Mouse Model of Chronic Post-Arthroplasty Infection: Noninvasive In Vivo Bioluminescence Imaging to Monitor Bacterial Burden For Long-Term Study

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Background

- 4 million arthroplasties will be performed annually in the US by 2030.
- Post-arthroplasty joint infections occur in ~1% of primary and 3-5% of revisions.
  - The most common infecting organism is *Staphyloccocus aureus*
- Implant infection is the most common cause of endoprosthetic failure
- Post-arthroplasty infections are clinically devastating, leading to reoperations, prolonged antibiotic therapy, extended disability/rehabilitation and significantly worse outcomes.
- Costs related to a post-arthroplasty infection average $144,514 -- this sums to an annual national healthcare burden of $8.63 billion by 2015.

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A Mouse Model of Post-Arthroplasty *Staphylococcus aureus* Joint Infection to Evaluate *In Vivo* the Efficacy of Antimicrobial Implant Coatings

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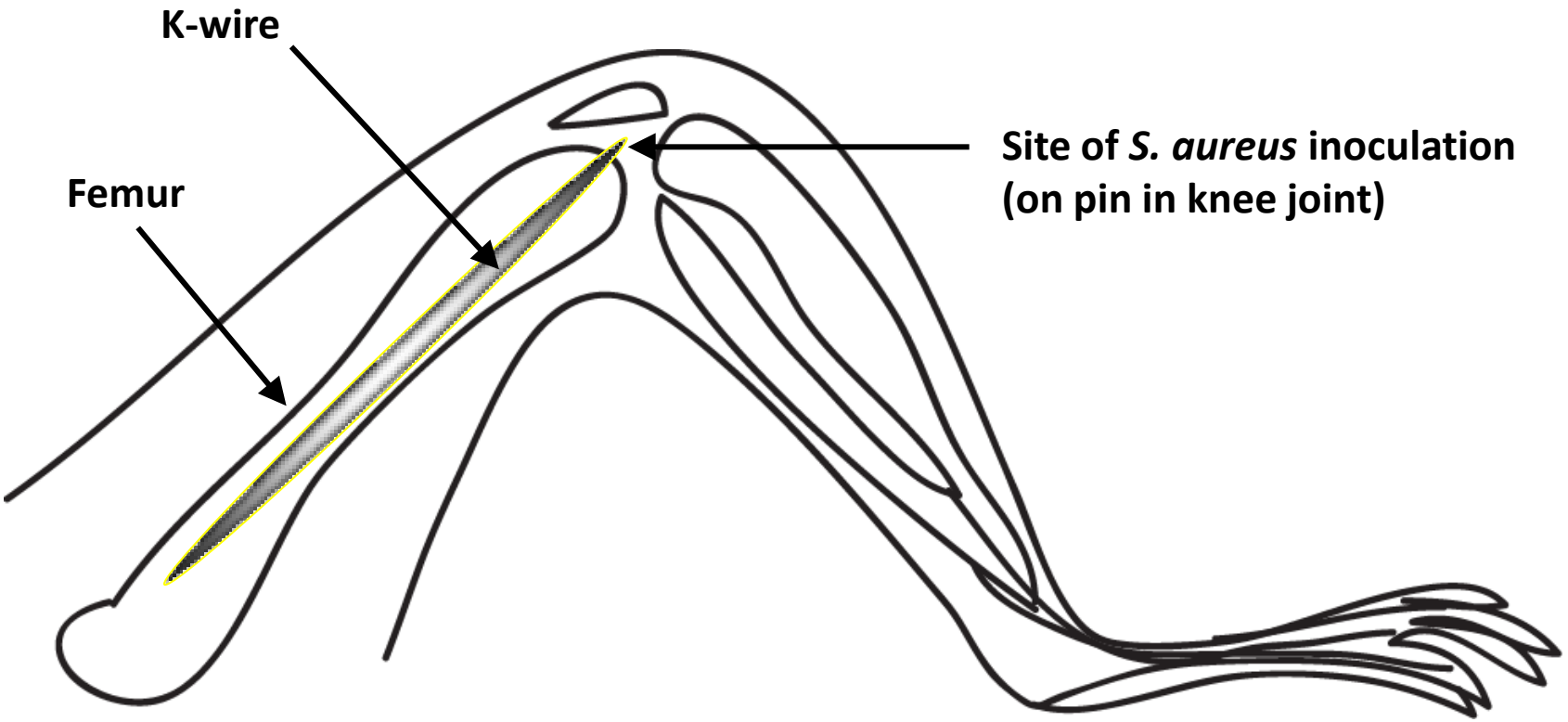

Surgical technique for placement of an intramedullary K-wire was modified from: Epstein,N.J., et al. 2005. *J. Orthop. Res.* 23:501-510.

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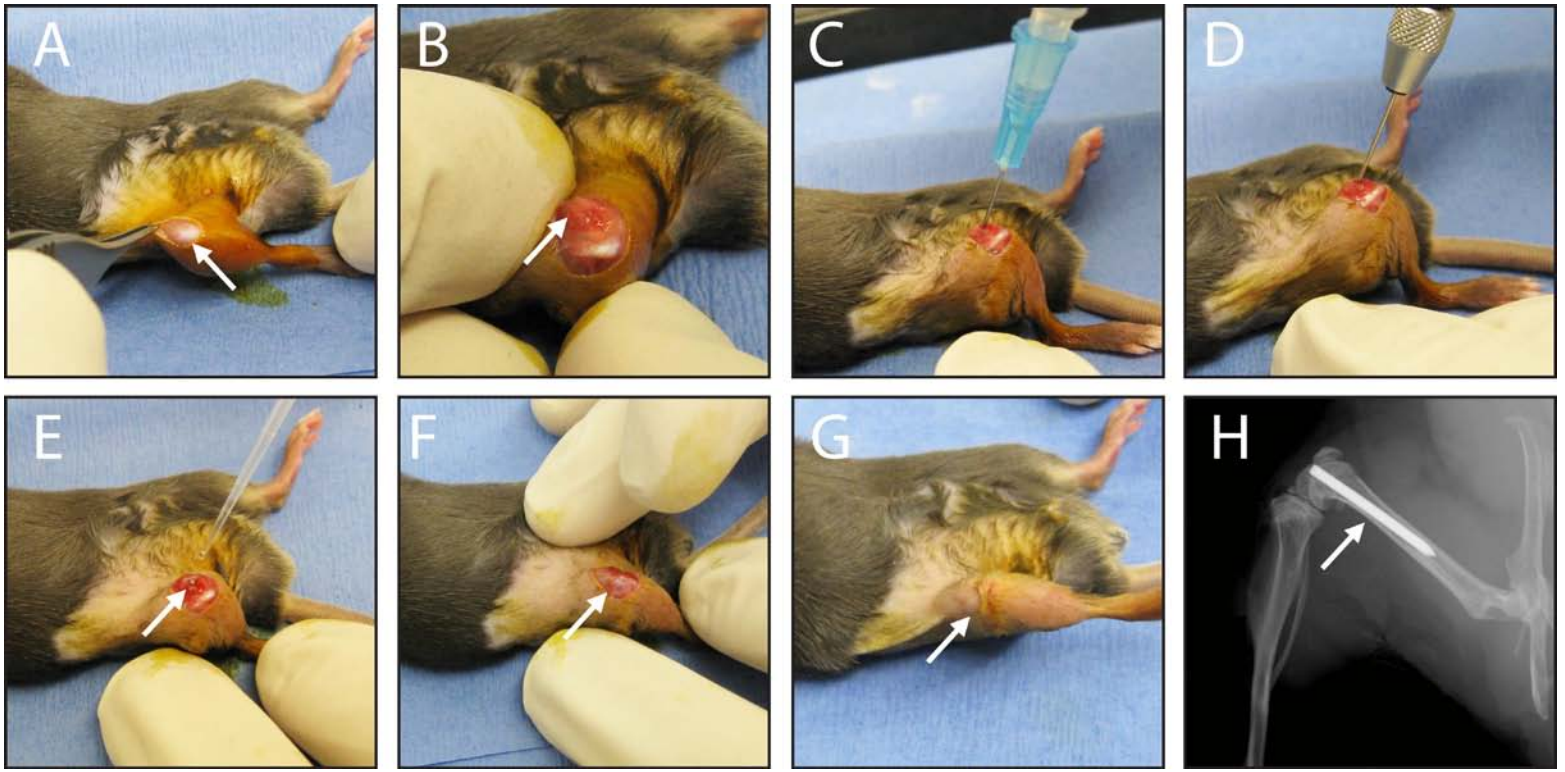

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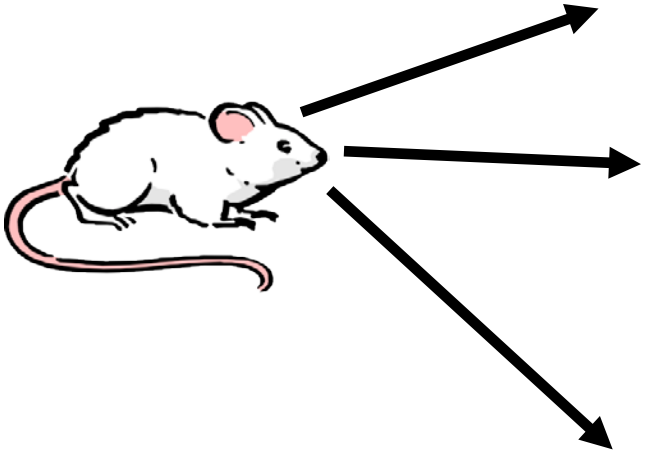
Intra-articular inoculation of bioluminescent *S. aureus*

Bacterial counts ***(in vivo*** **bioluminescence)** **(Xenogen IVIS®)**



Histology, immunohistochemistry and myeloperoxidase (MPO) assays

Variable Pressure Scanning Electron Microscopy (VP-SEM)

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- 4 commercially available strains of *S. aureus* containing the bioluminescent LUX operon:

  - ALC 2906
  - Xen 29
  - Xen 36
  - Xen 40

- These *S. aureus* strains naturally emit bioluminescent signals from live, actively metabolizing bacteria
- Our previous work correlated amount of bioluminescent signal with number of bacteria present in joint

- EGFP-Mice, genetically engineered possessing fluorescent neutrophils

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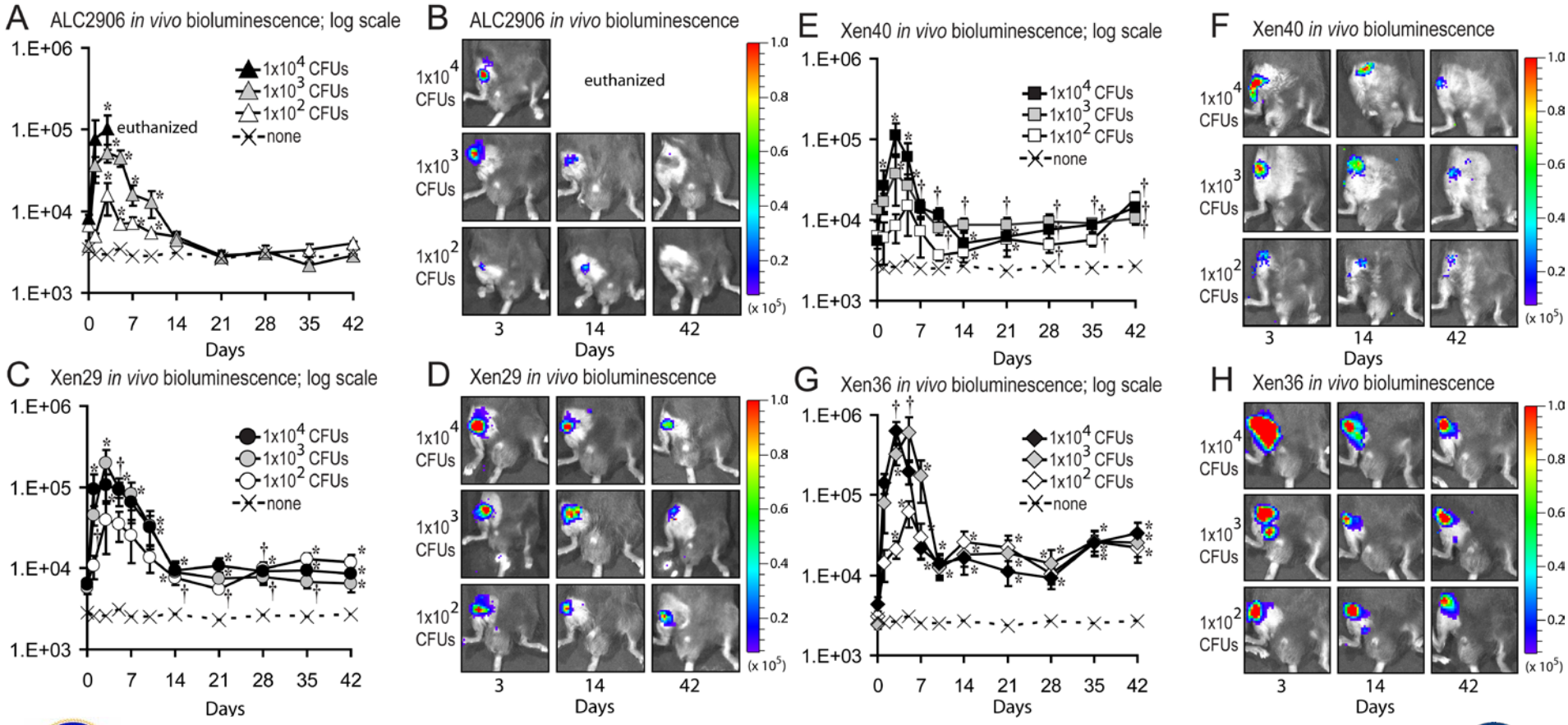
Bioluminescence



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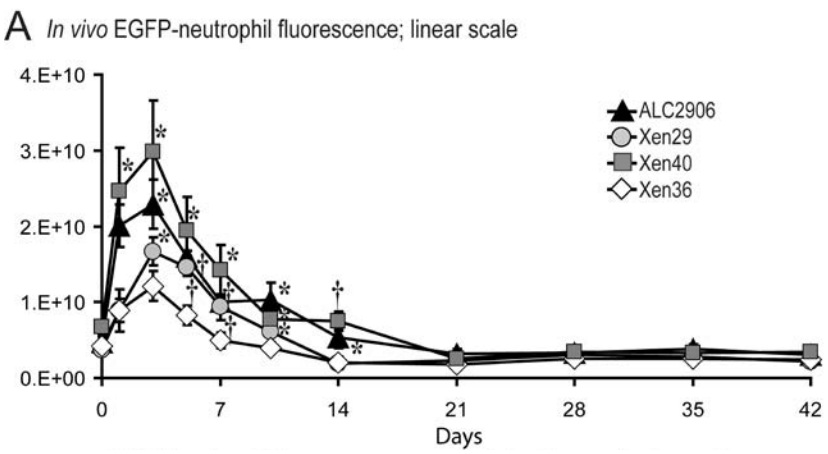
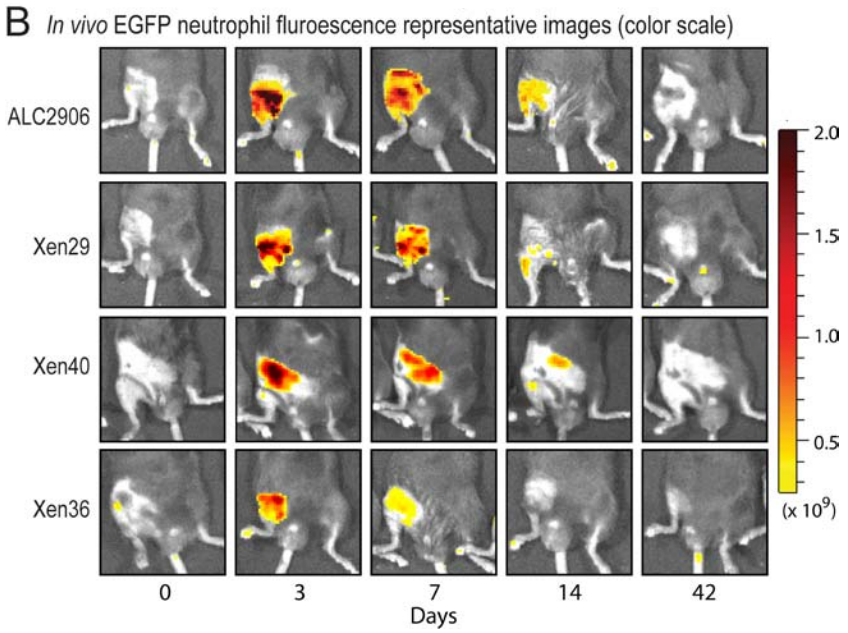
Neutrophil Recruitment





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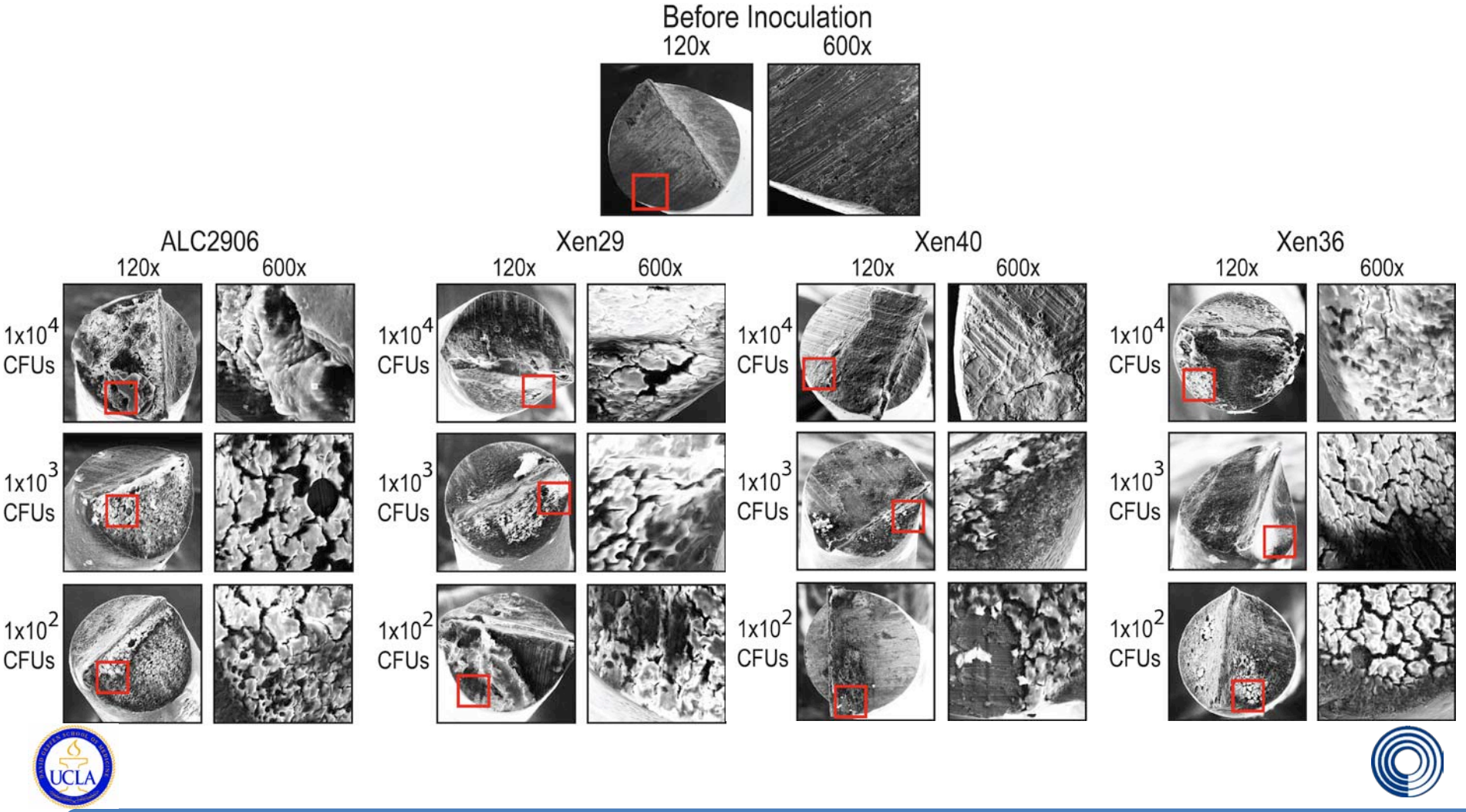
Variable Pressure Scanning Electron Microscopy



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Conclusions

S. Aureus **strains with a stable bioluminescent lux operon are useful in monitoring bacterial burden of post-arthroplasty joint infections in real time over a 6 week course, thus modeling a chronic infection.**

This model will allow the investigation of:

- **immune responses to chronic post-arthroplasty infection**
- **susceptibility to infection of commonly used orthopaedic materials (i.e. stainless steel, titanium, cobalt chrome)**
- **evaluation of antibiotic and antimicrobial coatings**

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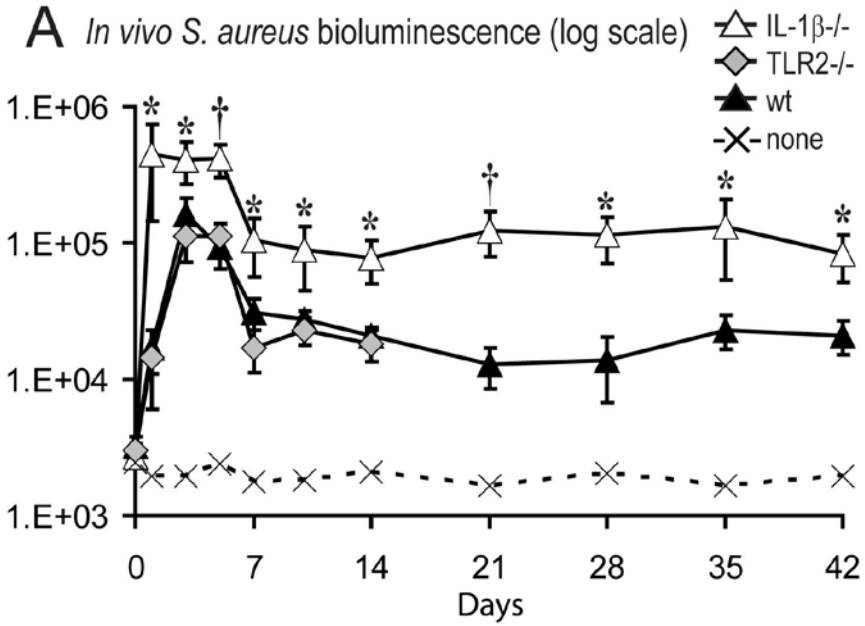
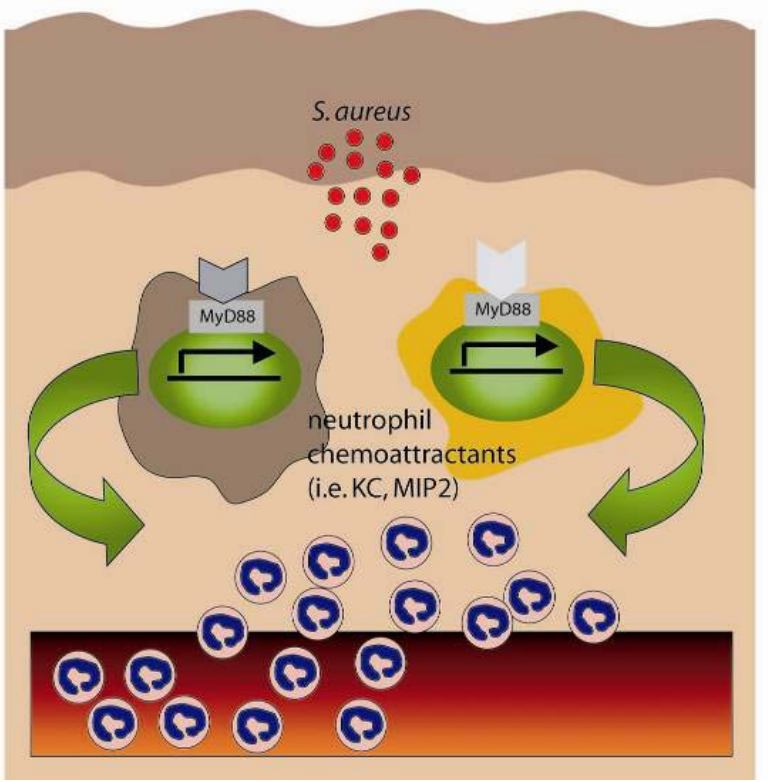
- Protective role of IL-1B by promoting neutrophil recruitment





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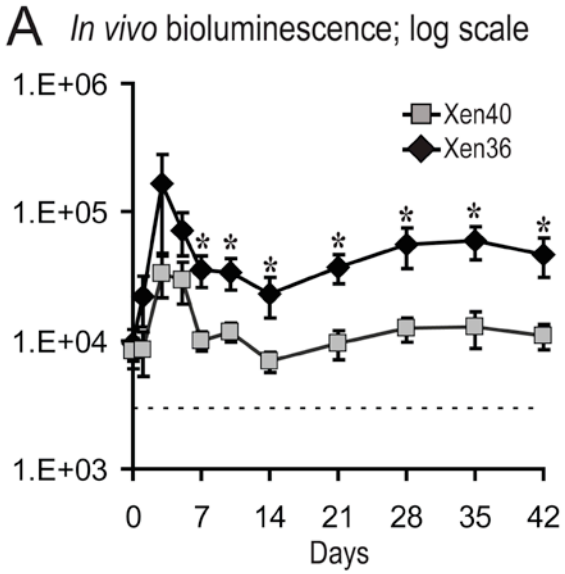
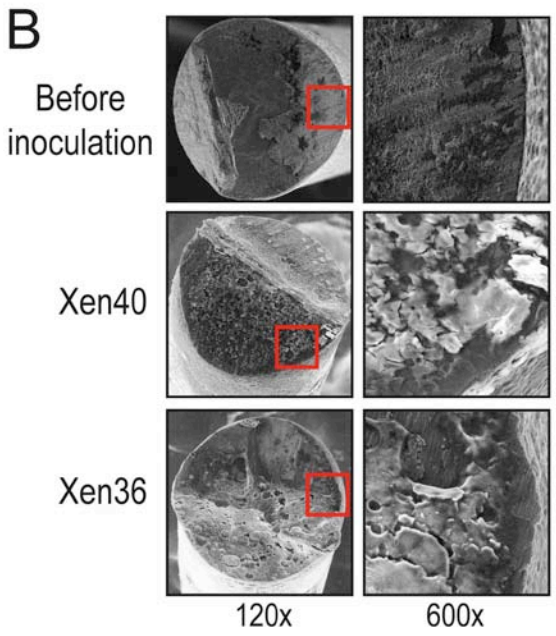
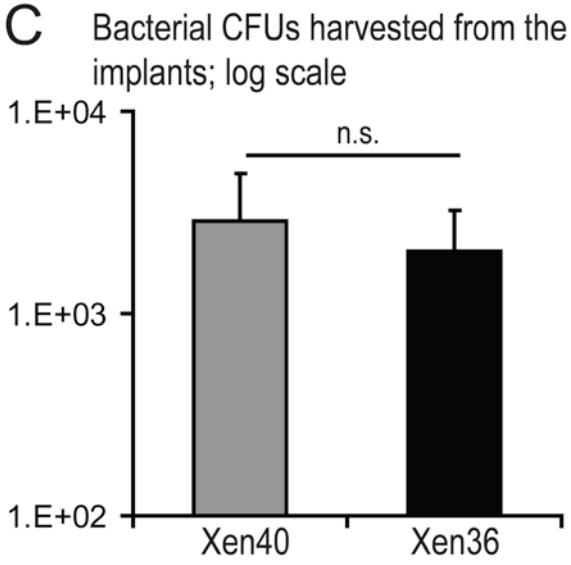
- Titanium Implants show similar infection rates as Stainless Steel Implants







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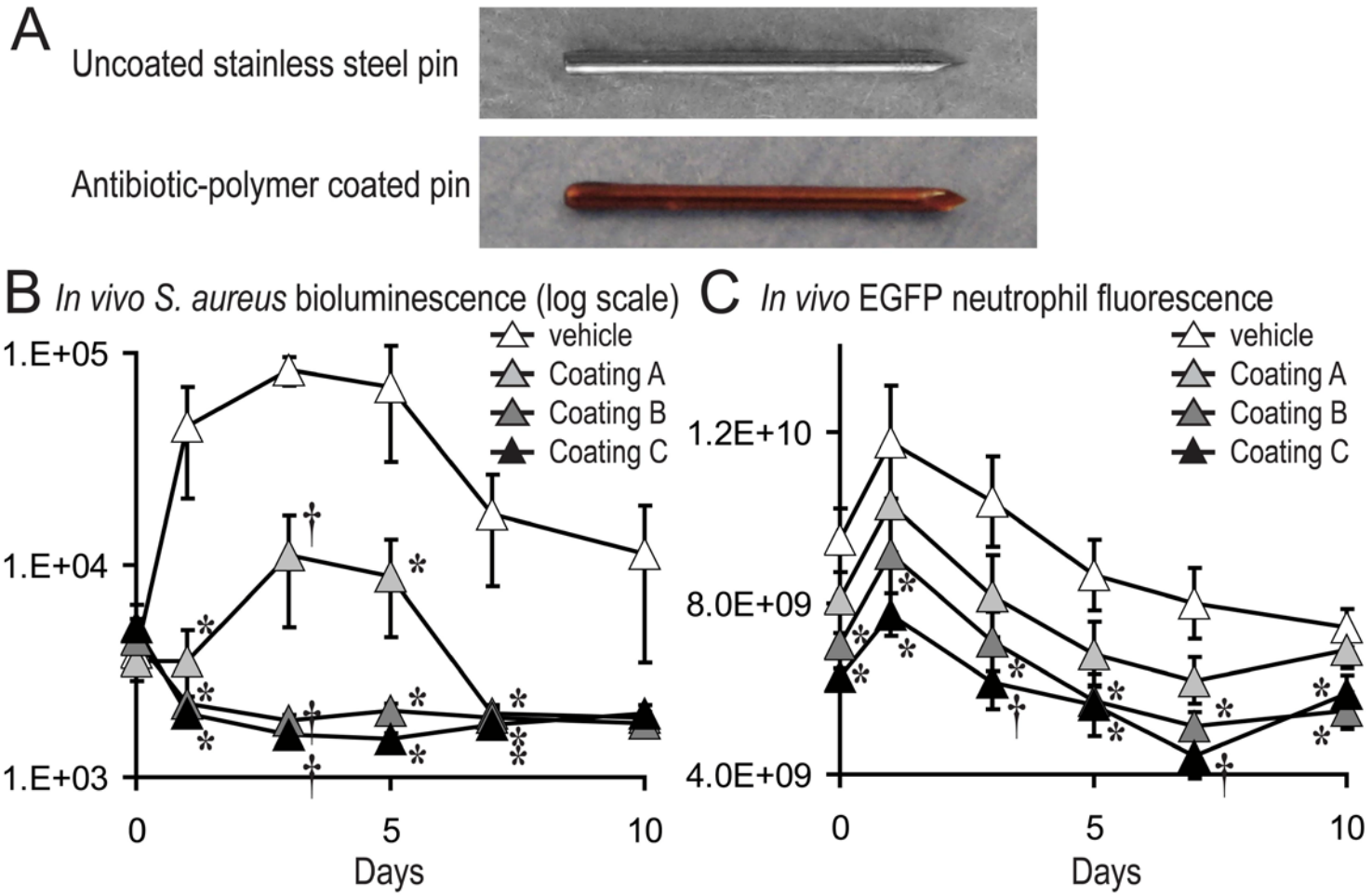
- Antibiotic Coated Pins to Prevent Post-Arthroplasty Infections



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Future Directions

- Implant infections are disastrous complications and any method to prevent them would be greatly beneficial to patients
- In Vivo bioluminescence offers a non-invasive, efficient means to longitudinally track infections
- Understanding host biology is essential
- Implant coatings are the holy grail!