Early Differential Diagnosis of Arthritis
Quantification of HDJ2 (DNAJA1) in Synovial Fluid

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Technology

We studied Hdj2 (DNAJA1) - a member of the J-protein family of chaperones - in a large number of synovial fluids (SF) taken before or after diagnosis of arthritis. Hdj2 occurred in high frequency in samples of patients with rheumatoid arthritis, including very early samples taken long before diagnosis. In contrast, samples from patients with other forms of arthritis contained Hdj2 less frequently, and only later in the course of the disease. We suggest an assay for the detection and quantification of synovial Hdj2 in early arthritis. This assay may contribute to the differential diagnosis of rheumatoid arthritis, thus allowing efficient treatment in due time.

Innovation

- new marker for differential diagnosis of rheumatoid arthritis at an early stage
- easy and reliable method
- efficient treatment at an early stage
- may allow prediction of the course of disease
- possibility to prevent severe disease

Application

- to develop mAbs for specific detection of Hdj2
- to develop specific detection assays (ELISA and other methods)
- to develop kits for early differential diagnosis of rheumatoid arthritis

Market Potential

Arthritis occurs in more than 20 % of the adult population, leading to activity limitations in 40 % of the patients. Without treatment, severe disability may follow. Specific markers for early differential diagnosis are required to ensure the best possible treatment.

Responsible Scientist

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Patent Status

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EARLY DIFFERENTIAL DIAGNOSIS OF ARTHRITIS BY QUANTIFICATION OF HDJ2 (DNAJA1) IN SYNOVIAL FLUID

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BACKGROUND

The J-protein Hdj2 (DNAJA1, Hspj, Hsdj, dj-2) is one of ~40 known human co-chaperones. Its highly conserved J-domain shows homology to E. coli DnaJ and cooperates with Hsp70 family members. HSP70/J-protein chaperone machines not only act as „foldases“ during protein synthesis and transport, but are also involved in many physiological processes like signal transduction, apoptosis or antigen presentation.

In healthy human joints (Fig. 2), the surface of synovial tissue (ST) is covered by a thin layer of synovial lining cells (SLC), and the joint space between cartilage and ST is filled with little synovial fluid (SF). During arthritis, the amount of ST, SLC and SF increases, leading to joint effusions which may be aspired for therapy and analyses.

Earlier we described an enhanced expression of Hsc70 (but not of the inducible Hsp70) and undefined J-proteins in ST from patients with rheumatoid arthritis (RA), but not from patients with osteoarthritis (OA) (1, 2). Here we show data on the expression of Hdj2 in SF and ST of patients with RA and other forms of arthritis.

MATERIAL & METHODS

Patients were diagnosed in the Department of Rheumatology and Clinical Immunology, University Medical Center, Freiburg. All diagnoses fulfilled the appropriate criteria, e.g. RA patients were characterized according to the ACR-criteria. All procedures were approved by the local ethics committee, and patients gave their informed consent to the study.

SF were collected from 130 patients with clinically apparent joint effusions. Samples were analysed for the presence of Hdj2 by 10 % SDS-PAGE, blotting onto nitrocellulose membranes, and detection with a specific murine monoclonal antibody (KA2A5.6) using HRP-labelled anti-IgG, substrate and phosphatase interaction with HSP70 proteins: ATPase stimulation and farnesylation.

RESULTS

I. The presence of Hdj2 in synovial fluid is significantly correlated with rheumatoid arthritis

<table>
<thead>
<tr>
<th>Disease</th>
<th>All N (%)</th>
<th>Hdj2 pos. N (%)</th>
<th>Hdj2 neg. N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unselected</td>
<td>130 (100)</td>
<td>80 (61.5)</td>
<td>50 (38.5)</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td>50 (38.5)</td>
<td>37 (74.0) *</td>
<td>13 (26.0) *</td>
</tr>
<tr>
<td>Other diseases</td>
<td>80 (61.5)</td>
<td>43 (53.8) *</td>
<td>37 (46.3) *</td>
</tr>
<tr>
<td>Reactive arthritis</td>
<td>24 (18.5)</td>
<td>12 (50.0)</td>
<td>12 (50.0)</td>
</tr>
<tr>
<td>Psoriatic arthritis</td>
<td>14 (10.6)</td>
<td>8 (57.1)</td>
<td>6 (42.9)</td>
</tr>
<tr>
<td>M. Bechterew</td>
<td>4 (3.1)</td>
<td>3 (75.0)</td>
<td>1 (25.0)</td>
</tr>
<tr>
<td>M. Reiter</td>
<td>4 (3.1)</td>
<td>3 (75.0)</td>
<td>1 (25.0)</td>
</tr>
</tbody>
</table>

Tab. 1. Expression of Hdj2 in SF of patients with RA or other diseases. The presence of Hdj2 is significantly correlated to the diagnosis RA (*p = 0.021).

II. Early detection of Hdj2 in synovial fluid of patients with rheumatoid arthritis

<table>
<thead>
<tr>
<th>Patients (N)</th>
<th>Hdj2</th>
<th>Diagnosis</th>
<th>Time of detection</th>
</tr>
</thead>
<tbody>
<tr>
<td>6</td>
<td>Present</td>
<td>RA</td>
<td>11-36 months before diagnosis</td>
</tr>
<tr>
<td>5</td>
<td>Present</td>
<td>RA</td>
<td>at diagnosis</td>
</tr>
<tr>
<td>8</td>
<td>Absent</td>
<td>No RA</td>
<td>at diagnosis</td>
</tr>
<tr>
<td>7</td>
<td>Present</td>
<td>RA</td>
<td>1-24 months after diagnosis</td>
</tr>
<tr>
<td>3</td>
<td>Absent</td>
<td>No RA</td>
<td>1-24 months after diagnosis</td>
</tr>
</tbody>
</table>

III. In RA patients, presence and amount of Hdj2 correlate with the degree of inflammation and the presence of autoantibodies

REFERENCES