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ABSTRACT OF DISSERTATION

Title	<p>The immunoregulatory role of p21 in the development of the temporomandibular joint- osteoarthritis (変形性顎関節症の進展におけるp21の免疫調節作用)</p>
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<p>Objective: We aimed to identify the immunoregulatory role of the cyclin-dependent kinase inhibitor p21 in the homeostasis of mandibular condylar cartilage affected by mechanical stress.</p> <p>Materials and Methods: Ten C57BL/6 wild-type (WT) and ten p21^{-/-} mice aged 8 weeks were divided into the untreated and treated groups. In the treated groups, mechanical stress was applied to the temporomandibular joint (TMJ) through forced mouth opening for 3 h/day for 7 days. The dissected TMJs were assessed using micro-CT, histology, and immunohistochemistry.</p> <p>Results: Treated p21^{-/-} condyles with mechanical stress revealed more severe subchondral bone destruction, with thinner cartilage layers and smaller proteoglycan area relative to treated WT condyles; untreated WT and p21^{-/-} condyles had smoother surfaces. Immunohistochemistry revealed significant increases in the numbers of Caspase-3, interleukin-1β, matrix metalloprotease (MMP)-9 and MMP-13 positive cells, and few aggrecan positive cells, in treated p21^{-/-} than in treated WT samples. Moreover, the number of TUNEL positive cells markedly increased in p21^{-/-} condyles affected by mechanical stress.</p> <p>Conclusion: Our findings indicate that p21 in chondrocytes contributes to regulate matrix synthesis via the control of aggrecan and MMP-13 expression under mechanical stress. Thus, p21 might regulate the pathogenesis of osteoarthritis in the TMJ.</p>	