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 (Bækkeskov *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).

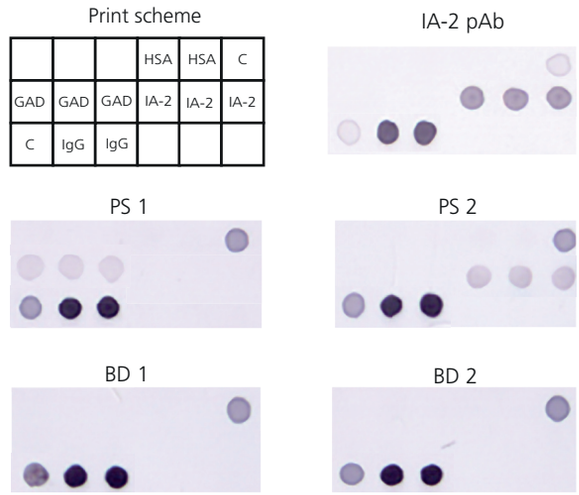

Figure: Immunodot analyses of GAD65 and IA-2 in triplicates using a polyclonal IA-2 antibody (pAb), sera from T1DM patients (PS1-2) and blood donors (BD1-2). As positive (serum) controls, goat anti-human IgGMA (C) and IgG were used. As negative control HSA was spotted on nitrocellulose membrane.

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

Ordering Information		
13800 13801	Glutamate Decarboxylase 65 kDa (GAD65)	0.1 mg 1.0 mg
20800 20801	GAD65 biotinylated	50 µg 0.5 mg
30500 30501	IA-2 (ICA 512)	0.1 mg 1.0 mg

References:
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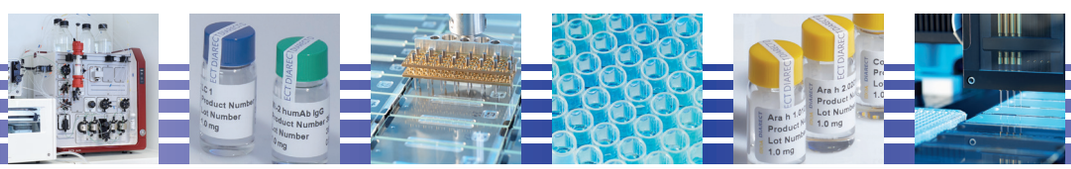

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