

## **Arthritis in a model for systemic lupus: Involvement of joints, inner organs and course of autoantibodies in pristane-induced lupus.**

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**Objective.** Arthritis is frequently seen in human lupus, but rarely in lupus models. Pristane-induced lupus (PIL) can be induced in various mouse strains such as BALB/c and C57Bl/6. We herein characterize clinical and histological features of arthritis in the context of systemic lupus and provide a prudent comparison with models of rheumatoid arthritis (RA).

**Methods.** 57 BALB/c mice received pristane i.p. and were analyzed for serum autoantibodies (anti-chromatin-, -histone, -Sm), as well as for clinical features of arthritis, while PBS-injected mice served as controls. All mice were analyzed for histopathology of joints, lungs and kidneys after an experiment period of 8 months. Joint pathology was quantified by an image analysis system and by tissue cytometry. 10 C57Bl/6 mice and historical groups of two different RA models (hTNF-tg and CIA mice, respectively) were analyzed accordingly.

**Results.** In BALB/c, clinical arthritis started at 3 months, occurred finally in 79% of PIL (but not in controls,  $p < 0.001$ ) and correlated with areas of inflammation, erosion, cartilage damage, osteoclast numbers and total severity score (for all:  $r > 0.7$ ,  $p < 0.001$ ). After 8 months, 58% of PIL (but no controls,  $p < 0.001$ ) had mild-erosive arthritis: In contrast to murine RA, the most frequent inflammatory cell type of the pannus was granulocytes (17.7%), PIL had lower numbers of osteoclasts, erosions rarely affected both layers of the cortical bone and there was no progression to complete joint destruction (even after 1 year of observation). Serum auto-abs preceded arthritis and became significantly elevated in all PIL; affected joints showed increased deposits of IgG (and IgM) within the inflammatory tissue, indicative for an antibody-mediated process. All PIL mice with arthritis also had pulmonary (100%) and renal (46%) lupus. In contrast to BALB/c, Bl/6 mice did not develop any signs of arthritis.

**Conclusion.** PIL in BALB/c mice is characterized by severe organ involvement, typical auto-abs and by a mild-erosive arthritis with similarities, but also with distinct differences to RA. PIL may help to study arthritis along with other key features of SLE after therapeutic interventions or in knockout models based on a BALB/c, but not on a B1/6 background.