Multifunctional Peptides for Infections Free Implant Surfaces

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Statement of Purpose: Opportunistic pathogens can get onto an implant surface during a surgical procedure and cause a major infection as implant surfaces are usually suitable for pathogen attachment. If surface is not properly treated, the infection may lead to implant rejection. The conventional approach to solve this problem is to apply common antibiotics, which brings an extra concern due to increased rate of antibiotic resistance development [1]. Here we propose a bio-inspired interface that utilizes a multifunctional chimeric peptide, composed of bi-directional domains: one domain self-assembles onto implant materials and another one having antimicrobial property [2]. While peptide induce their immediate antimicrobial activity, we also couple the implant material with bioactive glass (BAG) to tune the extended antimicrobial and BAG property with slow ion release [3]. This approach incorporates multiple antimicrobial mechanisms that may significantly reduce the incidence of resistance development while providing an infection free implant material [4]. Furthermore, molecular recognition-based self-assembling peptide system provides a flexibility in controlling the properties of implant interface upon changing a functional domain for further improvement of implant performance [5].

Methods: We use TiBP-AMP (antimicrobial peptide with titanium implant recognition domain that self assembles) and two types of BAG (BAG 71: 71 % Si, 21% Ca, 4% P, 3%, 1% B and BAG 75: 75 % Si, 21% Ca, 4% P).
The experimental procedures include: 1) Antimicrobial susceptibility (against *S. mutans* and *S. epidermitis*) determination for BAGs and TiBP-AMP separately and their combination. 2) Toxicity effect for each of the antimicrobial agents and their combination on Fibroblast/Osteoblast cells. 3) Bacterial adhesion to titanium implant material surface evaluation in presence of the antimicrobial agents in solution. 4) Antimicrobial testing of titanium surface, covered with BAG, decorated with TiBP-AMP both in solution and over the surface using engineered peptides that can self-assemble on the desired surfaces. For all the tests in solution AlamarBlue is used as bacterial viability indicator. For bacterial viability on the surface Invitrogen live/dead BacLight stain is used. Bacterial viability is quantified as percent of alive bacteria in comparison to Control (non-treated bacteria – 100% alive).

Results: The current results show almost 100% reduction in S. mutans colonies viability upon exposure to solution with 200 µM of AMP. After 24 hours of exposure *S. mutans* to BAG71 in solution at 10 mg/mL concentration, only less than 5% of viability is observed, giving a great potential for long-term antimicrobial properties. For BAG75, 60 mg/mL solution leaves about 7% of viable colonies. The combination of 200 µM of AMP and 10 mg/mL of BAG71 show almost zero of bacterial colonies alive after 24 hours of exposure in solution (Fig.1).

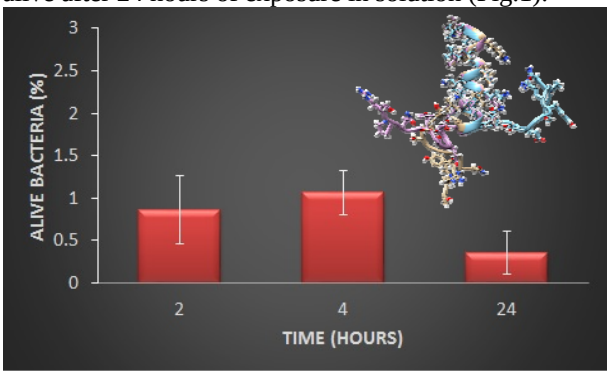

Figure 1. Effect of 200 µM AMP and 10 mg/mL BAG71 on S. mutans.

No bacterial colonies were observed on the Ti surface after 24 hours incubation of S. mutans bacteria in solution with 200 µM TiBP-AMP over a disk-shaped piece of titanium implant.

Conclusions: Antimicrobial peptide and in combination with BAG shows a significant antimicrobial effect against *S. mutans* and, potentially, against *S. epidermitis* (ongoing work). This system is very promising to fight against implant infections with reduced chance of resistance development in pathogenic bacteria. *NIH R21AR062249-02, KU #: NIH0071884 is greatly acknowledged.*

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