

## ABSTRACT OF DISSERTATION

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| Title  | <p><b>The immunoregulatory role of p21 in the development of the temporomandibular joint- osteoarthritis</b><br/> (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><b>Objective:</b> 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><b>Materials and Methods:</b> Ten C57BL/6 wild-type (WT) and ten p21<sup>-/-</sup> 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><b>Results:</b> Treated p21<sup>-/-</sup> 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<sup>-/-</sup> condyles had smoother surfaces. Immunohistochemistry revealed significant increases in the numbers of Caspase-3, interleukin-1<math>\beta</math>, matrix metalloprotease (MMP)-9 and MMP-13 positive cells, and few aggrecan positive cells, in treated p21<sup>-/-</sup> than in treated WT samples. Moreover, the number of TUNEL positive cells markedly increased in p21<sup>-/-</sup> condyles affected by mechanical stress.</p> <p><b>Conclusion:</b> 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> |  |