Active involvement of “alarmins” S100A8 and A9 in regulation of synovial activation and joint destruction during mouse and human osteoarthritis.

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Synovium and its role in osteoarthritis

Synovium | Joint cavity | Cartilage
---|---|---

S100 proteins

- Intracellular function: Calcium binding proteins
- Extracellular function: Danger signals (DAMPs)
  - Secretion after activation via unknown mechanism
  - Passive release after necrosis
- 9 members are secreted: S100B, A2, A4, A6, A7, A8, A9, A11, A12
- High levels of S100A8 and A9 in OA synovial fluid
- S100A8 and S100A9 produced by neutrophils, monocytes and activated macrophages

Aim

- To determine expression of S100A8/S100A9 in synovial biopsies of early and late OA patients.
- To determine the involvement of S100A8/S100A9 in synovial activation and cartilage destruction in experimental OA.
- To study whether S100A8/A9 levels are associated with progression of joint damage in human OA?

S100A8 and S100A9 are expressed by inflamed synovium during osteoarthritis: early and endstage.

<table>
<thead>
<tr>
<th>Protein</th>
<th>mRNA levels: RT-PCR</th>
<th>Protein levels: immunolocalisation</th>
</tr>
</thead>
</table>

S100A8 and S100A9 are expressed by inflamed synovium during osteoarthritis: early and endstage.

DISCLOSURE:
NOTHING TO DISCLOSE
**Murine osteoarthritis (OA) models**

Experimental "induced" OA
- Collagenase induced OA
- DMM induced OA

**Cartilage destruction**

**Synovial activation (macrophages) is involved in cartilage degradation and osteophyte formation during collagenase-induced OA**


**Kinetics of S100 expression in synovium during murine osteoarthritis**

S100A8 and S100A9 produced by monocyte/activated macrophages

**Strong reduction of OA pathology in S100A9ko mice**

Scorings method: Pritzker et al. 2006

**No effect of S100A8/S100A9 on cartilage destruction during DMM**

Poster number: 1012
S100A8/A9 serum levels are associated with progression of joint damage in human OA

CHECK (cohort hip and cohort knee): prospective cohort study of 1002 individuals with early symptomatic OA of knee or hip

Comparison of S100A8/9 levels in individuals without damage at baseline, which do or do not show progression of joint damage (K&L) after 2 years.

<table>
<thead>
<tr>
<th></th>
<th>S100A8/9</th>
<th>BMI</th>
<th>p-value</th>
<th>n/m/f</th>
<th>Age</th>
<th>SEX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-progressors</td>
<td>487</td>
<td>26.7</td>
<td>0.06</td>
<td>96</td>
<td>21/74</td>
<td>57.6</td>
</tr>
<tr>
<td>Progressors</td>
<td>580*</td>
<td>28.4</td>
<td>0.0075</td>
<td>82</td>
<td>15/67</td>
<td>57.4</td>
</tr>
</tbody>
</table>

Significance is indicated by * and tested by Mann-Whitney test.

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