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(54) Title (EN): MUC1 DECOY PEPTIDES FOR TREATMENT AND PREVENTION OF BACTERIAL INFECTIONS

(54) Title (FR): PEPTIDES LEURRES MUC1 POUR LE TRAITEMENT ET LA PRÉVENTION D'INFECTIONS BACTÉRIENNES

(57) Abstract:

(EN): *Pseudomonas aeruginosa* flagellin protein recruits the mammalian host sialidase enzyme neuraminidase- 1 (NEU1) to remove sialic acid residues from the extracellular domain of the mammalian cell-surface protein MUC l (MUC l -ED), thereby exposing a cryptic binding site on the MUC l -ED protein backbone for flagellin binding. NEU1 -driven MUC l -ED desialylation rapidly increases *P. aeruginosa* adhesion to the airway epithelium. MUCl -ED desialylation also increases MUC l -ED cleavage and shedding from the cell surface, where desialylated, shed MUCl -ED competitively blocks *P. aeruginosa* adhesion to cell-associated MUCl -ED. Presented herein are data showing that exogenously-administered, deglycosylated MUCl -ED peptides reduced adhesion of *P. aeruginosa* to airway epithelial cells. Also presented are data showing that administration of *P. aeruginosa* to mice in combination with deglycosylated MUC 1 -ED decreased *P. aeruginosa* recovered from the lungs at 48 hr and 72 hr post-infection. Such findings are extended to the methods of treatment and prevention of bacterial infections defined herein.

(FR): La protéine flagelline de *Pseudomonas aeruginosa* recrute l'enzyme sialidase neuraminidase-1 (NEU1) de l'hôte mammifère pour retirer les résidus d'acide sialique du domaine extracellulaire de la protéine de surface cellulaire de mammifère MUC1 (MUC1-ED), ce qui permet d'exposer un site de liaison cryptique sur le squelette de la protéine MUC1-ED pour la liaison de la flagelline. La désialylation de MUC1-ED dirigée par NEU1 augmente rapidement l'adhésion de *P. aeruginosa* à l'épithélium des voies respiratoires. La désialylation de MUC1-ED augmente également le clivage de MUC1-ED et son exfoliation de la surface cellulaire, MUC1-ED exfolié bloquant par compétition l'adhésion de *P. aeruginosa* à MUCl-ED associée aux cellules.

Dans la description sont présentées des données montrant que les peptides de MUC1-ED déglycosylés, administrés par voie exogène réduisent l'adhésion de *P. aeruginosa* aux cellules épithéliales des voies respiratoires. Dans la description sont également présentées des données montrant que l'administration de *P. aeruginosa* à des souris en combinaison avec MUC1-ED déglycosylé diminue la quantité de *P. aeruginosa* récupérée dans les poumons 48 h et 72 h après l'infection. Ces découvertes sont étendues aux procédés de traitement et de prévention d'infections bactériennes tels que définis dans la description.

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