

GAD65 and IA-2 Antigens

Insulin-dependent diabetes mellitus (IDDM) or type 1 diabetes mellitus (T1DM) is a T-cell mediated autoimmune disorder characterized by destruction of 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 the production of autoantibodies to cytoplasmic antigens of islet cells (ICAs) (Bottazzo *et al.* 1974). Using classic diagnostic ICA tests, polyclonal antibodies are detected in approximately 85% of children with recently diagnosed T1DM (Winter *et al.* 2002).

In the early 1990s, new antigens were identified including a 37/40 kDa tryptic fragment, which was identified to belong to the putative tyrosine phosphatase insulinoma-associated protein (IA-2), as well as the glutamate decarboxylase (GAD) antigen (Bækkeskov *et al.* 1990; Passini *et al.* 1995).

GAD is a pyridoxal phosphate-dependent enzyme that catalyzes the irreversible decarboxylation of glutamate to form gamma-aminobutyrate (GABA). Named according to its respective molecular weight, the pancreatic GAD65 isoform contains an N-terminal membrane-anchoring signal peptide and localizes in the proximity of the Golgi apparatus of islet cells and GABA-containing vesicles (Brilliant *et al.* 1990; Bu *et al.* 1992; 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 specific (Christie *et al.* 1994).

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 anti-GAD antibodies, anti-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 (ICA 512), are produced in the baculovirus/insect cell expression system.

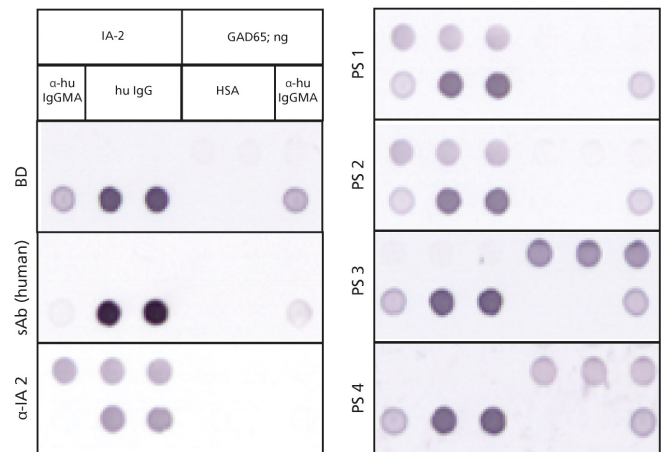


Figure: Immunodot analyses of new generation GAD65; ng and IA-2 in triplicates using a rabbit polyclonal anti-IA-2 antibody (α -IA-2), an anti-human secondary antibody (sAb (human)), sera from T1DM patients (PS1-4) and a blood donor (BD). As positive controls, goat anti-human IgGMA (α -hu IgGMA) and IgG were used. As negative control HSA was spotted on nitrocellulose membrane.

References:

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- Winter *et al.* (2002) *Clinical Diabetes*. 20 (4): 183-191
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- Ziegler *et al.* (2013) *JAMA*. 309 (23): 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

31900	Glutamate Decarboxylase 65 kDa	0.1 mg
31901	(GAD65; ng)	1.0 mg
30500	IA-2 (ICA 512)	0.1 mg
30501		1.0 mg

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