BATTLING AGAINST BIOFILMS

Kane Biotech fights source of hospital infections

BY RANDALL C WILLIS

WINNIPEG, Manitoba—In work described in *Antimicrobial Agents and Chemotherapy* and the *Journal of Industrial Microbiology and Biotechnology*, researchers at Kane Biotech made therapeutic and analytical progress against biofilms, a particularly intractable form of bacterial growth. According to the NIH, biofilms may be responsible for up to 80 percent of all human infections and has been implicated in almost all hospital-acquired or nosocomial infections.

"Once in a biofilm, bacteria can be several orders of magnitude more resistant to antibiotics than their planktonic [free-floating] counterparts," says Dr. Srinivasa Madhyastha, Kane Biotech's director of research. "Whatever the mechanism of drug resistance, bacteria in biofilms often outlive treatment. Once antibiotic treatment stops, just a few bacteria, sloughed off from the biofilm, can enter the planktonic, rapidly proliferating phase."

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Rather than try to tackle the microbes in the traditional manner, Kane Biotech opted to interrupt the process that holds the bacteria in the biofilm

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structure. In particular, they targeted GlmU, an enzyme involved in the biosynthesis of a precursor of bacterial cell-surface components. As such, the enzyme is also involved in the pathway responsible for the polysaccharide adhesion required for biofilm formation.

The researchers identified a GlmU inhibitor that showed stronger antibiofilm activity on urinary catheters—a prominent source of nosocomial infections—than the silver-hydrogel coating that is often applied for this purpose. According to Madhyastha, the findings offer a way to potentially avoid any complicating toxicological effects of the large quantities of metal used to inhibit bacterial growth.

"Furthermore, bacteria have already developed resistance to metals such as silver," he adds. "A method of long-term prevention from biofilm formation that acts at the level of biofilm formation is needed."

As part of their effort to develop new antibiofilm drugs, the company also worked to improve the widely used biofilm assay based on a simple staining protocol. The assay, however, involved many sample preparation steps, offered variable results, and required a lot of sample. The assay developed by Kane Biotech involved the spectrofluorometric quantification of the binding of a fluorescently tagged wheat germ agglutinin and bacterial surface structures. Monitoring the activity of two drugs against *E. coli* and *S. epidermidis*, the researchers found that the two assays offered similar responses but that the spectrofluorometric assay was more sensitive and specific.

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The assay opens the door to faster screening of new compounds as potential therapeutics against biofilms. Of the company's existing portfolio, Kane Biotech is looking for interested companies to either license the GlmU inhibitor or to develop it further in partnership.

"This is one of several candidate products that came out of the company's research program to develop and screen novel products with antibiofilm activity," Madhyastha says.

With the increasing prevalence of artificial medical implants and use of stents and catheters by aging Western populations, sooner will be better than later. ◆

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