Clinical relevance of the shared epitope (SE)

Rheumatoid arthritis (RA) possesses a prevalence of 1% and is the most common inflammatory systemic disease regarding joints in Germany. In severe cases, RA can lead to premature invalidity within a short period of time. Hence, early diagnosis and prognosis are vital in order to initiate suitable therapy and avoid consequential damages. There is a clear genetic pre-disposition regarding RA due to some HLA-DR4 sub-types. Associated with the disease are primarily some HLA-DR4 sub-types as well as some additional sub-types of HLA alleles DR1, DR10, DR11, and DR14. All of the RA-associated HLA-DR alleles code the so-called shared epitopes (SE), which are amino acid motives QKRAA, QRRAA or RRRAA. SEs have been detected in ca. 90% of RA patients. The prevalence in individuals without RA is ca. 20-30%. In case of existing SEs, the risk of falling ill from RA is 5-10 times higher in patients with one copy, while patients with two copies possess an elevated risk of up to 30%.

Hence, the detection of shared epitopes at an early stage can render the diagnosis a lot easier. The existence of a shared epitope is an important prognostic marker regarding future progress and severity, since there is a clear connection between HLA-DR status, SE type and the disease’s course. A gene dose effect has also been detected in patients, who are carriers of two disease-associated SE alleles. These patients suffer from a more severe course of the disease more often than patients with just one or no SE-HLA allele. Especially shared epitopes of HLA allele DR4 are predicative regarding a more progressive and destructive RA form with extra-articular organ manifestations.

The detection of shared epitopes provides information for drug-related therapy

With regard to medical treatment it has turned out that RA patients with SEs do respond more often to a combination therapy with Methotrexate-Hydroxychloroquine-Sulfonamide (94% responder) than to a Methotrexate mono-therapy (32% responder). Patients with two SE alleles usually respond better to Etanercept (76%) than to Methotrexate (48%). In patients with one SE-HLA allele, the response regarding Etanercept is comparable to that of Methotrexate (41%).

**Indication**
- Detection and differentiation of clinically unclear cases of RA
- Choice of therapy
- Treatment optimisation
- Family history of rheumatoid arthritis

**Molecular diagnostics / genetics**
Detection of HLA DR1/DR4-Shared Epitope

<table>
<thead>
<tr>
<th>Number of Shared Epitopes</th>
<th>Relative risk of falling ill from RA</th>
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<tbody>
<tr>
<td>0 SE</td>
<td>one-time</td>
</tr>
<tr>
<td>1 SE</td>
<td>5-10 times</td>
</tr>
<tr>
<td>2 SE</td>
<td>30 times</td>
</tr>
</tbody>
</table>

A shared epitope (SE) has been detected on both alleles; there is an increased risk of falling ill with rheumatoid arthritis (RA). Patients carrying two SE-positive alleles face a more severe course of disease than patients that possess only one or no SE. The detected constellation is commonly associated with extra-articular forms of RA.

**Medical report**

Do you have questions? Our serviceteam will be happy to support you: +49 (0)30 770 01-220.
HLA-association regarding the antibiotic-resistant course of Lyme disease (borreliosis)

It is a well-known fact that patients with HLA-DR2 or –DR4 possess a genetic predisposition regarding the development of antibiotic-resistant Lyme borreliosis (relative risk: 22-fold!). Latest research has shown that HLA-DR associations are not limited to so-called shared epitope-carrying HLA-DR alleles. Hence, in order to identify risk patients regarding the development of a therapy-resistant borreliosis, it is recommended to administer HLA-DR sub-typing. For further information, please read our diagnostic information No. 214: „What is the added value of HLA determination regarding diagnostics and assessment of the borreliosis’ course?"

Material

2 ml EDTA blood
Transport to the laboratory is not time-sensitive and can be sent by mail.

Invoicing

Costs of the test are 116,57 €.

Literature