LETTER TO THE EDITOR

Highlights from the Montana wound biofilm retreat

To the Editor:

Over the past several years, an increasing number of reports have investigated the potential role of biofilms in the delayed healing of chronic wounds. The Center for Biofilm Engineering (CBE) at Montana State University received a P20 Exploratory Research Center Grant from the National Institute of General Medical Science to investigate biofilms in chronic wounds. As part of our outreach program for this exploratory center, we held a Wound Biofilm Retreat in Bozeman, MT. This Retreat brought together scientists, clinicians, and company representatives to present the latest research on how microbial biofilms impact wound healing. Attendees included representatives from 25 companies and 12 universities with such diverse backgrounds as clinical practice, microbiology, and immunology.

To kick-off the retreat, Philip Stewart, Director of the CBE, gave a brief history of the biofilm hypothesis in chronic wound healing and illustrated how the recent spike in publications underscores increasing interest in the biofilm hypothesis within the wound healing community. Invited speakers included Thomas Bjarnsholt, from the University of Copenhagen, Denmark, who presented some of his recent work using in situ hybridization (peptide nucleic acid probes-fluorescence in situ hybridization) in clinical specimens to evaluate the ecology of biofilms in chronic wounds. Representing the clinical importance of biofilms in chronic wounds, Gerald Lazarus and Jonathan Zenilman of the Johns Hopkins Wound Center in Baltimore, Maryland, presented recent clinical work from their laboratories that demonstrated the need for a rapid, clinically relevant tool for identification and characterization of bacteria in chronic wounds. Importantly, Drs. Lazarus and Zenilman demonstrated that commonly used qualitative assays to assess microbial burden do not correlate well with quantitative assays, indicating a need for new analytic methods for chronic wounds.

Relevant chronic wound models are needed, and highlighted at the Retreat were multiple models using various organisms. Stephen Davis, from the Miller School of Medicine, University of Miami, highlighted his research with a porcine wound model in which he demonstrated that established bacterial biofilms in wounds slowed the response time for topical antimicrobial activity. Thomas Mustoe, Chief of Plastic Surgery at Northwestern Memorial Hospital in Chicago, presented work in which his group demonstrated delayed reepithelialization caused by the presence of bacterial biofilm in a murine cutaneous wound model. Dr. Mustoe also presented a rabbit ear dermal ulcer model his group is developing to study chronic wounds. Gregory Schultz, from the Institute for Wound Research at University of Florida in Gainesville, presented work from his group on the development and demonstration of an in vitro pigskin model. Testing this model with antimicrobial dressings, Dr. Schultz's group found that multiple antibiotics and antimicrobials, such as silver, were ineffective in killing mature bacterial biofilms; however, this model did identify cadexomer iodine as an effective antibiofilm treatment. Finally, Ge Alice Zhao from the University of Washington School of Medicine presented on a murine chronic wound model they are using to assess how bacterial biofilm affects wound healing in vivo.

In vitro wound modeling has the advantages of simplicity and environmental control. Mary Cloud Ammons of the CBE presented her recent work demonstrating the use of antimicrobial treatments that act synergistically against an established biofilm. Understanding host–pathogen interactions in the biofilm contaminated wound will improve our understanding of how chronicity develops. To this end, Kelly Kirker of the CBE presented an in vitro scratch model she has developed. In this model, Dr. Kirker demonstrated that the presence of biofilm could inhibit scratch closure and that antibiotic treatment of the biofilm improved the migration of keratinocytes.

As molecular techniques evolve, their utility in the field of wound care contributes to a greater depth of understanding of the processes of wound healing and chronicity in the presence or absence of bacterial biofilm. Taking a novel research approach, Chandan Sen, the Director of the Ohio State University Comprehensive Wound Center in Columbus, Ohio, presented work from his group that utilized a knockdown model in human endothelial cells (EC), which targeted the microRNA machinery. Using this model, Dr. Sen demonstrated the importance of microRNA in regulating redox signaling and thus the angiogenic properties of EC. Oxidative stress also influences the physiology of the biofilm as was demonstrated by Haluk Beyenal of Washington State University. Using an in vitro model developed by the CBE, Dr. Beyenal found that biofilms harbored anoxic niches for each of the wound isolates tested. Finally, Pat Secor of the CBE utilized molecular and microscopic methods to examine host/pathogen interactions in vitro. Using a transwell model, he demonstrated that bacterial biofilm induced cytoskeletal disruption in both human keratinocyte and human fibroblast cell cultures. These data have significant implications for the wound healing process in the presence of bacterial biofilms.

To conclude the daylong Retreat, the CBE moderated a roundtable discussion that included all academic and industrial participants. From this roundtable discussion emerged a clear consensus on where the field of biofilm research in wound care needs to proceed. First, the clinical participants emphasized the need for clinically relevant diagnostic tools for identifying and characterizing bacterial biofilm in the wound. From the academic participants emerged a clear interest in understanding the microbial ecology associated with

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wounds and a need for more intensive molecular analysis of the interface between the host and the pathogen in biofilm infected wounds. Finally, the industrial participants expressed a need for greater clarity on regulatory policies with regard to wound treatments. All in all, the Wound Biofilm Retreat successfully demonstrated how the field of biofilm research and the field of wound care have interwoven to create a new, emerging field of critical medical importance. There remain a great many questions to be answered, but at the conclusion of the Retreat the importance of biofilm research in wound healing was clear.

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