

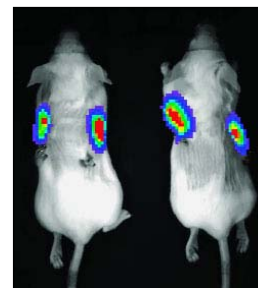
OVERVIEW SHEET

Applications in Biofilm Research

Xenogen has developed a rapid, continuous method for *in vivo* real-time monitoring of biofilms, through non-invasive imaging of bioluminescent bacteria. Luciferase-engineered strains developed by Xenogen Corporation constitutively produce light without the need for stimulation or excitation, making viable cells easily detectable.

The Features:

- **Improved data statistics:** The non-invasive procedure provides the ability to image the same animals over time, improving statistical analysis by providing an internal control.
- **More predictive data:** Improves data collection for *in vivo* animal models by sensitive real-time screening of medical device materials and/or drug compounds.
- **Quantitative monitoring of biofilms:** *In vivo* without the need for exogenous sampling and culturing.
- **Rapid and user friendly results:** Data collection is frequently accomplished in seconds to minutes. This can accelerate drug development at the animal model step.
- **Infections:** Could be studied with clinically relevant doses as low as 10^3 CFU/device.
- **Biofilm development and response to therapy:** With the ability to follow disease progression for weeks within the same animal.
- **Efficacy:** Allows examining efficacy or relapse and resistance development to therapeutic agents.



Xen5 *P. aeruginosa* colonized on catheters, imaged on Day 20

In Vivo Models

Currently Available: Subcutaneous Catheter Model

An *in vivo* mouse model of device-related biofilm infection is established by subcutaneous implantation of either pre- or *in vivo*-colonized catheters with bioluminescent, biofilm-forming pathogens. Xenogen's optical biophotonic imaging technology and biofilm-forming pathogens engineered to express light offer a method for studying chronic biofilm infection, pathogen burden and metabolic activity of biofilms, non-destructively, and directly on a support matrix. The model is useful for the study of pathogenesis and *in vivo* efficacy of therapeutic agents against both Gram-positive and Gram-negative bacterial pathogens in real-time. The imaging procedure can be repeatedly performed, thereby reducing the overall number of animals used, allowing each animal to act as its own control over time, overcoming the problem of animal-to-animal variations. The methodology is especially appealing for the analysis of efficacy of anti-microbial agents *in vivo*, as the effectiveness of the compound can be rapidly monitored without the need for exogenous sampling and culturing.

In Vivo Models Under Development

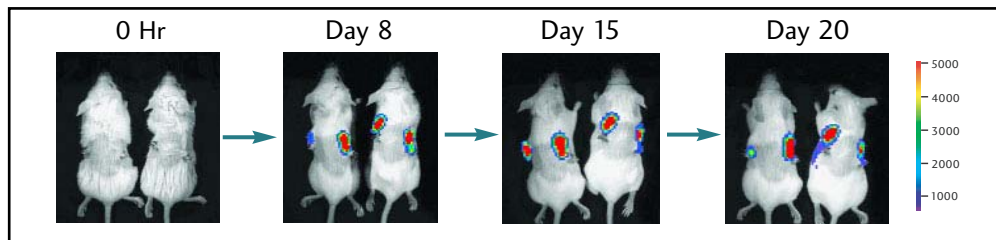
Rat Endocarditis Model (expected release date: 2Q 2003)

This is a bioluminescent adaptation of an established model, in which luminescent pathogens such as *Staphylococcus aureus* and *Pseudomonas aeruginosa* are used to infect rats with implanted cardiac catheters. Xenogen's technology can quantitatively monitor biofilm formation by these bioluminescent bacteria by repeated non-invasive imaging of the original animals throughout the disease course.

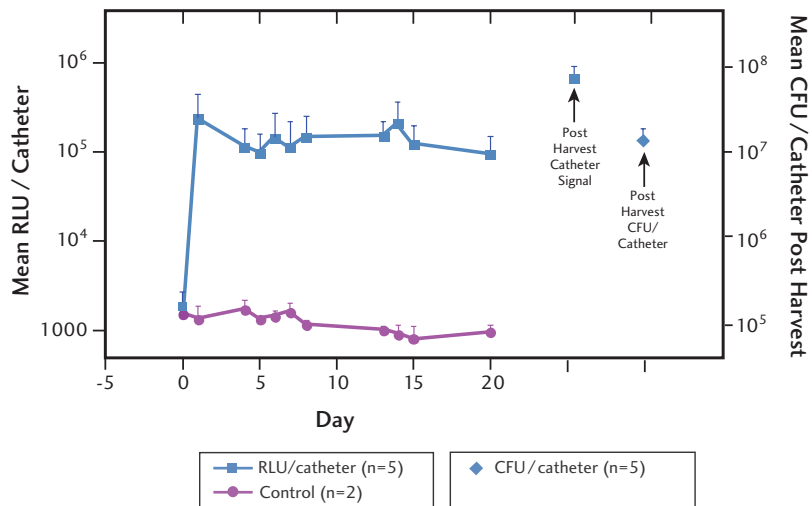
In Vitro Models

Currently Available: Biofilm Formation on Catheter Surfaces

Xenogen's optical biophotonic imaging technology and bioluminescent bacterial pathogens offers an efficient *in vitro* monitoring method to rapidly and effectively assess biofilm formation, prevention of colonization or efficacy of therapeutic agents on biofilm bacteria. The method provides information regarding physiological activities of bacteria within biofilm in real-time, thus allowing for optimizing of biofilm research.



Biofilm formed on catheters colonized by bioluminescent *S. aureus* Xen29 can be quantified *in vivo* with the Xenogen IVIS® Imaging System.



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