



Enter and Destroy the Biofilm Matrix: Dispersing Bacterial Biofilms with Engineered, Enzymatically Active Bacteriophage

Invention: Bacterial biofilms are sources of contamination that are difficult to eliminate in a variety of industrial, environmental and clinical settings. Hideki Kobayashi, Michihiro Araki, Mads Kaern and Jim Collins of Boston University have developed and successfully applied an engineered, enzymatically active bacteriophage T7 to eradicate mature biofilm formed by *Escherichia coli*. The engineered phage was designed to employ a two-pronged attack strategy: (i) its enzymatic activity targets and degrades the extracellular matrix of the biofilm, thus exposing the biofilm-embedded cells, and (ii) the phage infects and kills the exposed cells, releasing additional enzymatic phage in the process. The present invention will be the basis for a novel and highly effective treatment for dispersing and eliminating biofilms.

Introduction: Bacteria typically grow in surface-attached communities known as biofilms, which consist of cells encased in an extracellular matrix. Biofilms form on the surfaces of a variety of environmental, industrial, and biological systems, including water distribution systems, and fermenters. Bacterial biofilms are also associated with many human health issues. For instance, bacteria form biofilms on implanted medical devices (e.g., catheters, heart valves, joint replacements) and damaged tissue, such as the lungs of cystic fibrosis patients. Because bacteria in biofilms are highly resistant to antibiotics and host defenses, they are persistent sources of infection.

Because biofilm-encased cells have increased resistance to antibiotics and disinfectants, they are sources of contamination that are difficult to eliminate. There is a clear and growing need for novel technologies to reduce and control biofilms. To address this need, the inventors have engineered enzymatically active bacteriophage to disperse mature biofilm formed by *Escherichia coli*. While the encasing of bacterial cells in biofilms is normally thought to protect against phage infection, the inventors have employed a phage that is able to degrade the extracellular matrix allowing entry and infection releasing additional enzymatic phage in the process.

Features and Benefits:

- Proof-of-principle demonstration that phages can be engineered to significantly reduce biofilm levels by simultaneously degrading the extracellular matrix and infecting biofilm-embedded cells
- The multiplication of the engineered enzymatic phage during the subsequent lysis makes the biofilm reduction an efficient, autocatalytic process
- Treatment of mature biofilm with enzymatic phage has been shown to lead to a great reduction in biofilm levels that treatment with either purified cellulase or phage

Applications:

Engineered enzymatic phages may be useful for reducing and controlling biofilms in a variety of environmental, industrial and biomedical settings:

Infections Disease	Medical Devices	Industrial
Cystic fibrosis	Indwelling medical devices	Wastewater treatment plants
Native valve endocarditis	Implanted prosthetic devices	Water system piping
Otitis media (ear infections)	Urinary catheters	Food processing plants
Periodontitis	Endoscopes	Fermenters
Chronic prostatitis		

Intellectual Property: PCT patent application filed.

BU Case Number: BU04-61

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