A new hope for treating severe pneumonia

June 27 2016

Credit: Klaus Nielsen from Pexels

A biotech company involved in the PNEUMONP project – and responsible for the development of the antimicrobial peptide M33 – recently confirmed that the molecule at the heart of the project was now robust enough for industrial production. The new drug is hoped to help treat difficult lung infections like pneumonia.

Since it started investigating M33 antimicrobial peptide a few years ago, Italian company SetLance SRL has taken huge step forward. This optimised version of an artificial peptide sequence – which showed encouraging in-vitro results against multidrug-resistant Gram-negative bacteria – is increasingly thought to be the long-sought solution to treat pneumonia. It comes in an emergency context, as multidrug-resistant Gran-negative pathogens are on the rise and cause what the medical sector does not hesitate to call the 'antibiotic resistance crisis'.

Conscious of the need to find new antibiotics urgently, the European Union is supporting Setlance financially under the PNEUMONP project. The endgame is the development of a new formulation of M33, enhancing its antimicrobial activity, but also overcoming issues related to antimicrobial peptides' (AMPs) low selectivity for bacteria and certain degree of toxicity for eukaryotic cells in vitro, along with their short half-life in vivo.

Recently tested in mice inoculated with P. aeruginosa infections, the peptide and its Setlance-patented, pegylated form (SET-M33L-PEG) enabled a survival percentage of 60 to 80 % in sepsis and lung infections and completely healed skin infections when administered topically. The new formulation of M33 fights Gram-negative bacteria in three steps: It binds with the lipopolysaccharides (LPS) on the outer membrane of bacteria, forms a helix, and finally disrupts the membrane provoking cytoplasm leaking.

Unlike colistin—an antibiotic for the treatment of acute and chronic infections—SET-M33L did not select resistant mutants in bacterial cultures. It proved not to be genotoxic and had much lower in vivo toxicity than antimicrobial peptides already used in clinical practice.

Another interesting and recent finding was related to M33's use AMP in conjugation or combination with levofloxacin (LVFX) – a

fluoroquinolone antibiotic. While antibacterial assays showed no significant differences in activity when M33 and LVFX were used in in conjugation, their combination showed improved activity against Gram-negative bacteria. Combination treatment therefore opposes antimicrobial-resistance, restoring the effect of LVFX.

SetLance has scaled-up M33's synthesis route and is now able to produce several hundred milligrams per batch. The company is confident that its molecule is robust enough for industrial production, and expects that it will go on clinical development and validation at the beginning of 2018.

M33 is a key element of the PNEUMONP project, which aims to develop a new inhalable drug system, a new aerosol technology, an innovative treatment efficiency-test, and a new diagnostic kit for Gram-negative bacterial infections in lungs by the end of 2017.

More information: Project website: www.pneumonp.eu/

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