Novel bioengineered antimicrobial surgical implant coatings to prevent prosthetic joint infections

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Prosthetic joint infections

- Total joint replacements in the U.S. will increase from 1 to 4 million per year by 2030.

- Prosthetic joint infections occur in 1-2% of primary and 3-5% of revisions.

- Treatment of these infections involves extensive surgical and medical care.

- Increased morbidity/mortality and $25,000-$107,000 in additional costs per patient.

- The most common etiologic pathogens are staphylococcal species, including MSSA and MRSA.


Total Arthroplasties Performed and Prosthetic Infections

Bacterial biofilms form on the implanted materials


*Figure 1. Scanning Electron Micrograph of a *Staphylococcus epidermidis* Biofilm on Foreign Material.*

Bacteria grow in multicellular clusters. The scale bar represents 10 μm. (Photograph courtesy of Robin Patel, Mayo Clinic College of Medicine.)
Mouse model of MRSA prosthetic joint infection

Site of S. aureus inoculation (on pin in knee joint)
**In vivo** imaging to measure bacterial burden and neutrophil influx in real-time

1. S. aureus strain is bioluminescent (emits light)
2. Mice are LysEGFP that possess fluorescent neutrophils

*In vivo* imaging system was used to detect:

1. Bioluminescence (bacterial burden)
2. Fluorescence (neutrophil signal)

in the infected joints of live anesthetized mice.

Representative colonies of the bioluminescent S. aureus strain on a bacterial culture plate.
In vivo bioluminescent signals

Histology (post-operative day 1)

Bernthal, NM… Miller, LS. 2010. *PLOS ONE* 5(9): e12580
Biofilm formation

Bernthal, NM… Miller, LS. 2010. *PLOS ONE* 5(9): e12580
Periprosthetic osteolysis ($\mu$CT imaging)
Periprosthetic osteolysis (µCT imaging)

A  *S. aureus*-infected

B  Uninfected

Antibiotic/Antimicrobial coatings
**AIGIS$_{RX}^\text{TM}$ minocycline/rifampin polymer pouch**

Left (C) Infected implanted device with a biofilm-like material coating the surface

Right (D) An antimicrobial pouch (AIGIS$_{RX}^\text{TM}$) for cardiac implantable electronic devices protects against infection and biofilm formation

A novel antibiotic-impregnated implant coating results in reduced *S. aureus* infection and decreased inflammation.

Bernthal, NM... Miller, LS. 2010. *PLOS ONE* 5(9): e12580
A novel antibiotic-impregnated implant coating results in reduced *S. aureus* biofilm formation

Bernthal, NM... Miller, LS. 2010. *PLOS ONE* 5(9): e12580
Development of star poly(ethylene glycol)$_{44}$-poly(propylene sulfide)$_n$ (star PEG-PPS) implant coating
In vitro release of vancomycin from star PEG-PPS implant coating
In vivo efficacy of vancomycin- star PEG-PPS implant coating

A. in vivo bioluminescence (log scale)

B. CFU harvested from the joint tissue (log scale)

C. CFU harvested from the implants (log scale)
Development of poly(ε-caprolactone) PCL coating and poly(lactic-co-glycolic acid) PLGA
In vitro release of linezolid and rifampin from PCL and PLGA implant coating
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