

ABOUT AUTOIMMUNE DIABETES

What is Diabetes mellitus (DM)?

DM is a metabolic disorder of multiple etiology characterized by chronic hyperglycaemia. It results from defects in insulin secretion, insulin action, or both. Diabetes mellitus can be classified into two major types: type 1 diabetes, characterized by severe insulin deficiency, and type 2 diabetes, predominantly characterized by insulin resistance with relative but not absolute severe insulin deficiency. Whereas patients with type 1 diabetes are often insulin dependent, type 2 diabetes patients usually do not require insulin treatment for years after the onset of the disease.

Type 1 Diabetes mellitus (T1DM)

T1DM is the result of autoimmune destruction of insulin-producing beta-cells of the islets of Langerhans in genetically susceptible individuals. Patients suffer from increased thirst and hunger, polyuria, blurring of vision, fatigue, and weight loss. T1DM is characterized by the presence of autoantibodies that recognize antigens including insulin, glutamate decarboxylase (GAD65 kDa isoform) and tyrosine phosphatase-related protein IA2.

These autoantibodies appear to develop sequentially. Antibodies against insulin are often expressed first, especially in young children. Anti-GAD antibodies may represent a propensity for general autoimmunity whereas antibodies against IA2 are a more specific marker of beta-cell destruction.

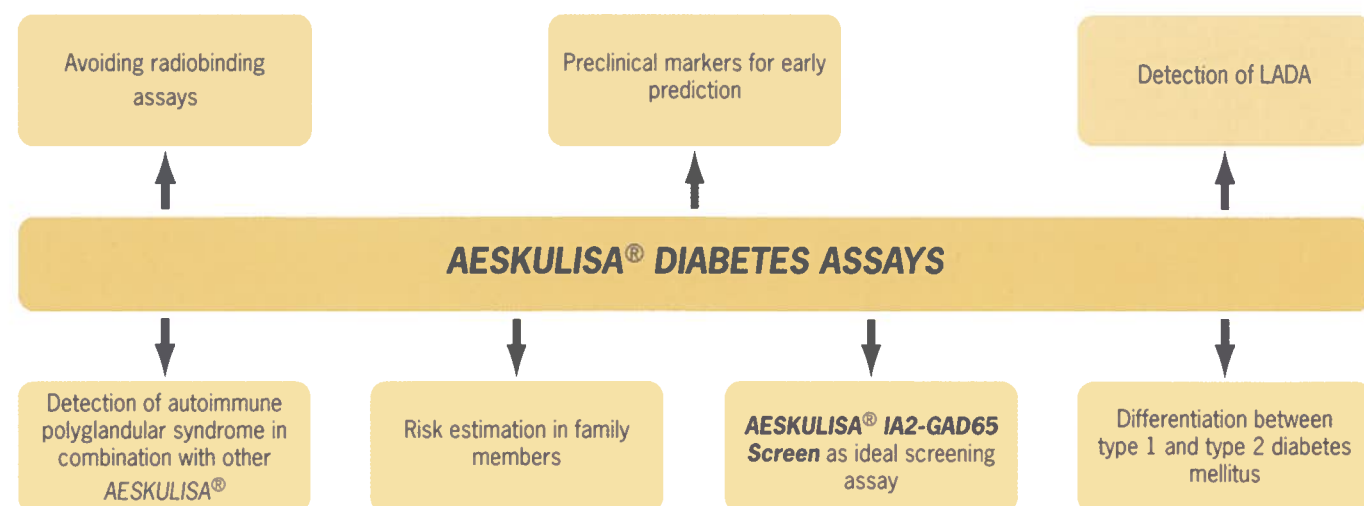
WHY MEASURE THE AUTOIMMUNE DIABETES MARKERS?

Preclinical markers - Autoantibodies against islet cell antigens are important preclinical markers as they may be present for years before diagnosis of diabetes and at a time where other metabolic assays show normal diagnostic findings. In approximately 90% of new-onset type 1 diabetes patients, one or more beta-cell autoantibodies are present.

Disease prediction - Detection of two or more islet autoantibodies is associated with a higher risk of T1DM than a single autoantibody. Also the risk for first degree relatives depends on the number and type of antibodies that are present. Therefore, the testing for multiple antibodies is important for risk assessment.

Classification of diabetes types - T1DM often develops in children and adolescents but can also manifest in adults. Special attention should be paid to the latter group of patients termed LADA (latent autoimmune diabetes of the adult) because they may be misdiagnosed as type 2 diabetes but have immunological and genetic features consistent with T1DM.

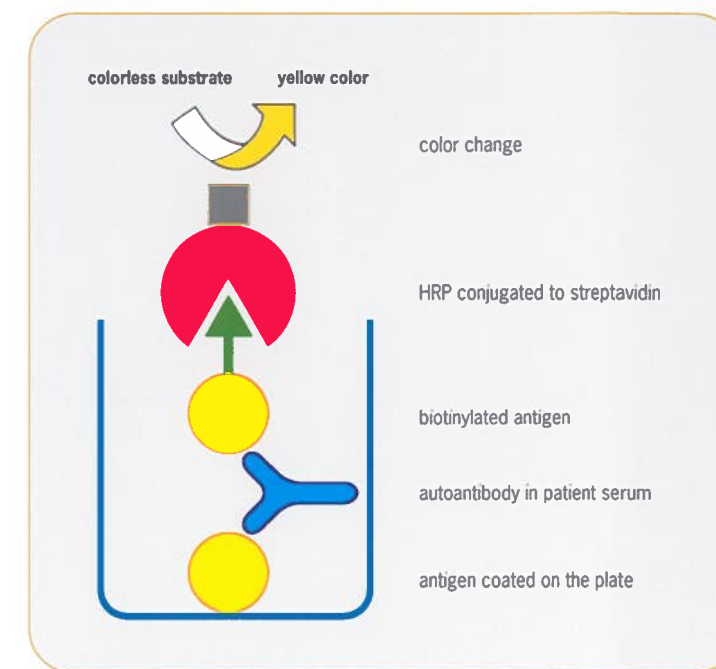
Identification of polyglandular syndrome - T1DM shows an increased prevalence of organ specific autoimmune disorders such as autoimmune thyroid disease, celiac disease, autoimmune gastritis, Addison's disease and vitiligo. Up to one third of T1DM patients develop an autoimmune polyglandular syndrome.



ASSAY PRINCIPLE

The AESKULISA® IA2, the AESKULISA® GAD65 and the AESKULISA® IA2-GAD65 Screen are based on the same principle. Microtiter plates are coated with the recombinant human antigen. Patient sera are applied to the plate and incubated overnight. Specific antibodies bind to the antigen coated on the plate and unbound sample will be washed off in the following washing step. Afterwards the respective biotinylated antigen is added to the plate that binds to the immune complex due to the second binding site of the antibody.

After a washing step the plate is incubated with peroxidase-conjugated streptavidin that binds to the biotin attached to the plate. After addition of the substrate a color formation will be visible and its intensity is proportional to the concentration of antibodies in the patient sample.



- Sample volume: minimum of 25 µl
- All diabetes assays can be run in parallel with the rest of the AESKULISA® autoimmune line

IA2	30'/30'/30' (with sample pre-incubation step of 16hrs)
GAD65	30'/30'/30' (with sample pre-incubation step of 16hrs)
IA2-GAD65 Screen	30'/30'/30' (with sample pre-incubation step of 16hrs)
Insulin	30'/30'/30'
AESKULISA® autoimmune line	30'/30'/30'
- AESKULISA® common reagents: sample buffer, wash buffer, substrate and stop solution
- AESKULISA® IA2 and AESKULISA® GAD65 are calibrated against the WHO reference reagent NIBSC code 97/550
- Calibration range for IA2 and GAD65: 0-500 IU/ml; for IA2-GAD65 Screen: 0-500 U/ml and for Insulin: 0-300 U/ml
- Choice of qualitative or quantitative interpretation

BENEFITS

Cost-effective

- AESKU.Diagnostics offers a complete Autoimmune Diabetes panel allowing simultaneous determination of autoantibodies against IA2, GAD65 and Insulin.
- AESKULISA® IA2-GAD65 Screen is a cost-effective screening assay useful to identify individuals with a high risk for type 1 diabetes because it allows the simultaneous measurement of GAD65 and IA-2 autoantibodies in the same sample.

Simplified workflow

- The AESKULISA® from the Autoimmune Diabetes panel have a comparable sensitivity and specificity to the radiobinding assays (RIA). Additionally, our ELISAs save the need for special equipment and complicated technical and regulatory requirements of the RIA.
- AESKULISA® IA2, AESKULISA® GAD65 and AESKULISA® IA2-GAD65 Screen share the same calibration range and the same cut-off value.

Automation friendliness

- All diabetes assays can be run in parallel with the rest of the AESKULISA® autoimmune line.
- Simplified automation due to the same test procedure, common reagents and easy handling.

STUDY RESULTS (EXAMPLE)

35 IA2-positive samples and 35 GAD65-positive samples (based on RIA) were tested in the Aeskulisa® IA2 and the Aeskulisa® GAD65, respectively. Additionally, all of these samples were tested in the Aeskulisa® IA2-GAD65 Screen. For all assays a control group was used consisting of 64 healthy donors and 32 sera from patients with other autoimmune diseases.

Aeskulisa® IA2	Diagnosis		Total	Aeskulisa® IA2
	Positive	Negative		
Positive	30	3	33	85.7% Sensitivity
Negative	5	93	98	96.9% Specificity
Total	35	96	131	

Aeskulisa® GAD65	Diagnosis		Total	Aeskulisa® GAD65
	Positive	Negative		
Positive	35	3	38	100% Sensitivity
Negative	0	93	93	96.9% Specificity
total	35	96	131	

Aeskulisa® IA2-GAD65 Screen	Diagnosis		Total	Aeskulisa® IA2-GAD65 Screen
	Positive	Negative		
Positive	70	5	75	100% Sensitivity
Negative	0	91	91	94.8% Specificity
Total	70	96	166	

REF 3604
Aeskulisa®
IA2-GAD65 Screen

Conjugate:
Streptavidin-HRP
Standard Range:
0 - 500 U/ml
Kit Configuration:
Screening-G

REF 3602

Aeskulisa®
IA2

Conjugate:
Streptavidin-HRP
Standard Range:
0 - 500 IU/ml
Kit Configuration:
Single-G

REF 3603

Aeskulisa®
GAD65

Conjugate:
Streptavidin-HRP
Standard Range:
0 - 500 IU/ml
Kit Configuration:
Single-G

REF 3601

Aeskulisa®
Insulin

Conjugate:
anti-human IgG-HRP
Equivocal Zone:
12 - 18 U/ml
Standard Range:
0 - 300 U/ml
Kit Configuration:
Single-G

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A COMPLETE PANEL FOR AUTOIMMUNE DIABETES TESTING



IA2-GAD65
INSULIN
GAD65
IA2

AESKULISA® DIABETES LINE

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THE DIAGNOSTIC TOOL THAT WORKS