OUEST VALORISATION

TECHNOLOGY OFFER

ANTI-ADHESIVE THERAPY FOR CROHN

MANNOSE DERIVATIVES

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TECHNOLOGY

Most *Escherichia coli* express the FimH adhesin, a mannose binding lectin produced at the tips of rod-shaped organelles called type-1 pili. FimH binds to high-mannose glycan structures at cell surfaces, allowing uropathogenic, fecal, and entero-hemorrhagic strains of E. coli to attach to the host cells.

This strategy has been particularly studied in the context of urinary tract infections (UTIs),in which the adhesion of pathogenic Escherichia coli strains to uroepithelial cells is prevented by blocking the FimH adhesin expressed at the tips of bacteria organelles called fimbriae.

We extended the antiadhesive concept, showing that potent FimH antagonists can block the attachment of adherent-invasive E. coli (AIEC) colonizing the intestinal mucosa of patients with Crohn's disease (CD).

We have designed a library of Heptyl-Mannosides based (HM) antiadhesive compounds against adherent-invasive *Escherichia coli* Bacteria associated with CD.

HM compounds show an high in vivo anti-adhesive activity, no cytotoxicity, and a stability in the gut. Despite its very simple structure, HM has a strong affinity for FimH, (best compound : Kd = 2,9 nM).

HM compounds show to reduce AIEC levels in the feces and in the colonic and ileal mucosa after oral administration in CD animal model. Signs of colitis and intestinal inflammation were also prevented.

APPLICATIONS

- Crohn's disease
- Urinary tract infection

KEY BENEFITS

- Decrease in bacterial load
- Reduction of colitis
- Prevention of instestinal inflammation
- Oral administration (water soluble compounds)
- No side effect

INTELLECTUAL PROPERTY

- WO201416361 / 2013-07-24
- Extensions : CA, US, EP, JP, KR, IN, BR

STAGE OF DEVELOPPEMENT

- Target validation
- In vitro and in vivo validation
- Pharmacology (safety, efficacy)

LABORATORY

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