In vivo fluorescent imaging: a novel technique for analyzing biocompatibility

Traditional methods for analyzing the biocompatibility of materials for medical use are dependent on slow histological analyses. In this study, researchers have validated a rapid, non-invasive method for quantification of biomaterial biocompatibility in vivo.

Three materials (alginate, polystyrene and saline) were placed subcutaneously into mice, in an array format, and the host response was imaged in vivo using fluorescent whole animal imaging. Alginate is a bio-inert material used in a variety of biomedical applications, polystyrene was chosen as a positive control as it induces a strong inflammatory response, and saline was used as a negative control.

Two markers of biocompatibility, macrophage recruitment and cathepsin activity, were monitored in vivo, in real time. To image cathepsin activity, researchers used PerkinElmer’s ProSense® 680 Fluorescent Pre-clinical Imaging Agent which becomes highly fluorescent when activated by the proteases plasmin, and cathepsins B, L and S. ProSense 680 (2 nmol in 150 µl sterile PBS) was injected into the tail vein 24 hr before imaging. In vivo fluorescence imaging was performed at different time points using an IVIS® Spectrum Imaging System from Caliper Life Sciences (excitation 680 ± 10 nm, emission 700 ± 10 nm).

The figure shows a time course for cathepsin activity in response to the injected materials, and is presented as fluorescence efficiency (defined as the ratio of the collected fluorescent intensity to an internal standard of incident intensity at the selected imaging configuration).

Quantitation of cathepsin activity provided an important non-invasive measurement which was used in comparisons with standard histological analyses to validate the in vivo imaging technique as a novel method for monitoring biocompatibility. The technique is novel in that it offers the ability to repeatedly analyze foreign body responses in the same animal, thus eliminating mouse-to-mouse variations that can occur during histological analyses. The researchers predict that in vivo fluorescence imaging could overcome the bottlenecks associated with analyzing biocompatibility by offering the ability to rapidly screen large libraries of polymers in vivo.

Cathepsin activity in response to injected materials.

In vivo fluorescent imaging using ProSense 680 to image cathepsin activity at various time points for saline (A), polystyrene (B), and alginate (C). The scale bar shows the range in standard deviation (SD) from 0-6 x 10^4. D and E show the quantified fluorescence efficiencies of cathepsin activities for polystyrene (D) and alginate (E), given as the mean with SD. Symbols represent data points and lines represent linear regressions.