Amicrobe, Inc
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AMICROBE
Engineering local antimicrobials

Antimicrobials standing guard

Amicrobe engineers biologics-as-materials that are applied locally in surgery and trauma to prevent and treat life-threatening infections.

When it comes to infectious diseases, the world knows well that an ounce of prevention is worth a ton of cure. But at points where patients are most vulnerable—with exposed tissues, as in surgery or following trauma—there are no ideal products for preventing infection or directly stopping its spread. Antiseptics are effective on intact skin, but see limited use on exposed tissues as they can get taken up into the bloodstream, with toxic effects. Antibiotics are safe to circulate, but are often ineffective when applied locally.

That's the sweet spot for Amicrobe, a California-based biotech that takes its cues from DuPont as much as Amgen. Amicrobe is the brainchild of co-founders Michael Bevilacqua, CEO and CSO, and Timothy Deming, Professor of Bioengineering and Chemistry at UCLA, who dreamt up the company's concept more than a decade ago. The big idea was Amicidins, synthetic proteins that would combine physical properties and microbicidal activity for a dual mode of action. Different arrangements of just two amino acids, lysine and leucine, could change the physical properties of the molecules, allowing Amicrobe to design and build different antimicrobials with distinct potential uses.

What are Amicidins?

Amicidins are cationic, designed with natural antimicrobial peptides like cathelicidins and defensins in mind. "We use what nature uses: positive charges," said Bevilacqua. "Through the course of evolution, bacteria went negative, and mammalian cells went positive to fight them." Bevilacqua and Deming envisioned antimicrobials with physical properties that could fill cracks, stay in place when needed, and be easily cleared by the body.

The difference between Amicidins and traditional antibiotics is intentional, says Daniel Huang, Amicrobe's VP of Operations. "Most antibiotics act like 'smart bombs,' targeting metabolic processes to disrupt bacterial cell machinery. But Amicidins are much broader," Huang explained. That's because Amicidins rely on positive charges of lysines to bind negative charges on microbes, disrupting membranes to affect function. "They work against both Gram-positive and Gram-negative bacteria, and we have millennia of evidence that it's very difficult for bacteria to develop resistance," Huang added.

The company says its two lead assets, Amicidin-α and Amicidin-β, will be regulated as biologics by the US Food and Drug Administration, but their function is as dependent on their physical properties as their antimicrobial characteristics. Amicidins are large molecules, built with hydrophobic ends that allow them to self-assemble into multimers. This becomes an inherent slow-release mechanism and prevents them from being absorbed intact into the bloodstream like smaller antiseptic molecules might. And because they are made from two amino acids, when the time is right, they are easily and safely broken down. "The simplicity of these molecules is key to their performance and safety," said Bevilacqua.

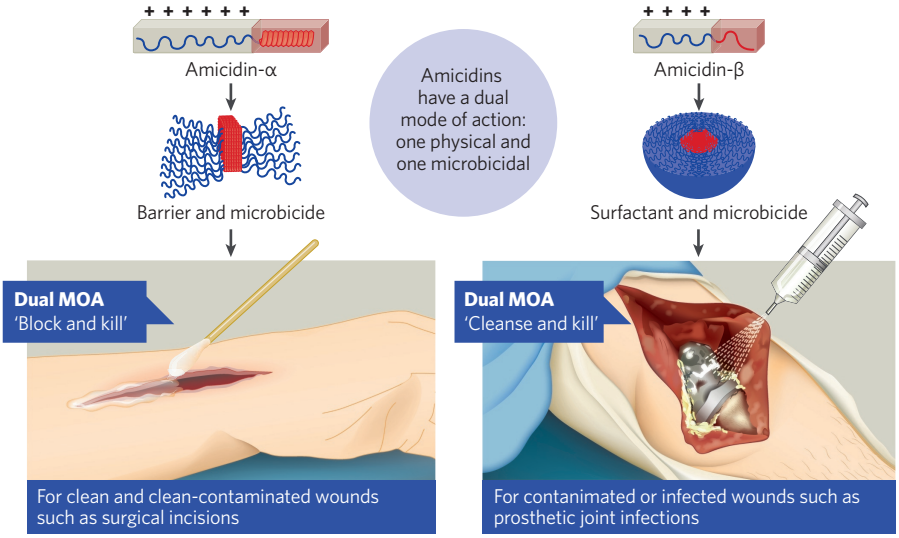

Fig. 1 | Dual mode of action of Amicidin-α and Amicidin-β. Employing a 'block and kill' strategy, Amicidin-α is formulated as a surgical gel that can be applied to tissues during surgery to prevent infection, whereas Amicidin-β is formulated as a solution to 'cleanse and kill' in active contamination or infections.

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Applications of Amicidin-α and Amicidin-β

Amicrobe's first product candidate is Amicidin-α formulated as a surgical gel—just synthetic protein and water—that can be applied to tissues during surgery to prevent infection, a 'block and kill' strategy. It will likely be tested first in humans undergoing mastectomy with breast reconstruction, and plans are in place to expand into open colorectal surgery trials. If it proves effective, Amicidin-α could be used in nearly all Class I (clean) and Class II (clean-contaminated) surgical procedures, which account for 87% of all surgeries.

Meanwhile, Amicidin-β is formulated as a solution to 'cleanse and kill' in situations where contamination or infection may have already occurred, including trauma. "We designed Amicidin-β to be a very good surfactant, with detergent activity like soaps," Bevilacqua said. It is planned to be first tested in patients with prosthetic joint or osteosynthesis site-associated infections, with plans to expand into patients with open tibial fracture. Both Amicidin-α and Amicidin-β are on track for clinical trials starting in 2022 (Fig. 1).

These two products are just the beginning. The company has received strong support from public funders, who have contracted with Amicrobe to develop formulations of their Amicidins for more specific applications. These vary from battlefield wounds to uterus-cleansing foams to be used in regions where fatal post-cesarean infection rates remain high. Amicrobe is now looking for corporate partnerships, both to help develop and commercialize its existing assets and to broaden uses for Amicidins into other products. "The key is stopping infections before they start, or when they're a local problem instead of a systemic one," Bevilacqua said. "If Amicidins work in human trials, we can be in every major surgical procedure and traumatic wound in the world, and have a million opportunities a day to protect lives."

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