

Lysando AG  
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## Innovative microbiome-friendly technology tackles antibiotic resistance

Lysando AG's Artilysin platform technology is producing novel antimicrobial proteins with a unique mode of action and a wide range of applications, from human and veterinary medicine to the food and cosmetics industry. Lysando is licensing the technology to companies all around the world.

Antibiotic resistance is one of the biggest public health challenges of recent times. When disease-causing bacteria become resistant to antibiotics, infections such as pneumonia, tuberculosis, gonorrhoea and salmonellosis are harder to treat. New strategies to combat antibiotic-resistant bacteria and prevent the development of resistance are urgently required.

Lysando AG is a leading biotechnology company based in Liechtenstein that has been developing antimicrobial proteins since 2009. Recently, Lysando acquired 2.7% of shares in the KOSDAQ-listed contract development and manufacturing organization Amicogen. Lysando's ground-breaking technology platform designs Artilysin that can target nearly every bacterial species, including the 'priority pathogens' identified by the World Health Organisation (WHO) as rapidly becoming resistant to a large number of antibiotics.

Since it was founded, the company has developed 450 Artilysin prototypes and signed 14 licences with leading global companies to help them overcome the challenges posed by pathogenic bacteria. "Our custom-designed molecules can be used to rapidly kill resistant or persistent bacteria in a way that they are very unlikely to develop resistance," said Markus Count Matuschka de Greiffenclau, CEO and co-founder of Lysando. "They are also environmentally friendly, as, unlike antibiotics, they degrade quickly and do not accumulate in the environment".

Artilysin are recombinant proteins with bacterial cell wall-binding and enzymatically active domains that are similar to those found in bacteriophages. These regions enable phages to degrade highly conserved cell wall peptidoglycans and cause bacteria to burst open. Artilysin are modified to modulate their range of targets and improve their stability. "Artilysin can be designed to target one specific species of bacteria, such as *Cutibacterium acnes*, the main cause of acne, or a particular type of bacteria, such as Gram-negative bacilli, the most common cause of sepsis," Matuschka de Greiffenclau explained.

Antibiotics often interfere with essential metabolic processes in bacteria, but, over time, bacteria can alter their metabolic networks to develop resistance. As the mechanism of action of Artilysin is independent of bacterial metabolism, they are effective against antibiotic-resistant bacteria. Moreover, evidence to date indicates



**Fig. 1 | Artilysin application observations in an otherwise 'incurable' person with atopic dermatitis.**

that bacteria are unable to become resistant to this mode of action. "Artilysin offer a long-term solution to antibiotic resistance and a promising alternative to antibiotics," said Matuschka de Greiffenclau.

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### Microbiome-friendly treatments

Bacteria comprise the bulk of the microbiome, that is, the genetic material of all the microbes (bacteria, fungi, protozoa and viruses) that live on and inside almost every part of the human body. These beneficial colonizers aid food digestion and help regulate the immune system. By killing

a wide variety of bacteria, antibiotics disrupt the composition of the microbiome, causing increased susceptibility to infection, gut problems, allergies, mood disorders and skin conditions.

The possibility of targeting very specific bacterial species with Artilysin means that the 'good', resident bacteria remain unharmed. Lysando has recently developed Artilysin for two topical applications that demonstrate this. One targets *Staphylococcus aureus*, which may represent up to 70 percent of the bacterial population on the skin of patients with atopic dermatitis. The other targets *C. acnes*.

"We can selectively kill pathogenic *S. aureus* while sparing commensal *Staphylococcus epidermidis* with Artilysin, and, thus, rebalance the natural human skin microbiome," Matuschka de Greiffenclau explained. The approach seems to be very effective.

When a patient with severe atopic dermatitis who had not responded to conventional treatments applied the Artilysin prototype spray on their hands, the itchiness and redness eased after only 2-3 days (Fig. 1). The symptoms remained at bay 2 months after a 13-day course of application, indicating that the effect is long lasting. Importantly, no allergic reaction was observed.

The results with an Artilysin against *C. acnes* in vitro and first application observations in patients with acne are also very encouraging. All patients in the observational trial experienced remarkable improvements.

"We now have tools on hand to manage, balance and optimize the microbiome," Matuschka de Greiffenclau said.

With more than 1,700 pathogens in its biobank and 3,000 constructs to start testing, Lysando can design antimicrobial proteins against potentially any Gram-positive or Gram-negative pathogen.

"We look forward to continue realizing the full potential of our Artilysin platform technology and helping patients and consumers," he concluded.

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