**TYPE II COLLAGEN DEGRADATION IS RESTRICTED TO LESION SITES IN SPONTANEOUS OSTEOARTHRITIS IN C57BL/6 AND BALB/C MICE**

*Stoop, R., Van der Kraan, P. M., Buma, P., **Poole A. R., **Billinghurst R. C., **Hollander, A.P., Van den Berg, W. B.* ** Orthopaedic Research Laboratory/Laboratory for Experimental Rheumatology, University Hospital Nijmegen. PO Box 9101, 6500 HB Nijmegen, The Netherlands. Fax: 243540230. E-mail: R.Stoop@orthp.azn.nl

**Introduction**

Osteoarthritis is considered to be a disease leading to localized destruction of articular cartilage. Degradation of type II collagen is thought to be a key step in this process, particularly since the rate of collagen turnover is very low\(^1\). In this study we investigated whether type II collagen breakdown is confined to the lesion site or elevated degradation of collagen can be seen throughout the tissue. Therefore we studied the localization of collagen degradation during spontaneous osteoarthritis in two mouse strains, C57bl/6 and Balb/c mice.

**Material and methods**

We used C57bl/6 mice (n=7) aged 2 years and Balb/c mice (n=8) aged 1 year, in which osteoarthritis develops spontaneously. After sacrifice, both knee joints were dissected, decalcified in 0.1M Tris, 10% EDTA and 7.5% polyvinylpyrrolidon (pH 7.4) and 7µm cryosections were made. All animal procedures were approved by the animal welfare committee.

HE stained sections were used to detect osteoarthritic changes. Osteoarthritic changes occurred during aging in C57bl/6 and Balb/c mice, although in different locations. Notwithstanding the difference in localization, in both strains type II collagen degradation during spontaneous osteoarthritis was restricted to areas with clearly damaged cartilage. In fibrillated areas and aligning erosions, both an upregulation of the collagenase cleavage site in type II collagen and of denatured type II collagen was observed. The staining of denatured collagen type II was more intense than the cleavage site staining. Remarkably, staining with both antibodies was restricted directly to the area where damage of the articular cartilage was seen on HE-stained sections. Areas further removed from the lesion sites (>1µm) did not show collagen degradation.

**Results**

Osteoarthritic changes could be observed in both C57bl/6 and Balb/c mice. However, a clear difference was present in the compartmental distribution of the degenerative changes (see table 1). In Balb/c mice, degenerative changes were mainly located in the patellar-femoral compartment, while in C57bl/6 mice damage was strongest on the lateral side of the tibial-femoral compartment.

<table>
<thead>
<tr>
<th>Compartment</th>
<th>C57bl/6/2yr</th>
<th>Balb/c-1yr</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrillation</td>
<td>0%</td>
<td>57%</td>
</tr>
<tr>
<td>Erosion</td>
<td>71%</td>
<td>100%</td>
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<tr>
<td>Fibrillation</td>
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<td>0%</td>
</tr>
<tr>
<td>Erosion</td>
<td>50%</td>
<td>0%</td>
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</tbody>
</table>

Table 1: Percentage of knee joints showing fibrillations and/or erosions in patellar-femoral and lateral tibial-femoral compartment.

**Discussion**

Osteoarthritic changes occurred during aging in C57bl/6 and Balb/c mice, although in different locations. Notwithstanding the difference in localization, in both strains type II collagen degradation was restricted to the lesion sites and could not be found outside damaged areas. A difficulty of studying collagen degradation by immunolocalization is that the epitopes are prone to further degradation. However, the observation that staining with both antibodies is restricted to the lesion site, where catabolism of collagen most probably is the highest, indicates that it is unlikely that the lack of staining in non-destructed cartilage is due to degradation of the epitopes. This study indicates that collagen degradation during spontaneous osteoarthritis in mice is a very local process, and that a general breakdown of articular cartilage collagen is not occurring in the affected knee joints.

**References**


**Joint Diseases Laboratory, McGill University, Montreal, Canada.**