Autoantibodies in Diabetes Mellitus Type 1

Insulin-dependent diabetes mellitus (IDDM) or type 1 diabetes mellitus (T1DM) is a T-cell mediated autoimmune disorder characterized by destruction of the pancreatic beta cells (Ziegler et al. 2013). Mostly starting in childhood, this leads to insulin deficiency and metabolic abnormalities (Pihoker et al. 2005). Patients require lifelong insulin treatment (Landin-Olsson et al. 1992).

In the 1970s it was described that beta cell destruction is associated with production of cytoplasmic autoantibodies to islet cells (ICAs) (Bottazzo et al. 1974). Using classic diagnostic ICA tests, polyclonal antibodies are detected in app. 85% of children with recently diagnosed T1DM (Winter et al. 2002).

In the early 1990s, new antigens were identified including 37/40 kDa tryptic fragments and the Glutamate decarboxylase (GAD) antigen (Bäkkeskov et al. 1990; Passin et al. 1995).

GAD is a pyridoxal phosphate-dependent enzyme catalyzing irreversible decarboxylation of glutamate to form gamma-aminobutyrate (GABA). Named according to its respective molecular weight, the pancreatic GAD65 isoform contains a N-terminal membrane-anchoring signal peptide and localizes in the proximity of the Golgi apparatus of islet cells and GABA-containing vesicles (Bu et al. 1992; Brilliant et al. 1990; Solimena et al. 1994). GAD65 autoantibodies appear in 70 – 80% of sera from recently diagnosed T1DM patients (Hagopian et al. 1993). However, they can also be present in nondiabetic individuals and are thus alone not strictly specific (Christie et al. 1994).

The 40 kDa antigen detected in 37/40 kDa tryptic fragments was considered to be another major target of autoimmune response in diabetes (Passin et al. 1995). The insulinoma-associated protein (IA-2), also called islet cell antigen 512 (ICA 512), is a catalytically inactive protein tyrosine phosphatase (PTP) (Bonifacio et al. 1995). It consists of an N-terminal extracellular signal sequence, a transmembrane domain and a long C-terminal intracellular tail, that harbors the majority of autoantibody epitopes (Lampasona et al. 1996). Similar to GAD it is expressed within secretory granules in neural, neuroendocrine and pancreatic islet cells (Solimena et al. 1996). Compared to GAD antibodies, IA-2 antibodies appear later and are therefore used as predictive value for upcoming T1DM onset in at-risk individuals (Achenbach et al. 2013). IA-2 autoantibodies are detected in 60 - 80% of sera from individuals with recent onset of the disease (Winter et al. 2011).

DIARECT’s antigens GAD65 and IA-2 (ICA512) are produced in the baculovirus/insect cell expression system.

References:
Achenbach et al. (2013) Diabetologia. 56: 1615-1622
Bäkkeskov et al. (1990) Nature. 347: 151-6
Bottazzo et al. (1974) Lancet. 2(7892): 1279–1283
Brilliant et al. (1990) Genomics. 6: 115-122
Bu et al. (1992) PNAS. 89: 2115-2119
Christie et al. (1994) Diabetes. 43: 1254-1259
Landin-Olsson et al. (1992) Diabetologia. 35: 1068-1073
Passin et al. (1995) PNAS. 92: 9412-9416
Pihoker et al. (2005) Diabetes. 54: 52–61
Solimena et al. (1994) J Cell Biol. 126: 331-341
Solimena et al. (1996) EMBO J. 15: 2102–2114
Ziegler et al. (2013) JAMA. 309: 2473–2479

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>Code</th>
<th>Name</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>13800</td>
<td>Glutamate Decarboxylase 65 kDa</td>
<td>0.1 mg</td>
</tr>
<tr>
<td>13801</td>
<td>GAD65</td>
<td>1.0 mg</td>
</tr>
<tr>
<td>20800</td>
<td>GAD65 biotinylated</td>
<td>50 µg</td>
</tr>
<tr>
<td>20801</td>
<td></td>
<td>0.5 mg</td>
</tr>
<tr>
<td>30500</td>
<td>IA-2 (ICA 512)</td>
<td>0.1 mg</td>
</tr>
<tr>
<td>30501</td>
<td></td>
<td>1.0 mg</td>
</tr>
</tbody>
</table>

Figure: Immunodot analyses of GAD65 and IA-2 in triplicates using a polyclonal IA-2 antibody (pAb), sera from T1DM patients (PS1-2) and blood donors (BD1-2). As positive (serum) controls, goat anti-human IgGMA (C) and IgG are used. As negative control HSA was spotted on nitrocellulose membrane.