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Imaging of lesions in a murine rheumatoid arthritis model with a humanized anti-interleukin-6 receptor antibody

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Rheumatoid arthritis (RA) has been attributed to the abnormal production of cytokine interleukin-6 (IL-6), which has a variety of physiological activities. *In vivo* IL-6-receptor imaging provides useful suggestions regarding the mechanism of anti-IL-6-receptor antibody action and indicates a basic therapeutic strategy for treating RA. Therefore, this study was designed to establish a method for radiolabeling anti-IL-6-receptor antibodies and to investigate the feasibility of using radiolabeled anti-IL-6-receptor antibodies in the scintigraphic imaging of lesions in an animal RA model. Anti-IL-6-receptor antibodies were conjugated with a bifunctional chelating agent, hydorazinonicotinamide (HYNIC), and radiolabeled with technetium-99m (^{99m}Tc) using the ligand exchange reaction of ^{99m}Tc-tricine complex. The binding affinity was estimated using the U266 cell line. Whole body scintigraphy, biodistribution and autoradiography were undertaken in mice containing synovial cells that had been transplanted from an RA patient. Our findings showed that the antibodies accumulated in the implanted tissue. When radiolabeled anti-IL-6-receptor antibodies are used in scintigraphic imaging, the distribution of the IL-6-receptors is associated with the inflammatory cell infiltration that is seen in the early stage of RA. Accordingly, imaging with humanized anti-IL-6-receptor antibodies appears to be useful for detecting early pathophysiological conditions and assessing the efficacy of antibody treatment as well as the prognosis of patients with RA.

Key words: rheumatoid arthritis, interleukin-6, HYNIC, technetium-99m, scintigraphic imaging