



Roma, 9-12 novembre 2017



ITALIAN CHAPTER



IL LABORATORIO NELL' INQUADRAMENTO DEL DIABETE

Auto-anticorpi: quali, come e quando

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Conflitti di interesse



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Ai sensi dell'art. 3.3 sul conflitto di interessi, pag 17 del Regolamento Applicativo Stato-Regioni del 5/11/2009, dichiaro che negli ultimi 2 anni non ho avuto rapporti diretti di finanziamento con soggetti portatori di interessi commerciali in campo sanitario



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Islet Autoantibodies



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Autoantibody	Acronym	Autoantigen	First evidence	Journal	Year
Anti-Islet Cells	ICA	Whole cell	Bottazzo GF, et al.	Lancet 2:1979-83	1974
Anti-Insulin	IAA	Insulin	Palmer J, et al.	Science 222:1337-9	1983
Anti-GAD65	GADA	Glutamic Acid Decarboxylase 2	Baekkeskov S, et al.	Nature 347;151-6	1990
Anti-IA-2	IA-2A	Tyrosine Phosphatase like Protein IA-2	Bonifacio E, et al.	J Immunol 155:5419-26	1995
Anti-ZnT8	ZnT8A	Zinc Transporter 8	Wenzlau JM, et al.	PNAS USA 104:17040-5	2007
Anti-TSPAN7	GLIMA	Tetraspanin family member 7	McLaughlin K, et al.	Diabetes 65:1690-8	2016

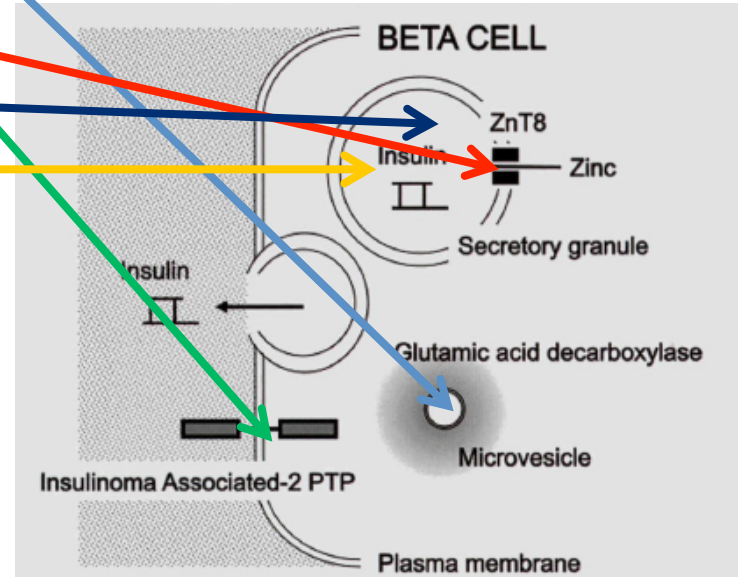


Islet Autoantigens



- Enzymes: Glutamic Acid Decarboxylase
- Enzymes: Tyrosine Phosphatase
- Transporters: Zinc Transporter 8
- Mediators: Tetraspanin 7
- Hormones: Insulin

Lampasona V, Liberati D.
Curr Diab Rep 2016;16:53





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Islet autoantibodies: methods of detection/measurement



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Autoantibody	Method
ICA	Indirect Immunofluorescence (human/non-human primate pancreas)
IAA	Radio-immunoprecipitation, ELISA, CLIA
GADA	Radio-immunoprecipitation, ELISA, CLIA
IA-2A	Radio-immunoprecipitation, ELISA, CLIA
ZnT8A	ELISA



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Islet autoantibodies

(Winter WE, Pittman MD, 2013, modified)



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AAb	Frequency at diagnosis (%)	Persistence following diagnosis of T1DM	Ease of detection	Recommended for screening
ICA	70-80	Least persistent	+ (manual)	Test for ICA if the subject is positive for ≥ 1 other islet Aab
IAA	49-67	Not defined	++ (middle automated)	Test for IAA if the subject is positive for ≥ 1 other islet Aab
GADA	80-83	Most persistent	+++ (high automated)	Yes
IA-2A	41-68	Least persistent	+++ (high automated)	Yes
ZnT8A	39-61*/**	Most persistent	+++ (high automated)	Test for ZnT8A if the subject is positive for ≥ 1 other islet Aab

*Kawasaki E. Clin Pediatr Endocrinol 2014;23:99-105

** Fabris M, et al. Auto Immun Highlights 2015;6:17-22



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Ruolo diagnostico degli auto-anticorpi associati al diabete



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Quando non è possibile distinguere clinicamente il DMT2 dal DMT1



Pazienti con iperglicemia

Pazienti con DM Tipo 2, per identificare il LADA

Pazienti con diabete gestazionale, per identificare il DM1 autoimmune

Pazienti con iperglicemie transitorie o intermittenti

Soggetti con alterazione della tolleranza ai carboidrati

Soggetti con pre-diabete autoimmune



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Ruolo predittivo degli auto-anticorpi anti-insula



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- Familiari di soggetti con DM1
- L'insorgenza di diabete è strettamente correlata al numero di anticorpi rilevati



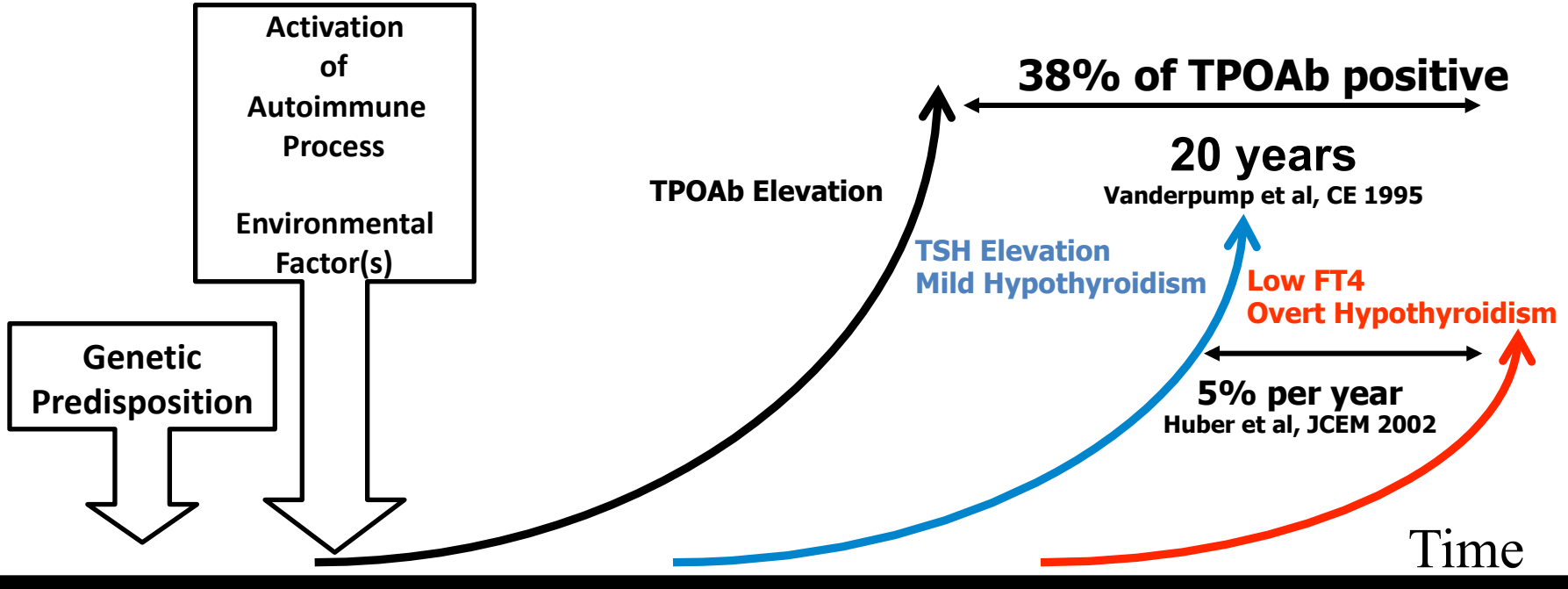
TPOAb as predictors of hypothyroidism in Hashimoto's thyroiditis

Tozzoli R. The diagnostic role of autoantibodies..... Clin Chem Lab Med 2008



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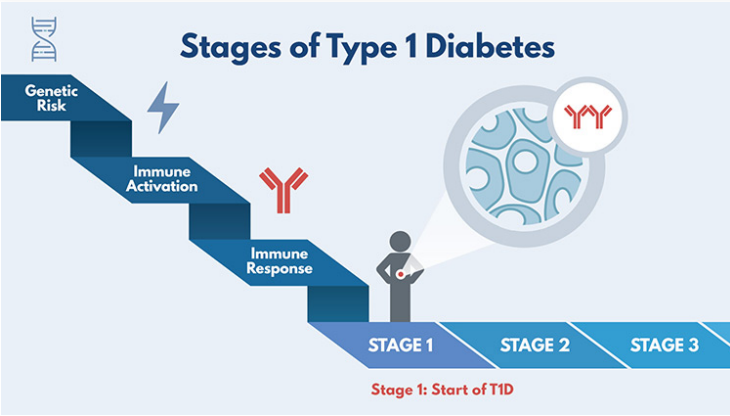


Natural history of T1DM



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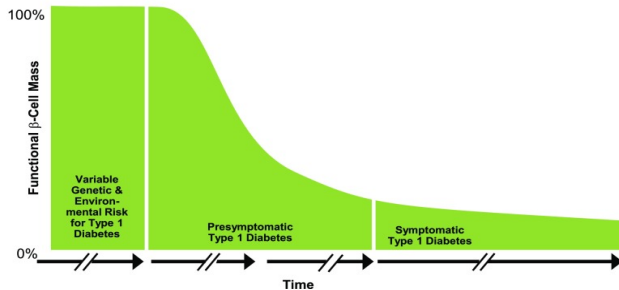
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Statement of JDRF, ES, ADA
 Insel RA, et al. Diabetes Care 2015;38:1964-74

Immune response: Development of a single autoantibody
 Stage 1: Normal blood sugar; ≥ 2 autoantibodies; no symptoms
 Stage 2: Abnormal blood sugar; ≥ 2 autoantibodies; no symptoms
 Stage 3: Clinical diagnosis; ≥ 2 autoantibodies; symptoms

Proposed Nomenclature	Stage 1	Stage 2	Stage 3
Phenotypic Characteristics	β -Cell Autoimmunity Normoglycemia Presymptomatic	β -Cell Autoimmunity Dysglycemia Presymptomatic	β -Cell Autoimmunity Dysglycemia Symptomatic
Phase in Natural History			




Greenbaum C, et al. Emerging concepts on Disease-Modifying Therapies in Type 1 Diabetes. Curr Diab Rep 2017;17:119



Quali test autoanticorpali?



- L'opinione del clinico (Winter WE, et al, 2013)
 - Pannello pediatrico (ICA, IAA, GADA, IA-2A, ZnT8A)
 - Pannello adulto (ICA, GAD, IA-2A, ZnT8A)
 - Pannello LADA (GADA, ZnT8A)
- 
- L'opinione del Patologo Clinico (Autoimmunologo)
 - Eliminazione di ICA
 - Ragioni tecniche, gestionali, economiche