

P2262 Multivalent fucosides with affinity for the *Aspergillus fumigatus* lectin FleA prevent spore adhesion and delay *in vivo* dissemination

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Background: *Aspergillus fumigatus* is an opportunistic pathogen and source of increasing concern due to the emergence of antifungal-resistant strains. Airborne conidia (spores) are typically found in decaying organic matter in soils, but can disperse widely and are easily inhaled into the respiratory tract. FleA (or AFL), a fucose lectin, was recently identified in the opportunistic mold *Aspergillus fumigatus*.

Materials/methods: The anti-adhesive potency of the fucosides was evaluated *in vitro* for their capacity to prevent the adhesion of *A. fumigatus* spores to human A549 pneumocytes. The better compound was used to treat *A. fumigatus* spores before intratracheal administration to immunodepressed swiss mice.

Results: The hexavalent fucosides were significantly more powerful anti-adhesives compared with divalent fucosides. Satisfactory dose-responses were observed on conidium anti-adhesion, with a significant decrease starting at 1 μ M. Hexavalent fucosides reached around 50% adhesion inhibition (IC₅₀) at a fucoside concentration of 10 μ M. Thus, when expressed in mol of molecules, a low IC₅₀ of around 1.7 μ M can be calculated. Treatment of spore by the hexavalent compound before infection lead to a significant decrease of fungal burden in the lung 12 hours after infection.

Conclusions: The anti-adhesive effect observed can be ascribed to binding to FleA and to the formation of conidium aggregates. These fucosides are promising tools to better understand the role of FleA in conidia pathogenicity and host defenses against invasive aspergillosis. Furthermore, preventive strategy by inhibitors nebulization must be explored.

