

individual mouse level of different measurements of inflammation and tissue damage locally or systemically in CIA. We evaluated the impact of treatment with dexamethasone, etanercept, abatacept and zoledronic acid. Quantification of disease severity by clinical scoring of paw swelling over time is a standard method, usually followed by histological examination of the knee joint or back paws to assess inflammation, cartilage and bone loss. We evaluated alternative methods of assessing bone loss based on scoring of x-ray or micro-CT images, because they can be used for longitudinal follow-up and are less time-consuming than histology. Surprisingly, our analysis showed that scoring of x-rays rather than micro-CT images is a valuable tool for studying bone erosions in CIA and for evaluating the impact of therapy. In a second part of the study we investigated the significance of 13 locally (inflamed paws) and 10 systemically (serum) expressed proteins to be used as biomarkers to quantify disease severity. The expression of both inflammatory mediators and chemokines such as interleukin (IL)1, IL17, tumour necrosis factor α , matrix metalloproteinase (MMP)-3, KC and CxCL1 as well possible indicators of cartilage and bone damage such as COMP, CTXII, CTXI and MMP-13 were studied for their value in representing clinical symptoms. One of the most striking associations with disease severity was found with local as well as systemic levels of MMP-3, which strongly correlated with clinical disease severity and histological signs of inflammation, and responded very well to therapeutic intervention. By contrast, other frequently used markers to monitor CIA such as COMP or anti-collagen responses appeared to be less reliable in assessing response to therapy. Overall, this search for reliable read-out parameters to monitor disease activity and therapeutic responses will lead to a more optimised utility of CIA as a preclinical model for RA.

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A MULTIPARAMETER APPROACH TO MONITOR DISEASE ACTIVITY IN COLLAGEN-INDUCED ARTHRITIS

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Mouse models of rheumatoid arthritis (RA) are widely used to study initiation and progression of joint inflammation and for preclinical evaluation of new therapeutic agents. Collagen-induced arthritis (CIA) is the most widely used mouse model for RA, yet it is not clear which read-out parameters (histology, x-ray, biomarkers, microCT) are most useful in assessing CIA. We therefore undertook a comparative analysis on an