In Vivo Imaging of Inflammation, Bone Formation, and Bone Resorption In A Mouse Model of Post-Traumatic Osteoarthritis

In this study we validated the use of in vivo optical imaging to track local inflammation, and the activation of osteoblasts and osteoclasts following traumatic joint injury. These techniques allow us to non-invasively and longitudinally determine the time course and spatial activity of inflammation, bone resorption, and bone formation, which previously required expensive and destructive histological analysis.

Methods: The right legs of mice were subjected to non-invasive knee injury as previously described (Christiansen et al., Arthritis Rheum, submitted). Additional mice were injected with fluorescence imaging agents, but were not injured (uninjured controls). Based on our previous data, mice were imaged at the time point of greatest inflammation (1 day post-injury), bone resorption (3 days), or bone formation (6 days). Mice were imaged using in vivo fluorescence reflectance imaging (FRI) performed on a Maestro 2 system (CRi, Woburn, MA). Mice were injected intravenously with Cat K 680, MMPSense 680, ProSense 750, or OsteoSense 800 (80 nmol/kg in 150 µL sterile saline administered via tail vein injection) 48 hours prior to imaging. Throughout imaging, mice were anesthetized via 2% isofluorane inhalation and positioned with both knees centrally located in the imaging field of view (Figures).

Results: All fluorescence imaging agents were easily detectable in both injured and uninjured mice at the time of imaging. The agents that detect inflammation (ProSense, MMPSense) had relatively higher activation in the injured knee than in the uninjured knee. However, for these agents there was widespread activation throughout field of view. In contrast, the fluorescence agents that tracked bone resorption (Cat K Sense) and bone formation (OsteoSense) were considerably more specific to the knee joints. However, there was no discernable difference between the injured and uninjured knees for these mice.

Discussion: We investigated the possible use of fluorescence imaging agents for the in vivo quantification of inflammation, bone resorption, and bone formation following knee injury in a mouse model of PTOA. We observed widespread inflammation following knee injury, with relatively higher activation in the injured knee. This is consistent with our previous results (Christiansen et al., Arthritis Rheum, submitted), which showed rapid subchondral bone loss in the uninjured limb as well as the injured limb. These data suggest that in vivo optical imaging may be a useful method for tracking inflammation following traumatic joint injury in mice.

We also observed highly localized activation of OsteoSense and Cat K Sense in both injured and uninjured knees. This is likely due to the high level of bone formation/resorption activity at the growth plates, which never close in mice. It is possible that the intense signals from the growth plates will obscure the signal produced by bone formation and resorption near the knee joint, therefore these methods may not be useful for tracking the activity of bone cells following knee injury in mice.