

Improve Islet Autoantibody Assay

New Assay Development

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Symposium on General Population Screening for T1D

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Barbara Davis Center for Diabetes
UNIVERSITY OF COLORADO ANSCHUTZ MEDICAL CAMPUS

Conflict of Interest

None.



Improve Islet Autoantibody Assay

New Assay Development

1. Electrochemiluminescence (ECL) Assay
2. New Bridging ELISA

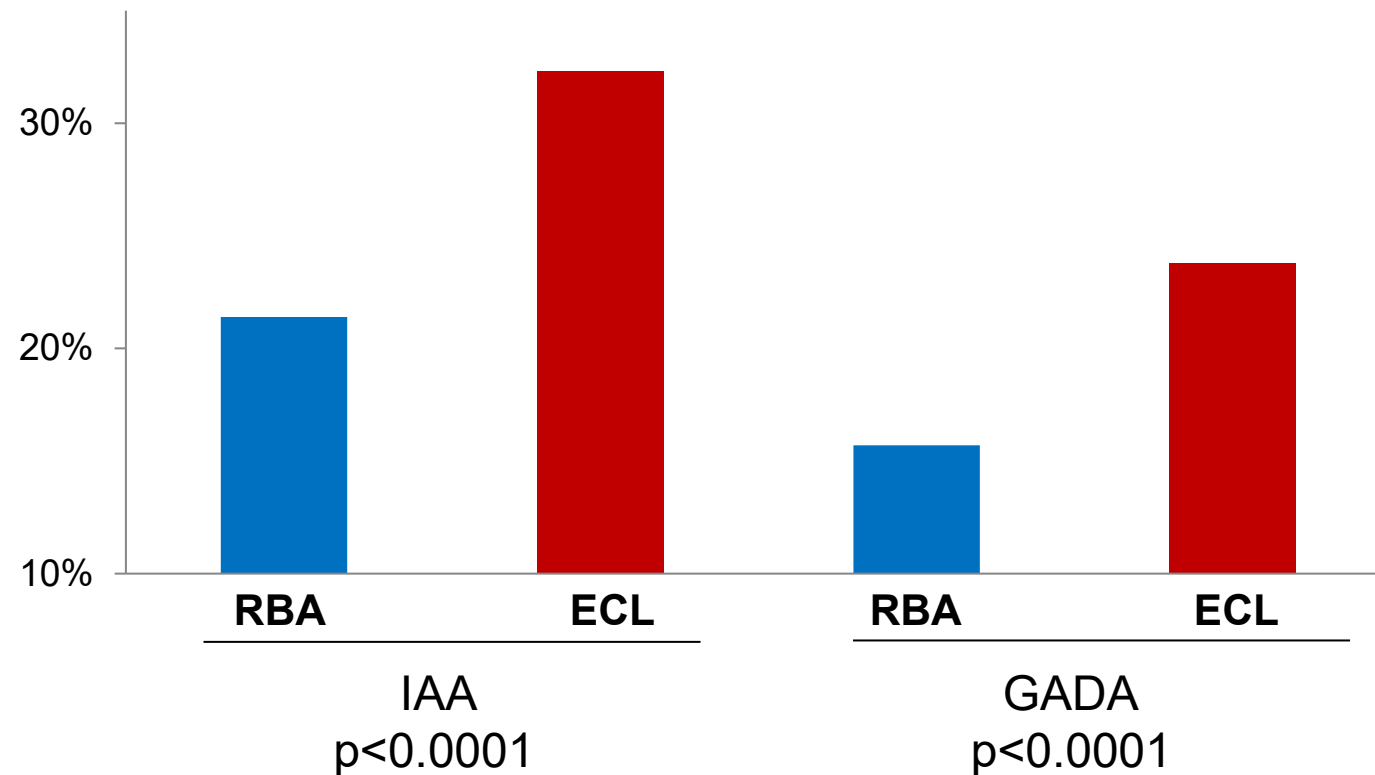


Improve the Predictive Values for Islet Autoantibodies

TrialNet Ancillary Study – 1 (ECL assay --- 2015)

N=3,484
FU to T1D 384
Multi-IABs 571
Single IAb 1,727

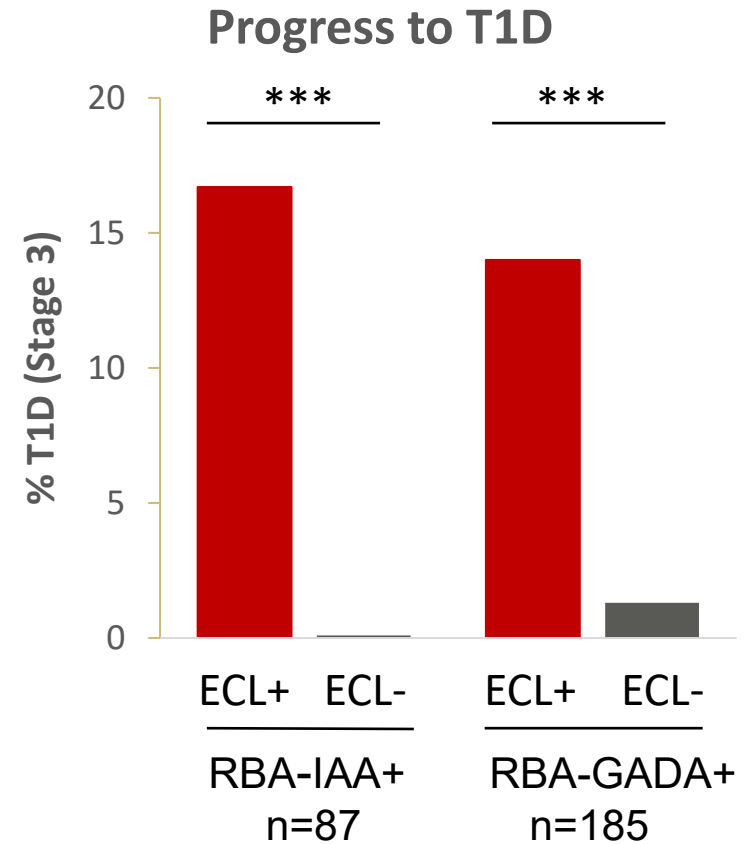
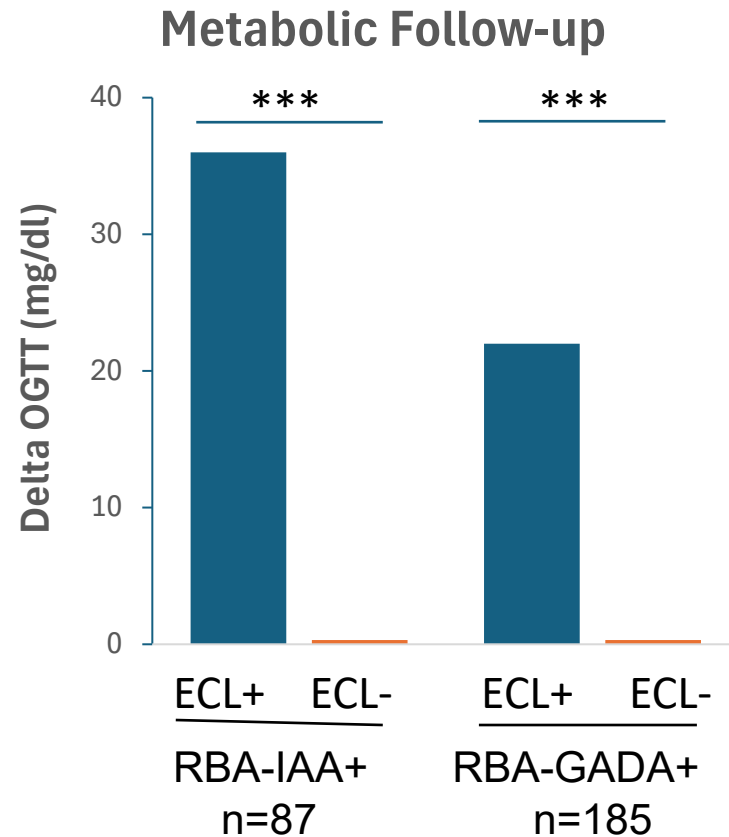
Overall Predictive Values T1D (TrialNet Initial Screening)



Improve the Predictive Values for Islet Autoantibodies

TrialNet Ancillary Study – 2 (ECL assay --- 2017)

Persistent 1 IAb
N=263
GADA: 185
IAA: 87

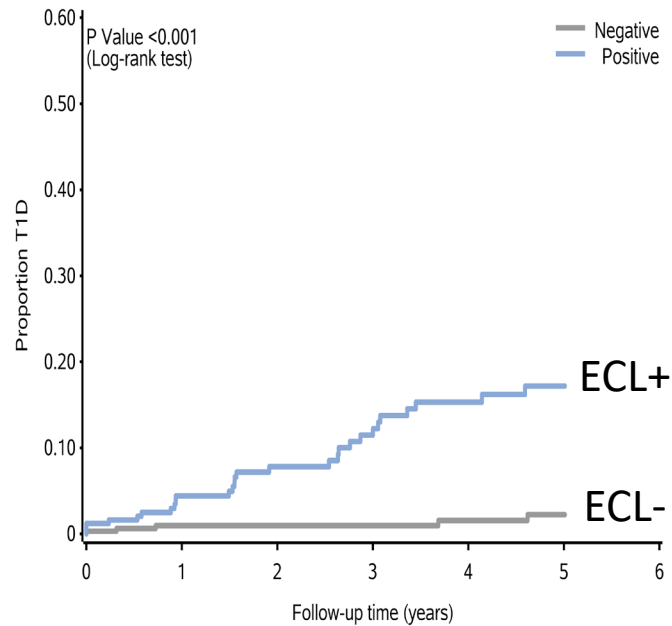


Improve the Predictive Values for Islet Autoantibodies

TrialNet Ancillary Study – 3 (ECL assay --- 2025)

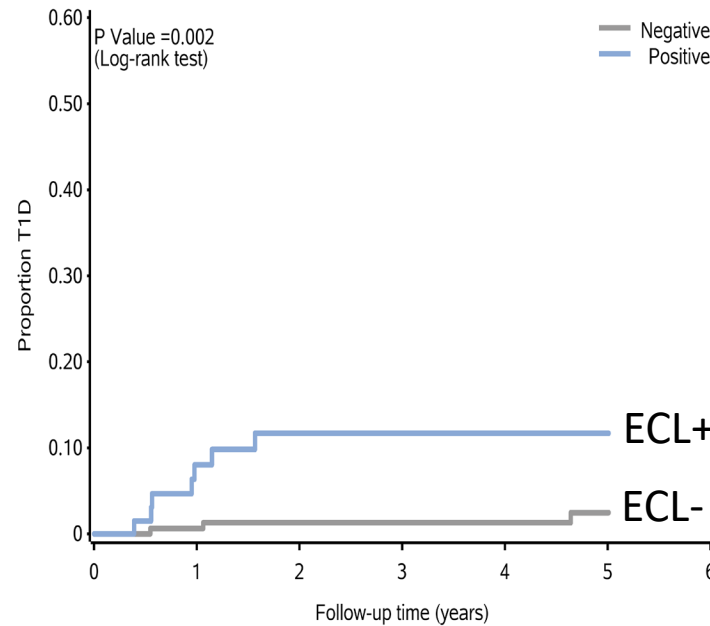
Confirmed Single IAb+, n= 877	GADA	586
	IAA	245
	IA-2A	44

GADA



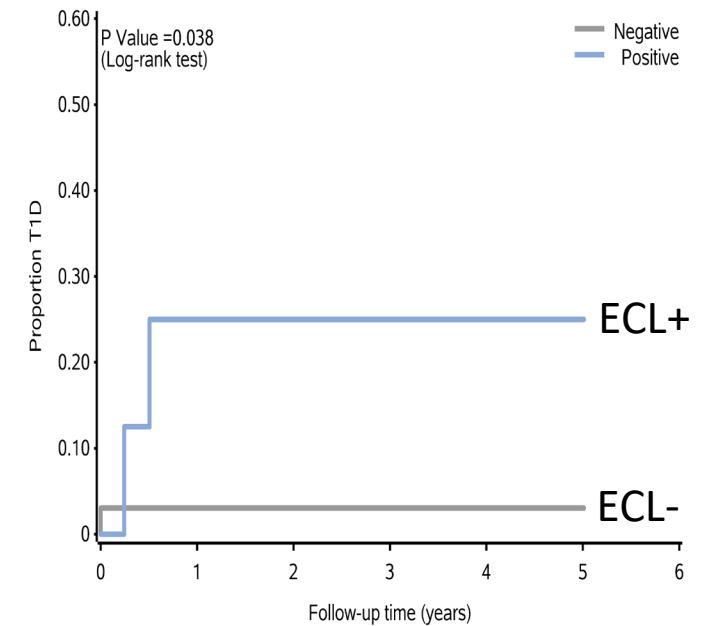
Number at risk:						
Negative	326	285	229	192	156	136
Positive	247	194	145	118	99	75

IAA



Number at risk:						
Negative	168	147	126	110	91	81
Positive	67	54	45	38	32	29

IA-2A

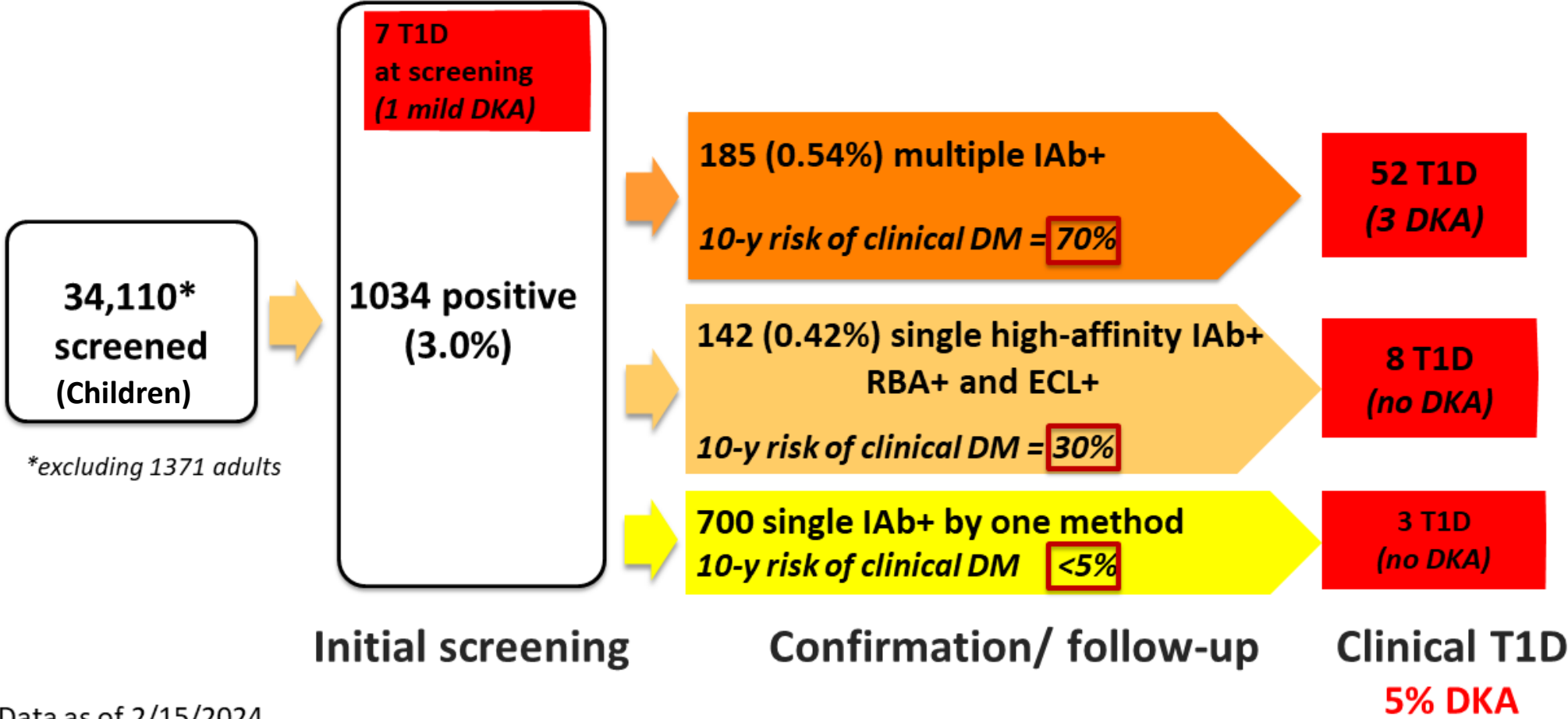


Number at risk:						
Negative	33	28	26	24	19	16
Positive	8	6	5	3		



Improve the Predictive Values for Islet Autoantibodies

ASK Results: Islet Autoimmunity and Stage 3 Type 1 Diabetes (T1D).



Data as of 2/15/2024

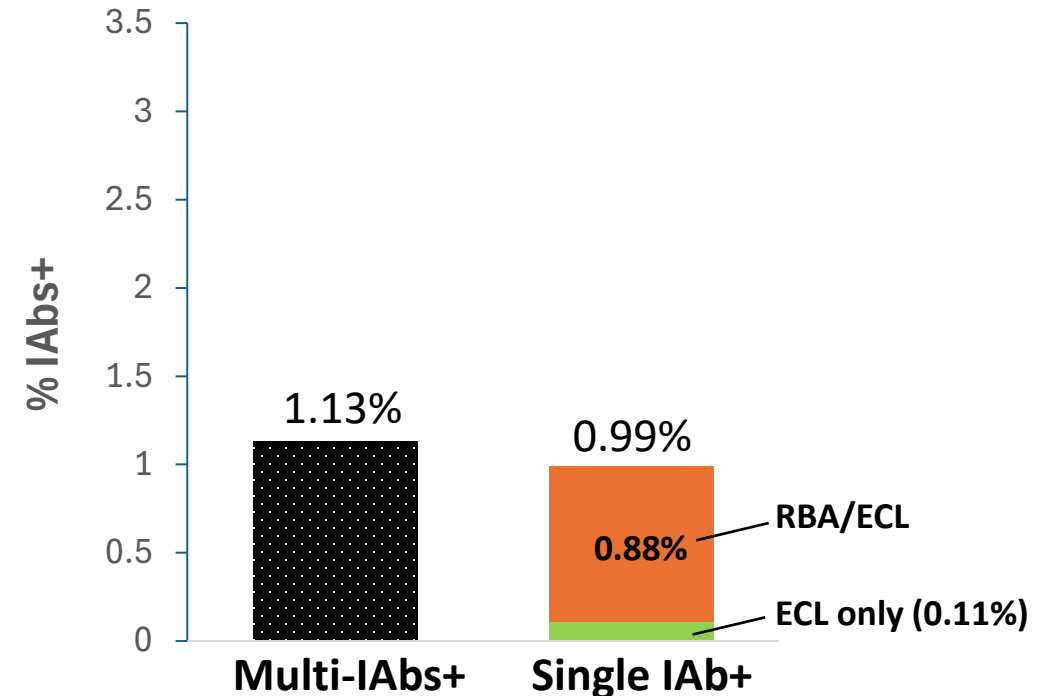
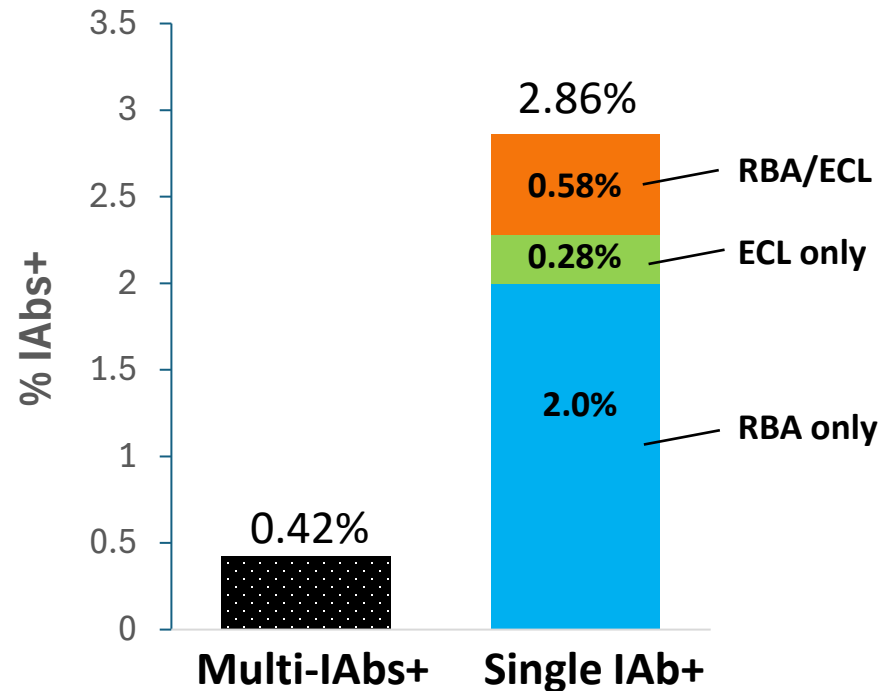


Improve the Predictive Values for Islet Autoantibodies

ASK Screening

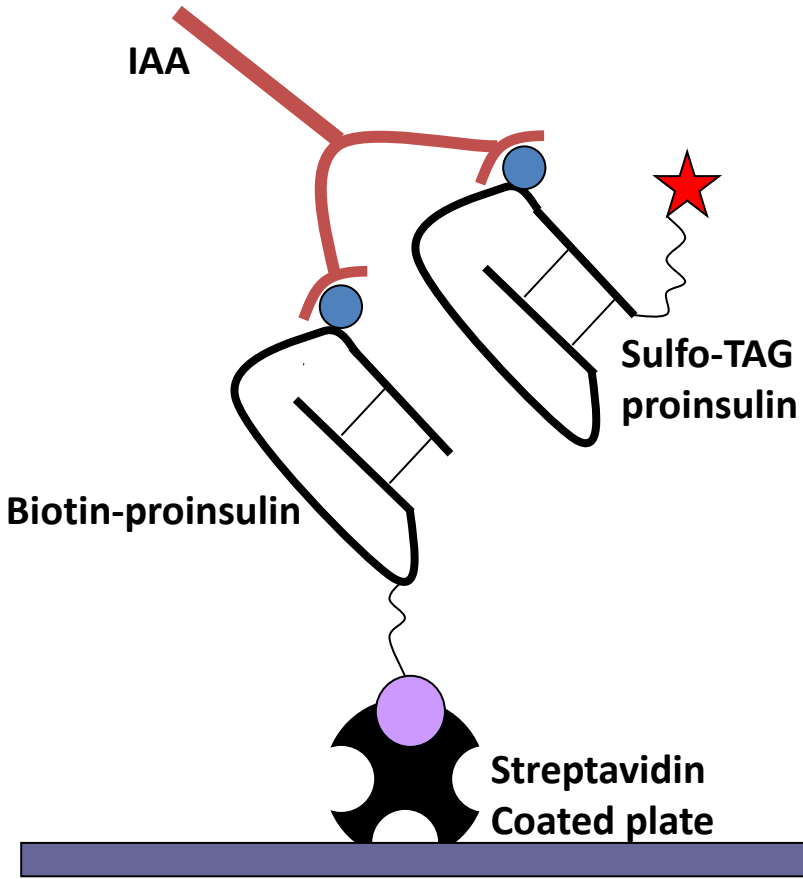
2017 – July 2021
RBA/ECL in Parallel
N= 29,196

Aug 2021 – 2025
ECL Primary, RBA on Positives
N= 14,730

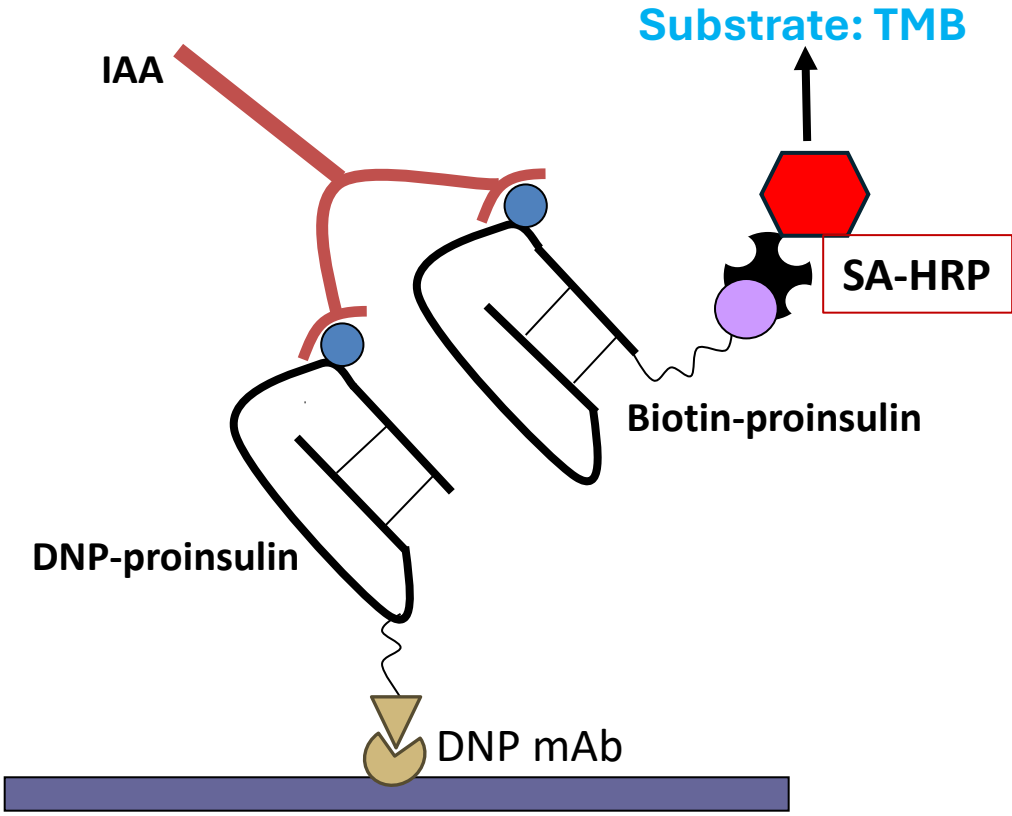


New Bridging ELISA-IAA

ECL-IAA



ELISA-IAA



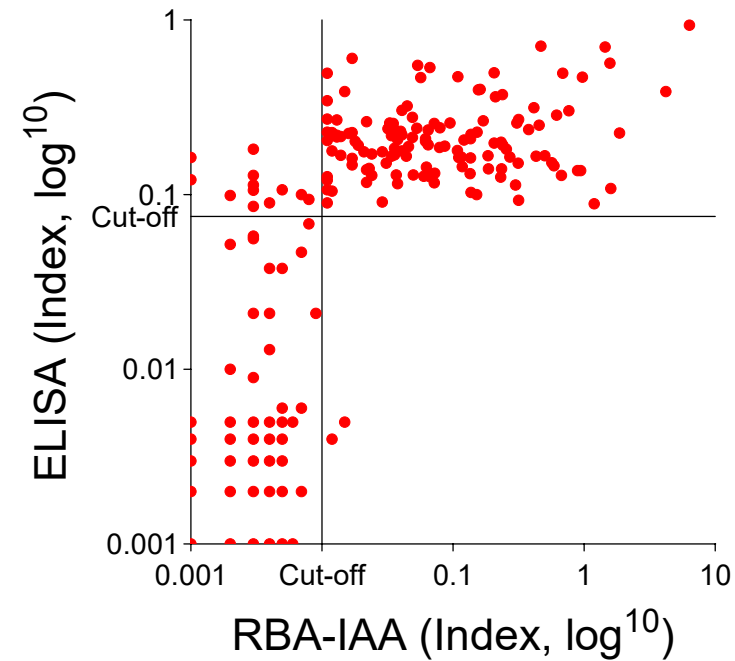
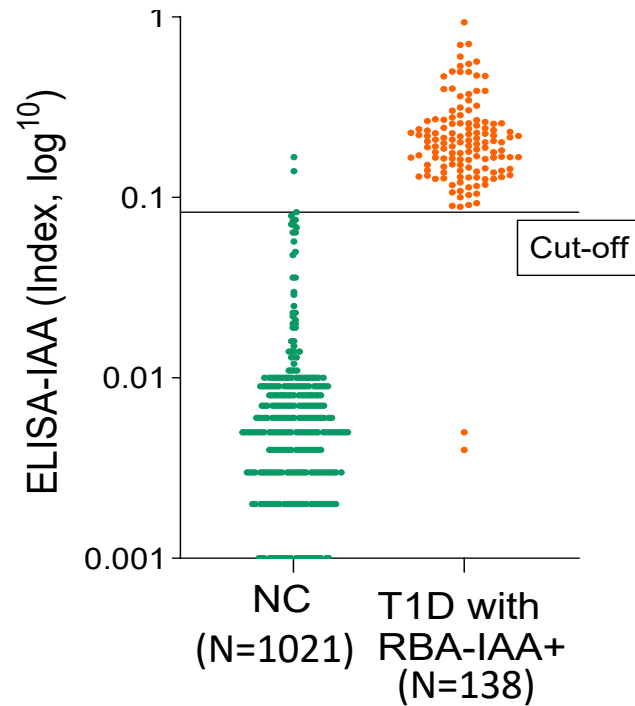
New Assay Development

New Bridging ELISA-IAA

Randomly Selected 227 New-onset T1D

Specificity 99.5%	Positivity 98.6%
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RBA-IAA: 60.8% ECL-IAA: 65.2%
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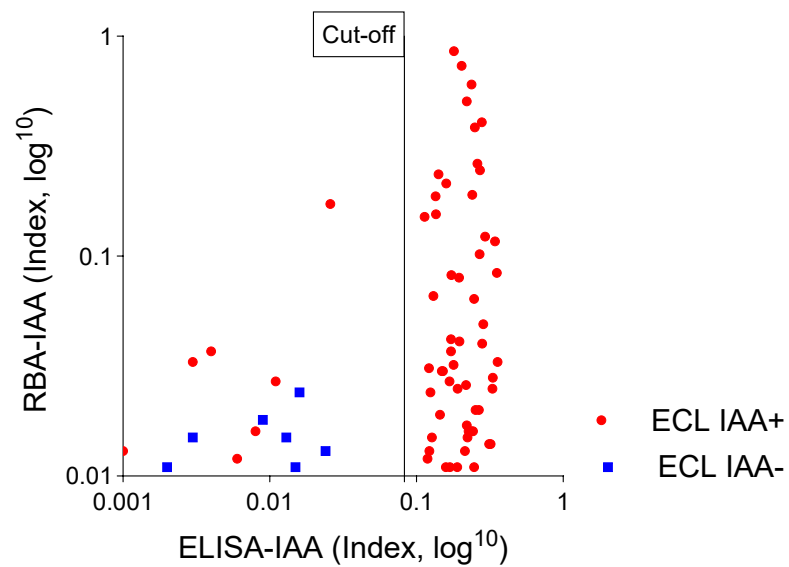


New Assay Development

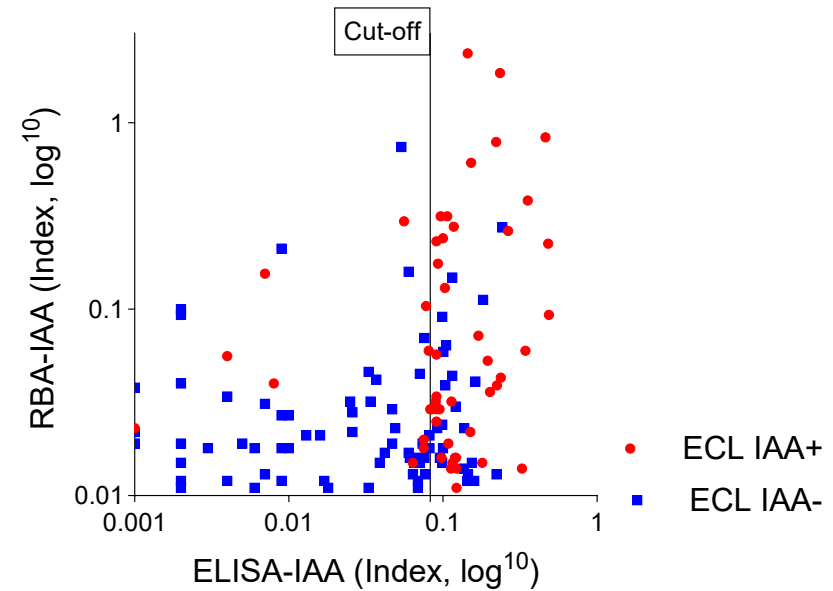
New Bridging ELISA-IAA

202 at-risk subjects
from the ASK with IAA+

Multi-IAbs+



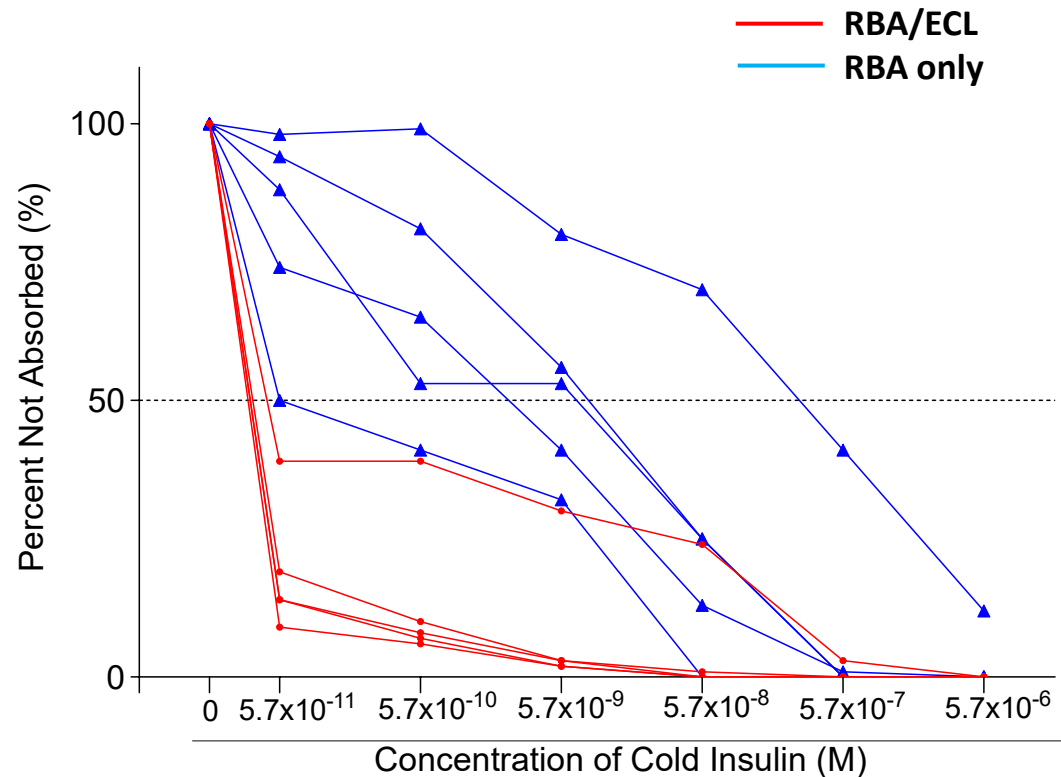
Single IAA+



New Assay Development

New Bridging ELISA-IAA

IAA affinity analysis



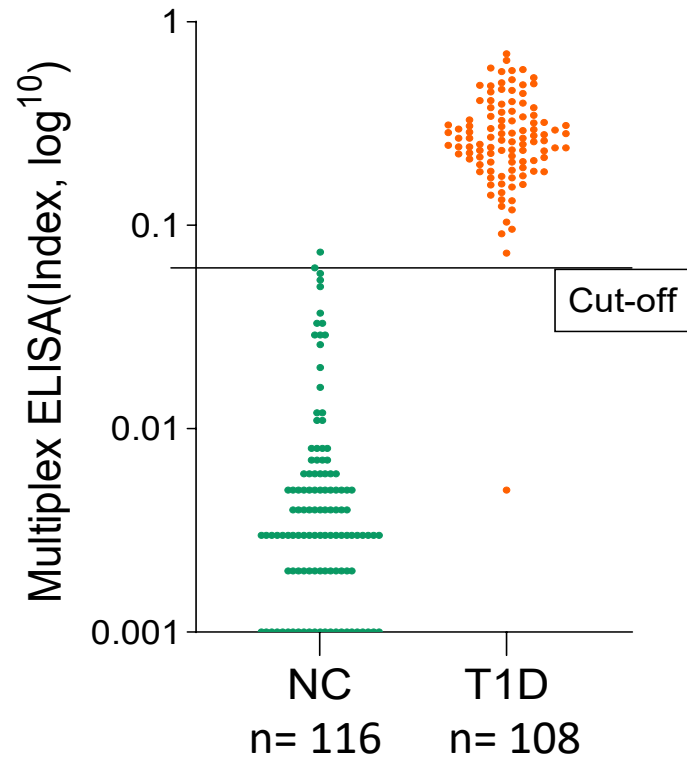
Assays	Samples	50% Inhibition by cold insulin (M)
RBA ⁺ &ELISA ⁺	H1	$<5.7 \times 10^{-11}$
	H2	$<5.7 \times 10^{-11}$
	H3	$<5.7 \times 10^{-11}$
	H4	$<5.7 \times 10^{-11}$
	H5	$<5.7 \times 10^{-11}$
RBA ⁺ &ELISA ⁻	L1	5.7×10^{-9}
	L2	5.7×10^{-10}
	L3	5.7×10^{-7}
	L4	5.7×10^{-9}
	L5	5.7×10^{-10}



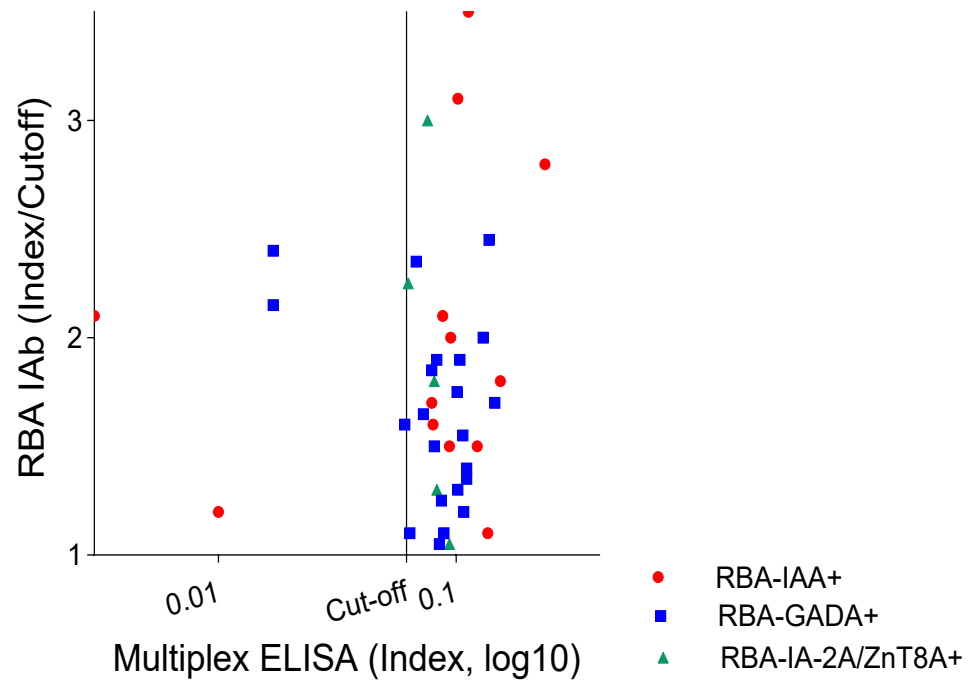
New Assay Development

New Bridging Multiplex ELISA, 4-Pex

Randomly Selected New-onset T1D



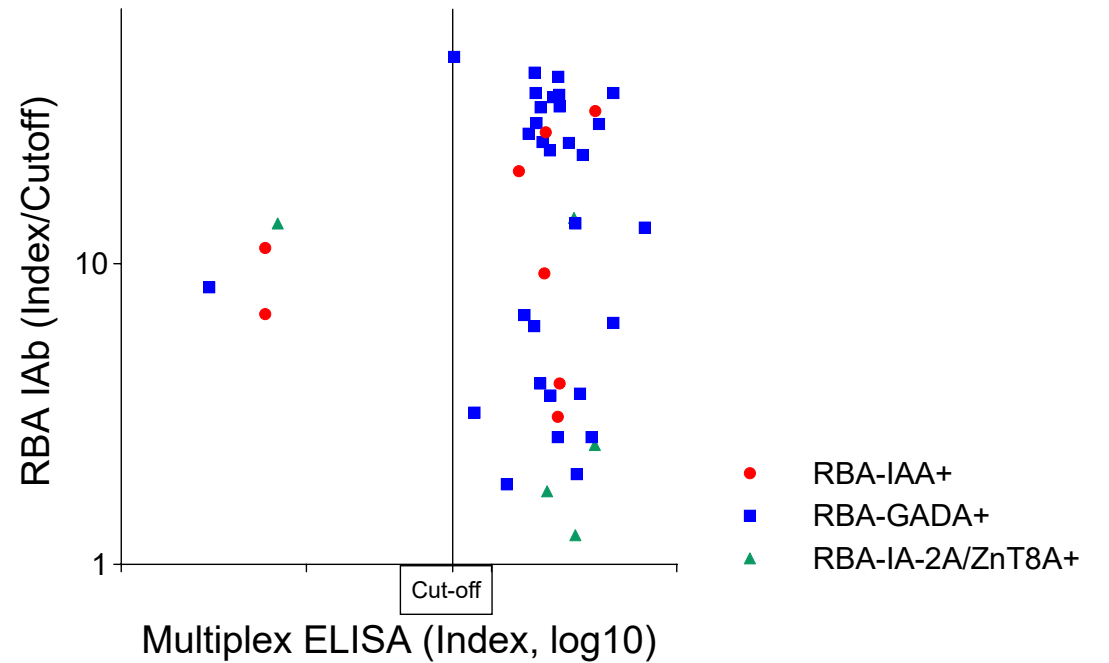
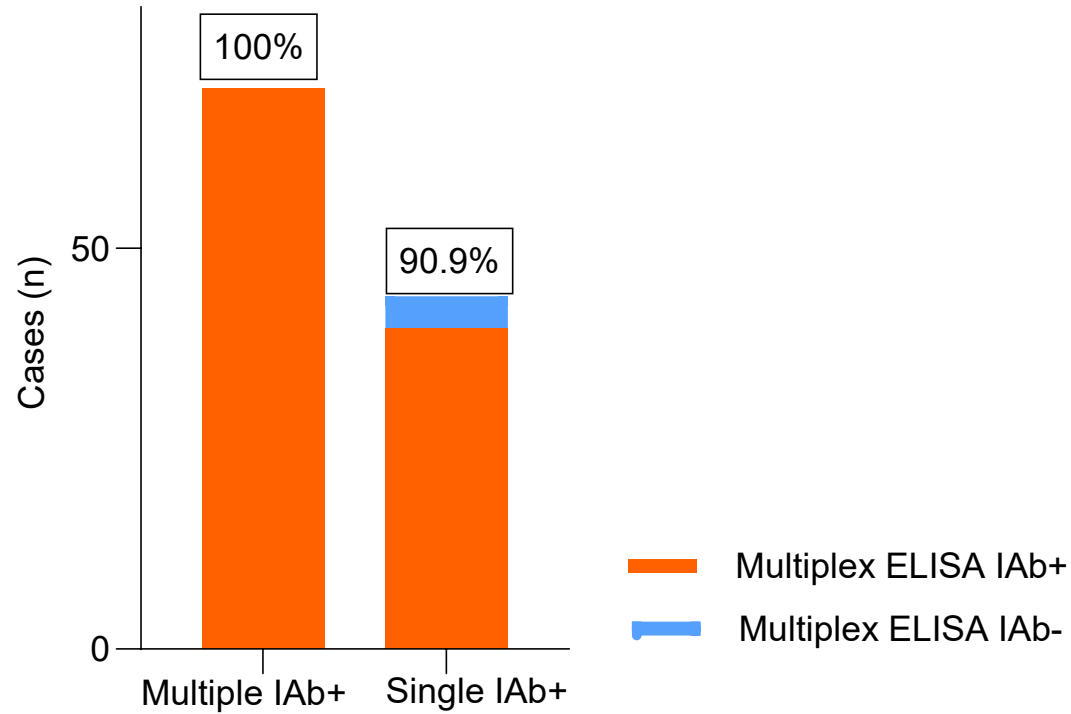
40 New-onset T1D with Ultra-low single IAb



New Assay Development

New Bridging Multiplex ELISA, 4-Pex

114 at-risk subjects from the ASK

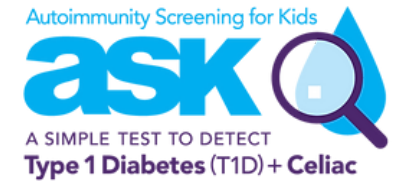
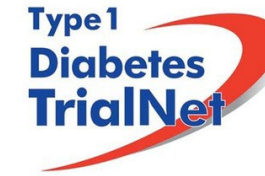


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Yu's Lab



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