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In vivo bioluminescence, fluorescence, µCT and photoacoustic imaging to noninvasively evaluate pathogenesis, therapeutics and diagnostics in an experimental orthopaedic implant infection

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Infection is a devastating complication following orthopaedic surgical procedures. Bacteria form bio-films on the implanted materials, creating chronic infection and inflammation that leads to periprosthetic osteolysis, implant loosening and failure. These infections are challenging to diagnose and treatment is difficult and typically requires re-operations, prolonged systemic antibiotic courses, extended disability and rehabilitation. To study these infections, we developed a mouse model of an orthopaedic implant infectionin which a bioluminescent strain of *Staphylococcus aureus* was inoculated into a post-surgical knee joint of LysEGFP mice (expressing fluorescent neutrophils) that contained a titanium Kirschner-wire extending from the femur. *In vivo* bioluminescence and fluorescence imaging was used to noninvasively quantify the bacterial burden and neutrophil recruitment, respectively. We found that bioluminescent bacteria persisted for the 48 day experiment whereas EGFP-neutrophil signals decreased within the first 14-21 days. Using µCT imaging, the outer bone volume of the femur doubled, which was associated with low-density signals and bone loss, consistent with peri-implant osteolysis. This model was used to evaluate optimal antibiotic combinations to treat an existing infection as well as the novel antimicrobial implant coatings. Finally, as a new diagnostic approach, near-infrared fluorescent probes were used in combination with advanced techniques of photoacoustic imaging. This imaging modality has the potential for clinical translation since photo acoustic signals can be detected several centimeters into tissue. Taken together, bioluminescence, fluorescence, µCT and photoacoustic imaging represent valuable noninvasive techniques to study the pathogenesis of orthopaedic implant infections and to evaluate novel therapeutic and diagnostic strategies.

Biography

Lloyd S Miller completed his MD and PhD degrees from SUNY-Downstate Medical Center and Clinical Residency & Post-doctoral fellowship training at UCLA School of Medicine. He currently is an Associate Professor in the Johns Hopkins Departments of Dermatology, Medicine (Division of Infectious Diseases) and Orthopaedic Surgery. He has published over 30 peer-reviewed manuscripts, including high impact publications in *Immunity* and *Journal of Clinical Investigation*. For more than 10 years, he has been a pioneer in utilizing *in vivo* whole animal optical (bioluminescence and fluorescence imaging), µCT and photoacoustic imaging to study infectious diseases, including orthopaedic implant infections.

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