

Featured Publication Note

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In vivo imaging of the effects of dexamethasone on the host response to biomaterials

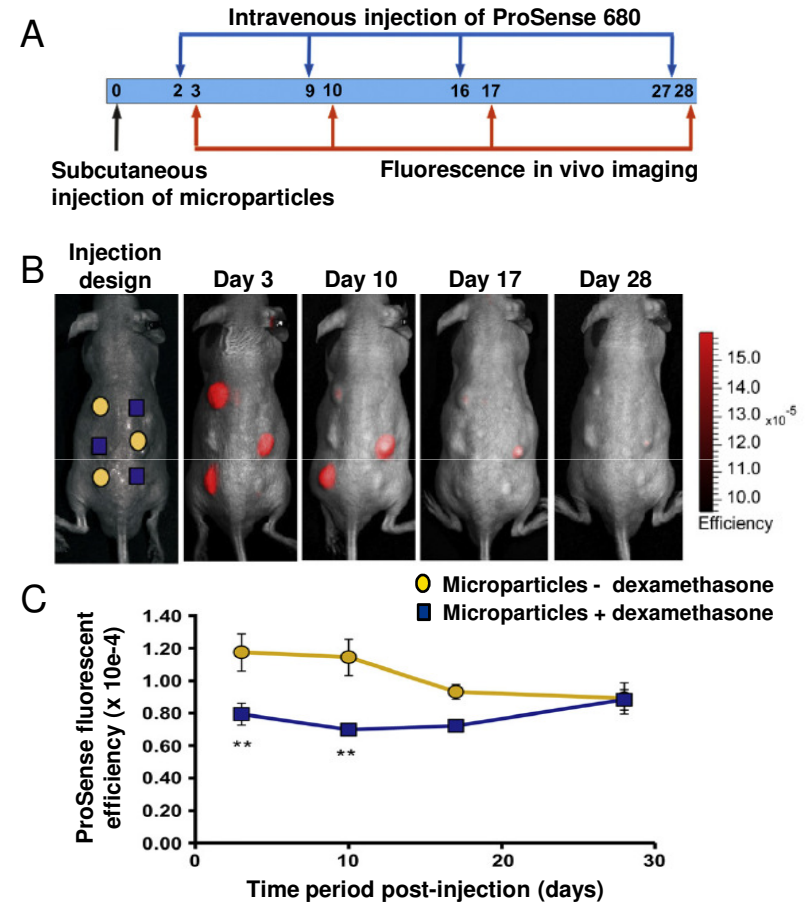
The implantation of biomedical devices into the body can induce a non-specific host response which inhibits the function of the device. This major clinical challenge can be circumvented by the incorporation of controlled-release anti-inflammatory drugs, such as dexamethasone, into the device. Previous studies into dexamethasone delivery systems have only focused on histological analyses *ex vivo* and there is a need to better understand the effects of dexamethasone on the activity of inflammatory cells *in vivo*.

In this study, researchers used non-invasive *in vivo* fluorescence imaging to investigate the spatiotemporal effects of dexamethasone on the inhibition of the innate immune response to implanted microparticles. The activity of cathepsin (an inflammatory protease secreted by immune cells) was used as an early marker of inflammation.

Dexamethasone-loaded microparticles were subcutaneously injected in an array format on the dorsal side of mice. To measure cathepsin activity, researchers injected PerkinElmer's ProSense® 680 Fluorescent Pre-clinical Imaging Agent into the tail vein of mice (2 nmol in 150 μ l sterile PBS). After 24 hr, *in vivo* fluorescent imaging was performed using an IVIS® Spectrum Imaging System from Caliper Life Sciences (excitation 650 nm, emission 720 nm). The data showed for the first time *in vivo* that controlled-release formulations of dexamethasone exhibited specific and localized inhibition of cathepsin activity in response to implanted microparticles.

To measure the temporal effects of controlled-release dexamethasone, cathepsin activity was imaged in mice over a period of 28 days (figure). The data is presented as fluorescence efficiency (the ratio of the collected fluorescent intensity to an internal reference to account for variations in the distribution of incident light intensity). Inhibition of cathepsin activity by dexamethasone was observed at the earliest time points. This result showed that monitoring cathepsin activity is useful in detecting the anti-inflammatory effect in the early phase of the host response.

The researchers believe that using controlled-release anti-inflammatory systems to modulate early cellular dynamics will improve the biocompatibility of implanted biomedical devices.



Quantitative monitoring of cathepsin activity over 28 days

(A) Timeline (days) of ProSense 680 administration and *in vivo* imaging following injection of microparticles. (B) Fluorescent images of a representative mouse at each of the time points shown in part A. All figures are of the same colour scale. (C) Quantification of fluorescent signals from four replicates over the time period shown in part A. (**) indicates $P < 0.05$ by the Student's two-sample two-tailed t -test.