Autoantibodies against Glutamate Decarboxylase 65 kDa (GAD65)

Glutamate decarboxylase (GAD) catalyzes the decarboxylation of glutamate yielding in the production of gamma-aminobutyrate (GABA) and CO₂. In humans, two genes encoding different GAD isoforms have been identified. Named according to its deduced molecular weight, the pancreatic GAD65 isoform contains an N-terminal membrane-anchoring signal and localizes in the proximity of the Golgi apparatus and GABA-containing vesicles (Bu et al. 1992; Karlsen et al. 1991; Brilliant et al. 1990; Solimena et al. 1994).

Insulin-dependent diabetes mellitus (IDDM) or type 1 diabetes mellitus (T1DM) is an autoimmune disease caused by the destruction of the insulin-synthesizing pancreatic beta cells (Eisenbarth 1986). While the presence of autoimmune antibodies against pancreatic autoantigens has been associated with IDDM, their role in the pathogenesis of this disease is still under debate (Morran et al. 2015). In 1982, Baekkeskov et al. identified a 64 kDa protein, which was immunoprecipitated from lysates of human islet cells using sera from children diagnosed with IDDM. Follow-up studies confirmed this observation and revealed that the immunoprecipitated protein possessed GAD activity (Baekkeskov et al. 1989; Baekkeskov et al. 1990). Shortly thereafter, the cDNA of the GAD protein expressed in human islet cells was cloned and identified to code for GAD65 (Karlsen et al. 1991). Using sera from patients diagnosed with IDDM and recombinant human GAD65, Hagopian et al. (1993) demonstrated autoantibodies present in these sera primarily detect GAD65 rather than GAD67. Overall, GAD65 autoantibodies have been reported to be present in approximately 70 – 80 % of the sera from patients recently diagnosed with IDDM and to be detectable even before the onset of clinical symptoms (Morran et al. 2015; Hagopian et al. 1993; Seissler et al. 1993; Velloso et al. 1993).

Analyzing the interaction between human GAD65 and anti-GAD65 autoantibodies, Richter et al. (1993) identified the corresponding epitopes to be mostly conformation dependent and to be localized within GAD65’s middle and C-terminal region. These conformation dependent epitopes are also considered a possible explanation for the diminished sensitivities often observed when using standard solid-phase assays (Mauch et al. 1993; Uibo and Lernmark 2008; Törn et al. 2008; Tuomi et al. 1994). In addition, the identification of anti-idiotypic antibodies masking anti-GAD65 autoantibodies further highlights the potential limitation of conventional methods in detecting anti-GAD65 autoantibodies (Oak et al. 2008; Larsson et al. 2013).

DIARECT’S GAD65 is produced in the baculovirus/insect cell system.

References:
Baekkeskov et al. (1989) Diabetes. 38:1133-1141
Brilliant et al. (1990) Genomics. 6:115-122
Bu et al. (1992) Proc Natl Acad Sci USA 89:2115-2119
Larsson et al. (2013) PloS One. 8:e65173
Solimena et al. (1994) J Cell Biol 126:331-341
Törn et al. (2008) Diabetologia. 51:846-852
Velloso et al. (1993) J Clin invest. 91:2084-2090

In some countries the use of certain antigens in diagnostic tests may be protected by patents. DIARECT is not responsible for the determination of these issues and suggests clarification prior to use.

Ordering Information

<table>
<thead>
<tr>
<th>Lot</th>
<th>Description</th>
<th>Quantity</th>
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<tbody>
<tr>
<td>BD</td>
<td>Glutamate Decarboxylase 65 kDa (GAD65)</td>
<td>0.1 mg</td>
</tr>
<tr>
<td>A</td>
<td></td>
<td>1.0 mg</td>
</tr>
<tr>
<td>B</td>
<td></td>
<td></td>
</tr>
<tr>
<td>C</td>
<td></td>
<td></td>
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<tr>
<td>Neg. control</td>
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</tbody>
</table>

Figure: Immunodot analyses of three different lots of recombinant GAD65 using sera from a blood donor (BD) and patients (1-3) with presumed autoimmune diabetes.