Synergy with tobramycin in chronic *P. aeruginosa* murine lung infection model
- ***In vivo* PK:** High oral bioavailability, good plasma exposure, urinary excretion, high dose of 150 mg/kg/d without signs of toxicity

COMMERCIAL OPPORTUNITY

The technology is available for co-development and in-licensing partnerships.

DEVELOPMENT STATUS

In vivo proof-of-concept for frontrunners of LecB inhibition in chronic lung infection model, LecA inhibitors effective *in vitro*, LecA/LecB targeting demonstrated in murine infection model.

PATENT SITUATION

Three patent families (WO2016151066, WO2021089729, WO2023104922) with granted patents in EU, US, JP, CN, AU, IL and a pending application in CA. Additional pending applications exist in EP, US, JP, CA, AU, IL, and CN.

FURTHER READING

Zahorska, *et. al., JACS Au* 2024, *4*(12); Zahorska et al., *Angew. Chem. Int. Ed. Engl.* 2023, 62(7); Mala *et al., J. Med. Chem.*, 2022, 65(20); Meiers, *et. al., Journal of Medicinal Chemistry* 2020 *63*(20)

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