Enzymatic Inactivation of Antibiotics to Combat Antimicrobial Resistances

Marik M. Müller, Katja M. Arndt

Molecular Biotechnology, University of Potsdam, Karl-Liebknecht-Str. 24-25, 14476 Potsdam, Germany

Email: marik.m.mueller@gmail.com; katja.arndt@uni-potsdam.de

Antibiotics are an important milestone in medicine; however, their increased use has resulted in an alarming rise of antimicrobial resistances. Antibiotics are used in large quantities not only in human medicine but also in animal farming and agriculture, where they enter the environment through waste products, feces, or milk of treated cows, promoting antimicrobial resistance, and ultimately leading to untreatable multidrug-resistant pathogens threatening also human health. Importantly, antibiotic-resistant bacteria often activate export mechanisms that result in resistance to various structurally unrelated antibiotics.

We devised a novel strategy for the enzymatic inactivation of antibiotics in different media such as salt water or milk. Using a combinatorial approach and metabolic selection, we optimized a hydrolase enzyme (EstDL136) for cleavage of the antibiotic florfenicol. Time-resolved nuclear magnetic resonance spectroscopy revealed significantly improved reaction kinetics for the optimized variant. Importantly, the hydrolase remained active in different media such as saltwater or cow milk.

Various environmentally-friendly application strategies for florfenicol inactivation were developed using the optimized hydrolase. As a potential filter device for cost-effective treatment of waste milk or aquacultural wastewater, the hydrolase was immobilized on Ni-NTA agarose or silica as carrier materials. In two further application examples, the hydrolase was used as cell extract or encapsulated with a semi-permeable membrane. This facilitated, for example, florfenicol inactivation in whole milk, which can help to treat waste milk from medicated cows, to be fed to calves without the risk of inducing antibiotic resistances.

In general, our strategies for enzymatic inactivation of antibiotics enable therapeutic intervention without promoting antibiotic resistances.

Reference

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