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14.6 MRP-Targeting in experimental rheumatoid arthritis allows monitoring of disease activity with optical molecular imaging

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Purpose

Monitoring disease activity of chronic arthritis is still a major challenge in clinical praxis. Activated macrophages play a crucial role during joint inflammation. Expression of myeloid related protein 14 (MRP14) by activated macrophages correlates with disease activity in different forms of arthritis. We analyse the use of Cy5.5-labelled antibodies against MRP14 for monitoring of inflammation activity in experimental model of arthritis using optical molecular imaging.

Methods

Anti-MRP14 antibody was coupled to Cy5.5-NHS-ester. Collagen-induced arthritis was analysed in male DBA/1lacJ-mice. Fluorochromes (anti-MRP14-Cy5.5. or IgG-Cy5.5 as control) were injected in amounts of 2 nm Cy5.5 per animal at day 25 and Fluorescence Reflectance Imaging (FRI) was performed from day 26 to 30 and signal-to-noise-ratios (SNR) were calculated. For correlation of imaging findings expression of MRP14 was confirmed by immunohistochemistry of inflamed tissue and determination of serum levels of MRP14 by ELISA. A one-way ANOVA was performed for statistical analysis.

Results

Injection of Anti-MRP14-Cy5.5 resulted in SNR which was more than three-fold higher compared to those after IgG-Cy5.5-injection (6359.2 vs. 2087.5, $p < 0.01$), confirming that the measurable signal was due to probe-to-target-binding. Fluorescence intensity correlated with clinical disease score and MRP14 serum levels: highly symptomatic mouse (clinical score 3/4) vs. asymptomatic mouse (1/4): Fluorescence Intensity 10256 vs. 4459 AU; MRP14 serum level 1450 vs. 83 ng/ml.

Conclusion

Anti-MRP14-Cy5.5 combined with FRI allows sensitive and specific detection of inflammatory activity represented by MRP14 expression in vivo. Thus imaging disease activity of inflammatory arthritis at high resolution in living animals is feasible using this approach.