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Production of protegrin-1 with a matrix metalloproteinase/elastase cleavage site and its therapeutic potential for skin wound infections

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Clinically-relevant pathogens are rapidly developing resistance to conventional antibiotics making infection control difficult. Methicillin-resistant *Staphylococcus aureus* (MRSA) is a gram-positive bacterium commonly found to be multidrug-resistant. As infections incited by MRSA are associated with increased rates of mortality compared to drug-sensitive strains, their presence in healthcare settings and emergence in the community is of growing concern. Protegrin-1 (PG-1) is a broad spectrum antimicrobial peptide effective against bacteria and antibiotic-resistant bacteria. PG-1 may be a potential alternative to conventional antibiotics and its promising therapeutic abilities have been previously demonstrated in infection models and in the reduction of inflammation in chemically-induced murine colitis. In the current study, proform PG-1 (ProPG) was designed to include a novel cleavage site and recombinantly generated for more efficient activation at sites of tissue inflammation. A widely selective matrix metalloproteinase (MMP) cleavage site was

inserted into ProPG 5' to the native neutrophil elastase site to allow for the more efficient release of mature PG-1 at skin inflammation sites where MMPs are abundantly expressed. *Pichia pastoris* served as the expression host for the constructed expression vector and fermentation parameters were adjusted for optimal ProPG expression and secretion. Cleavage studies of the introduced MMP site performed with recombinant mouse MMP-3, demonstrated the functionality of the inserted MMP-3 site. Future studies will verify the selectivity of the MMP site and the therapeutic potential of ProPG against MRSA infected skin wounds.

Speaker Biography

Emily K Hill is in the process of completing her MSc (Animal Biosciences) from the University of Guelph in Dr. Julang Li's laboratory. She is scheduled to defend in August 2017 and has one publication so far. An aspiring veterinarian, she will begin her DVM degree at the Ontario Veterinary College in the Fall Semester.

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