PRESS RELEASE

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Antimicrobial peptide therapy for tuberculosis infections

Hamlet BioPharma, the innovative pharmaceutical company currently advancing several phase II trials targeting infectious diseases and cancer, along with an extensive project and patent portfolio, is delighted to announce progress for the tuberculosis project. A PhD thesis entitled ''Antimicrobial peptide therapy for tuberculosis infections'', from the group of Professor G. Godaly, was successfully defended by Komal Umashankar Rao.

Tuberculosis is a major cause of mortality in all parts of the world, not least in patients whose immune system is compromised as in HIV infected individuals. The treatment options are becoming more limited, due to escalating antibiotic resistance. The group of Professor G. Godaly are developing a novel antimicrobial peptide, NZX, as a potential drug for pulmonary tuberculosis treatment, in collaboration with Hamlet BioPharma. The new, peptide-based drug has shown promising treatment effects against lung tuberculosis in animal models, both against antibiotic sensitive and antibiotic resistant bacteria.

The bacteria causing tuberculosis, *Mycobacterium tuberculosis*, have a unique, thick cell wall, which is difficult for anti-bacterial compounds to penetrate. The effect of the peptide NZX on the bacterial cell was studied to understand NZX's membrane interaction in live bacteria. NZX displayed a pull-and-aggregate mechanism on the inner membrane of mycobacteria, disrupting cell integrity. In drug interaction studies, NZX showed an additive effect with traditional tuberculosis therapies such as isoniazid and ethambutol, which may be essential for defining future clinical protocols.

In addition, the peptide NZX demonstrated broad-spectrum activity against non-tuberculosis mycobacteria and drug-resistant *Staphylococcus aureus*. These findings emphasize NZX's potent effects against mycobacteria, with a notable absence of antibiotic resistant mutants in resistance development studies.

Pharmacology parameters analysed included stability of NZX after exposure to proteolytic molecules or human serum. Directed therapy of NZX was achieved by loading NZX onto nanoparticles, which proved effective for directed intracellular therapy and enhanced antimicrobial activity.

Despite the international efforts to expand access to TB treatments, the problem of multi drug resistant bacteria is limiting the effects and tuberculosis remains a major public health threat with high mortality rates. There is a need to find new ways to battle drug resistant TB infections. These comprehensive studies position NZX as a promising candidate against drug resistant TB infections.

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