



PRESS RELEASE

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Immunotherapy - a new approach to treating bacterial infections, including antibiotic resistant strains

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 treatment of antibiotic resistant bacteria in a murine model relevant to human disease. A recent paper, clearly shows that treatment with the drug anakinra (IL-1RA) prevents severe infections of the urinary tract, including kidney infections that may cause sepsis. The treatment was efficient also against infections caused by antibiotic resistant bacteria, defining this therapy as an alternative or complement to antibiotics. Ambite I et al. (2024) Pathogens 13(1), 42 <https://doi.org/10.3390/pathogens13010042>.

The treatment of bacterial infections has largely focused on the bacteria and how to remove them with antibiotics. This approach is increasingly difficult, due to the development of antibiotic resistance. Here we propose an alternative way of treating bacterial infections by strengthening the anti-bacterial defense of the host. Rather than killing bacteria directly with antibiotics, we used immunotherapy to accelerate bacterial clearance in mice with urinary tract infection with the added benefit of reducing the inflammatory responses in infected tissues. Immunotherapy showed similar efficacy against infections caused by antibiotic sensitive or antibiotic resistant bacterial strains.

The World Health Organization (WHO) has declared antibiotic resistance one of the “biggest threats to global health, food security, and development today”, highlighting the need for novel solutions (WHO. Antibiotic Resistance. Available online: www.who.int/news-room/fact-sheets/detail/antimicrobial-resistance). Hamlet BioPharma’s publication clearly demonstrates exceptional immunotherapy results in *E. coli* infected mice with severe acute cystitis (see figure below). The results show that infections can be treated with therapies, other than antibiotics. This is an important conceptual advance that highlights the potential for future solutions to anti-infective therapies.

Hamlet BioPharma’s development strategy is focused on pursuing this important area of drug development, with our promising drug candidate IL-1RA, as well as other compounds in our project pipeline. This recently published study illustrates the versatility of Hamlet BioPharma’s project portfolio and the importance of the health issues addressed by the company. The global urinary tract infection therapeutics market was valued at USD 8.7 billion in 2021 and is expected to reach USD 10.7 billion by 2028 with a 3.0% CAGR (Coherent Market Insights - urinary tract infection therapeutic market analysis).

IL-1RA – Urinary tract infection treatment

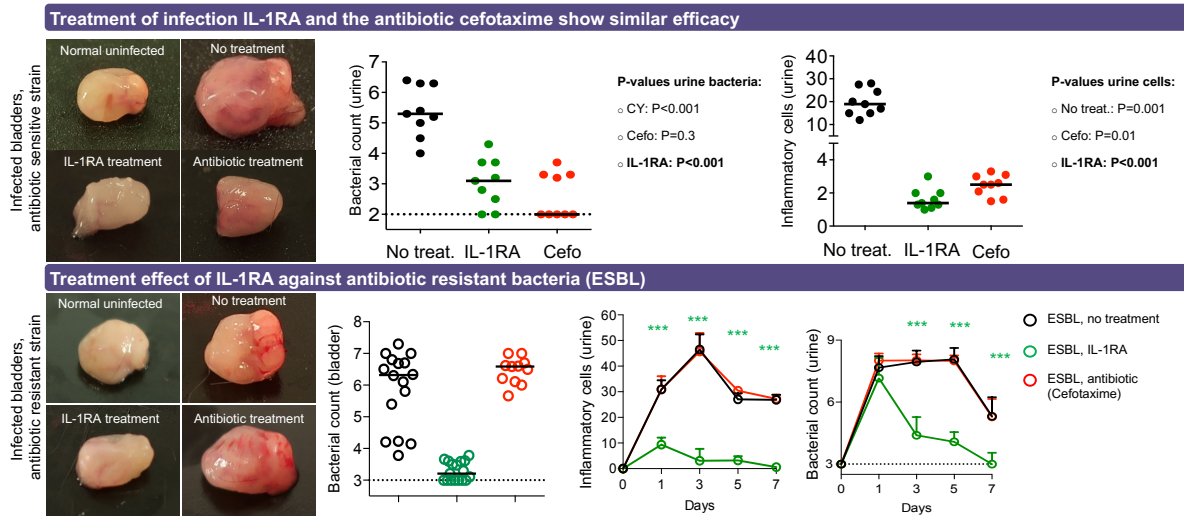


Figure legend. In this study, immunotherapy was shown to prevent excessive innate immune activation and restore the anti-bacterial defense.

Upper panels. *E. coli*-infected mice develop severe urinary bladder infection, defined by high bacterial counts and extensive tissue pathology (black dots). Here, the interleukin-1 receptor antagonist (IL-1RA, green dots) was identified as a more potent inhibitor of inflammation and pain than cefotaxime (red dots).

Lower panels. Unexpectedly, IL-1RA treatment also accelerated clearance of antibiotic-resistant bacteria from infected bladders and kidneys, including *E. coli* (ESBL), where cefotaxime treatment was inefficient. The treatment effects were also significant after long-term follow-up suggesting that IL-1RA therapy might have a lasting protective effect.

Due to antibiotic resistance many infections are difficult to treat

Urinary tract infections are among the most prevalent infectious diseases globally. Resistance is spreading rapidly. Infections with antibiotic-resistant *E. coli* account for one-half of the estimated global burden of antibiotic resistance, with about 90% of *E. coli* strains being resistant to at least one antibiotic. In Europe, *E. coli* isolates are resistant to third-generation cephalosporins and fluoroquinolones (11.8% and 22.3%, respectively), and fluoroquinolone-resistant *E. coli* represented 31.3% of the isolates in hospitalized patients (Antimicrobial Resistance Collaborators (2022). *The Lancet* 399(10325). [https://doi.org/10.1016/S0140-6736\(21\)02724-0](https://doi.org/10.1016/S0140-6736(21)02724-0)).

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