

Streamlining Basophil Activation Tests (BAT): Addressing Methodological Limitations to Close Gaps in Allergy Clinical Research

Bridging the Gap from Expert to Everyday Use

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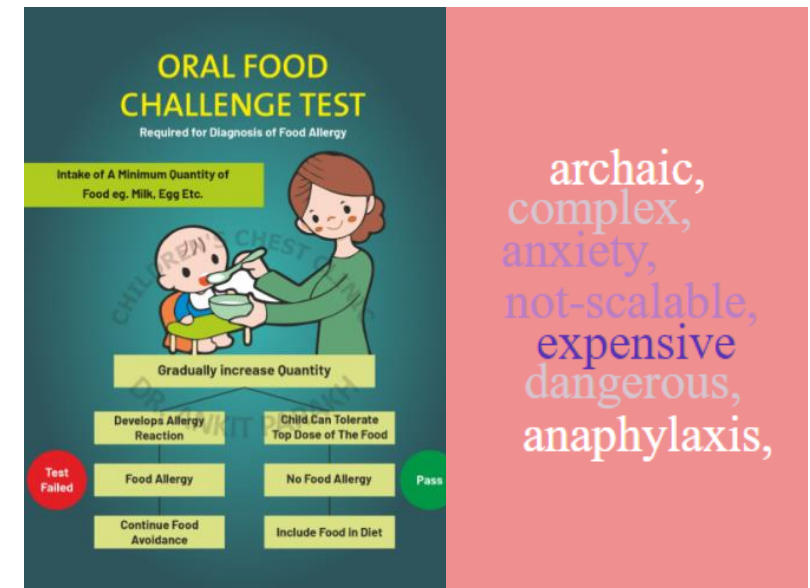
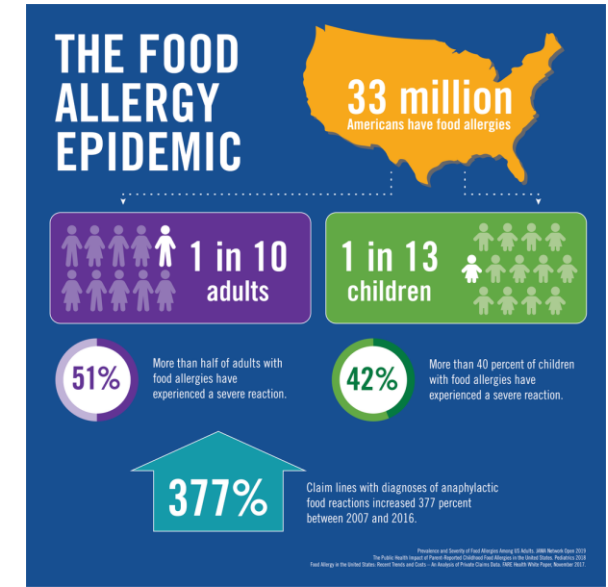


A Valuable Problem To Solve

- Global Food Allergy Population = **220M**
- Oral Food Challenges (OFC) are the gold standard for food allergy diagnostics despite being an archaic diagnostic procedure
- Current in vitro methods are great for screening but lack specificity

		Likelihood of allergy from test results		
		Low	Intermediate	High
Likelihood of allergy from clinical history	High	Possible allergy	Probably allergic	Likely to be allergic
	Intermediate	Possible allergy	Possible allergy	Probably allergic
	Low	Unlikely to be allergic	Possible allergy	Possible allergy

2023 EAACI guidelines on the diagnosis of IgE-mediated food allergy



A Valuable Problem To Solve

- A gap impacting the complete allergy testing ecosystem
- Current tools are not up to the current challenges and opportunities

Diagnosis

- OFC is the only accurate method to diagnose allergies, remains the gold standard

Clinical trial

- Allergy drug development hindered by the need for OFC

Monitoring & Treatment efficacy

- Most patients are not monitored, OFC not amenable for monitoring: patients ordering unreliable test

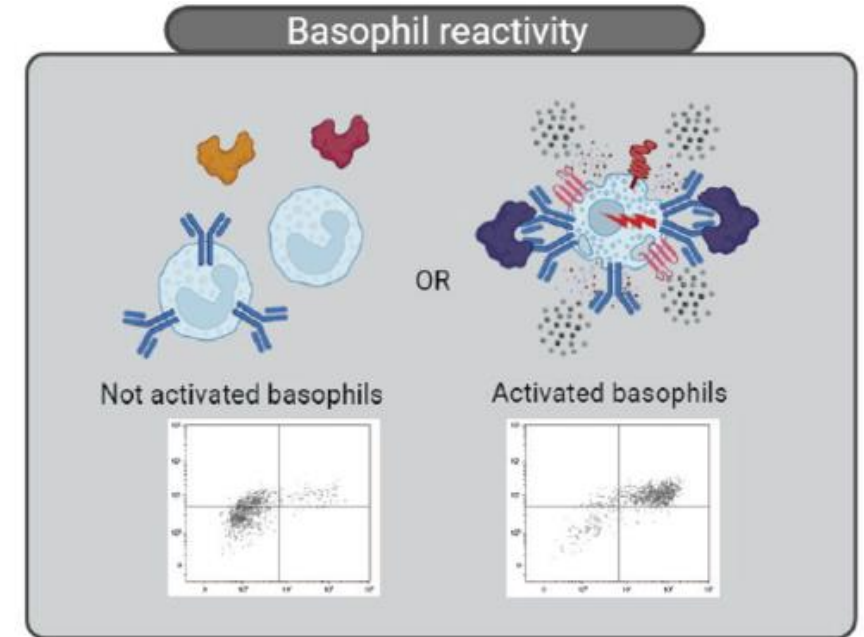
Desensitization monitoring

- Families keep restrictive regimens due to absence of alternative to OFC

What is a Basophil Activation Test (BAT)

BAT is a functional assay to measure basophil activation in response to specific allergens/stimuli. It assesses how basophils respond to an allergen by using flow cytometry to measure expression of activation markers on their surface.

While BAT provides valuable insights in the study of allergies, its adoption has been limited due to the perceived complexity and lack of reproducibility associated with the assay.



2023 EAACI Guidelines

- The 2023 EAACI guidelines on the diagnosis of IgE-mediated food allergy included BAT within the recommended diagnostic algorithm
- Conditional inclusion, acknowledging that BAT data are not accessible to many allergists

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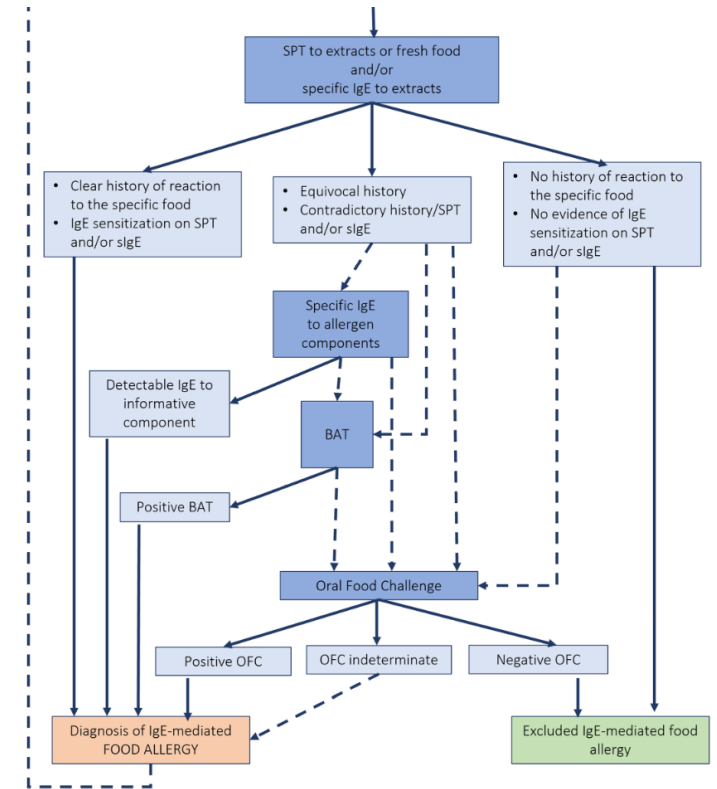
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DELINE



EAACI guidelines on the diagnosis of IgE-mediated food allergy

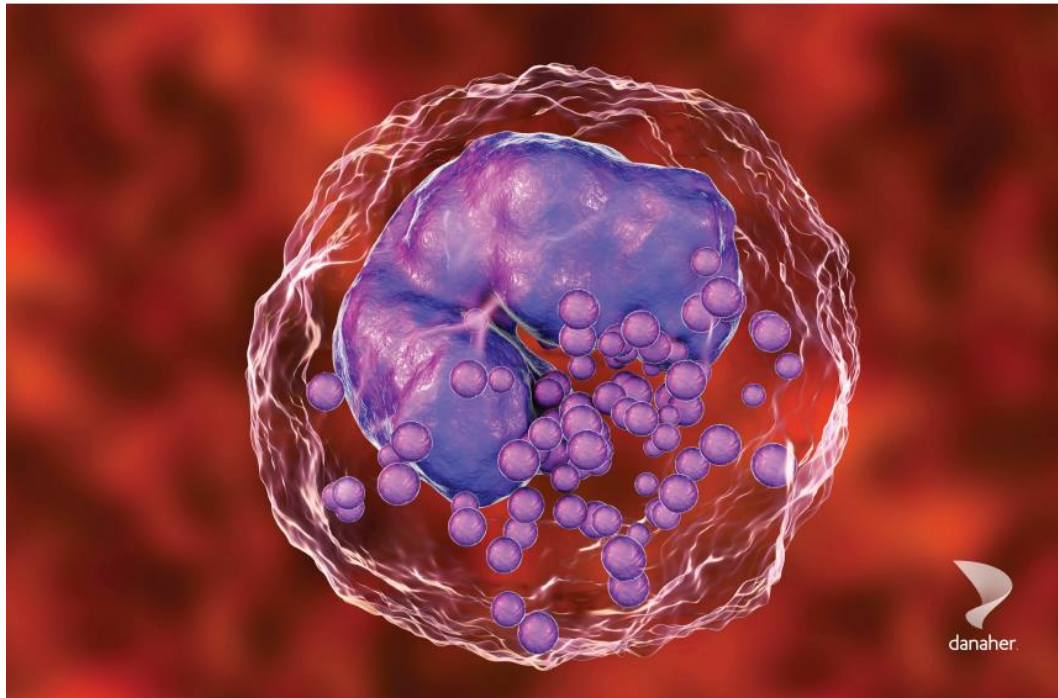
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Next Gen Basophil Activation Test

Introducing the Next-Generation Basophil Activation Test (BAT)

Leveraging dry technology to
overcome traditional BAT challenges

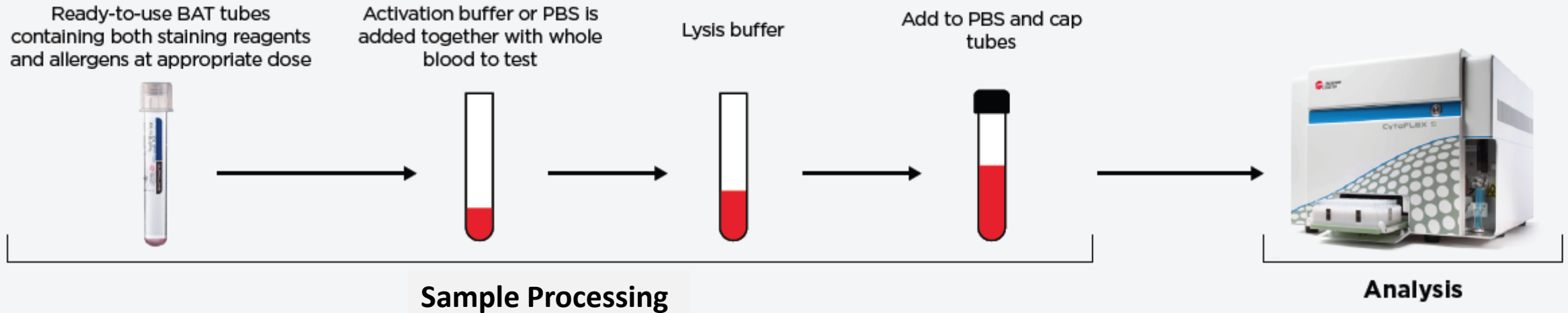


Leveraging Dry Technology to Overcome Traditional BAT Challenges

- Standardized
 - Antibodies and allergens are premixed at desired doses and dried down in a single tube
 - Negative/positive controls can be included
- Straightforward
 - Simply add your sample to the tube, lyse and acquire on your flow cytometer
 - Only 4 pipetting steps required
- Easy to Use
 - No compensation
 - No centrifuge
 - Compatible with any flow cytometer
 - Prolonged post-processing stability
- Customizable
 - Define your own combination of antibodies and allergens, and number of doses with specifications and format of your choice



A Smarter Workflow For BAT



The centrifugation-free protocol, consisting of only 4 pipetting steps, can be implemented to prepare the tubes, resulting in a streamlined, robust and standardizable approach to BAT that can be used in most laboratories, regardless of flow cytometry expertise.

Streamlining Basophil Activation Testing to Enable Assay Miniaturization and Automation of Sample Preparation
Arif-Lusson R, Agabriel C, Carsin A, Cabon I, Sénéchal H, Poncet P, Vitte J, Busnel JM, *Journal of Immunological Methods* 2020, 481, 112793

Possible alternative strategies to implement basophil activation testing in multicentric studies
Bourgoin P, Dupont T, Agabriel C, Carsin A, Verles A, Cabanski M, Vitaliti A, Busnel JM, *Cytometry Part B* 2024, 106, 392-404

A novel approach to the basophil activation test for characterizing peanut allergic patients in the clinical setting
Agyemang A, Suprun M, Suarez-Farinas M, Boina F, Arif-Lusson R, Grishin A, Busnel JM, Sampson HA, *Allergy* 2021, 76, 2257-2259

A streamlined strategy for basophil activation testing in a multicenter phase III clinical trial
Suarez-Farinas M, Grishin A, Arif-Lusson R, Bourgoin P, Matthews K, Campbell DE, Busnel JM, Sampson HA, *JACI-IP* 2024, 24, 2198,

Award Winning Product Concept

FARE Innovation Award Diagnostic Challenge

A multi-million-dollar competition designed to promote the development of an innovative and accessible food allergy diagnosis

An Easy-to-Use, Accurate Alternative to the Oral Food Challenge

Attracting the Best Minds

The FARE Innovation Award Diagnostic Challenge will attract the best minds to develop innovative technologies that will lead to a simple point-of-care test to diagnose food allergy

Opportunity to Prove Concept

Investigators participating in the Diagnostic Challenge will be offered an opportunity to prove their concept and receive modest financial incentives during stage one

Opportunity for Funding

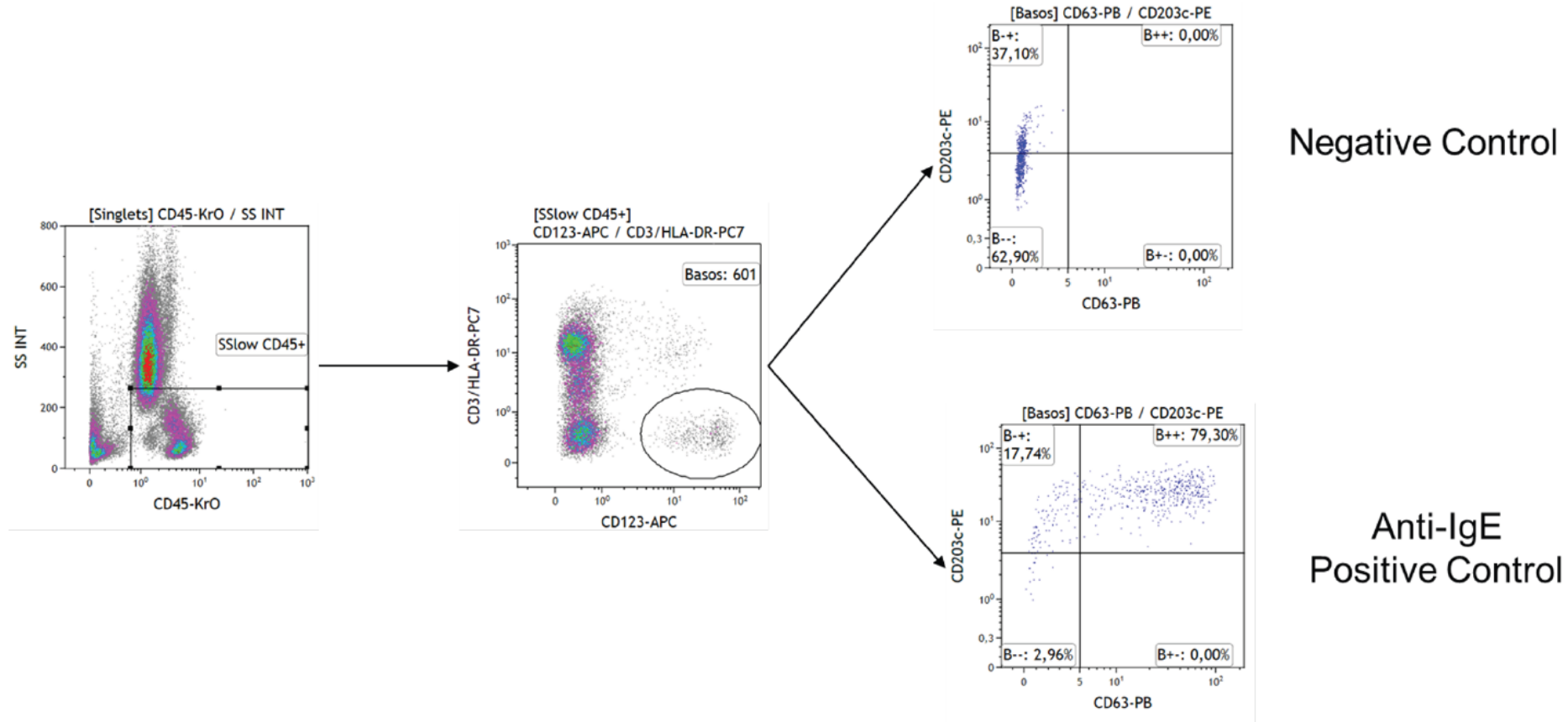
Those that move their concept forward will have the opportunity for increased funding and ultimately the opportunity to offer an alternative to the oral food challenge, or OFC

MEDIA ROOM | October 13, 2022

FARE Innovation Award Diagnostic Challenge Presented to Beckman Coulter Life Sciences

\$1,000,000 Awarded to Advance Innovation in Food Allergy Diagnosis

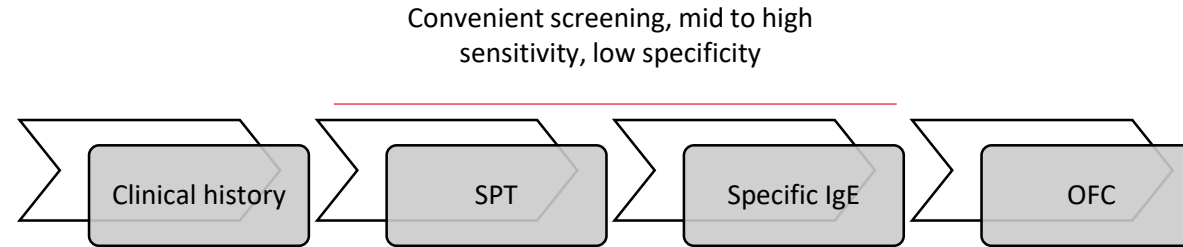
BAT Data Example



Representative results, on a Navios Flow Cytometer, using dry, ready-to-use, room temperature-stable reagents. Panel included CD203c-PE, CD3-PC7, HLA-DR PC7, CD123-APC, CD63-PB, CD45-KO. In the next generation BAT, activators used for positive control (anti-IgE, fmLP, etc.) or test condition with allergenic extracts, purified or recombinant allergens, are formatted together using the dry DURAClone technology.

Possible Workflow

TODAY



TOMORROW



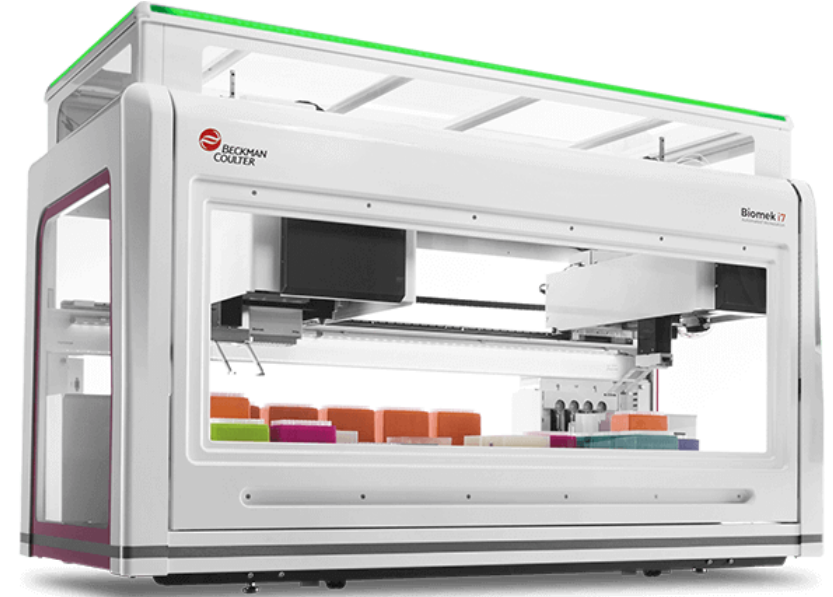
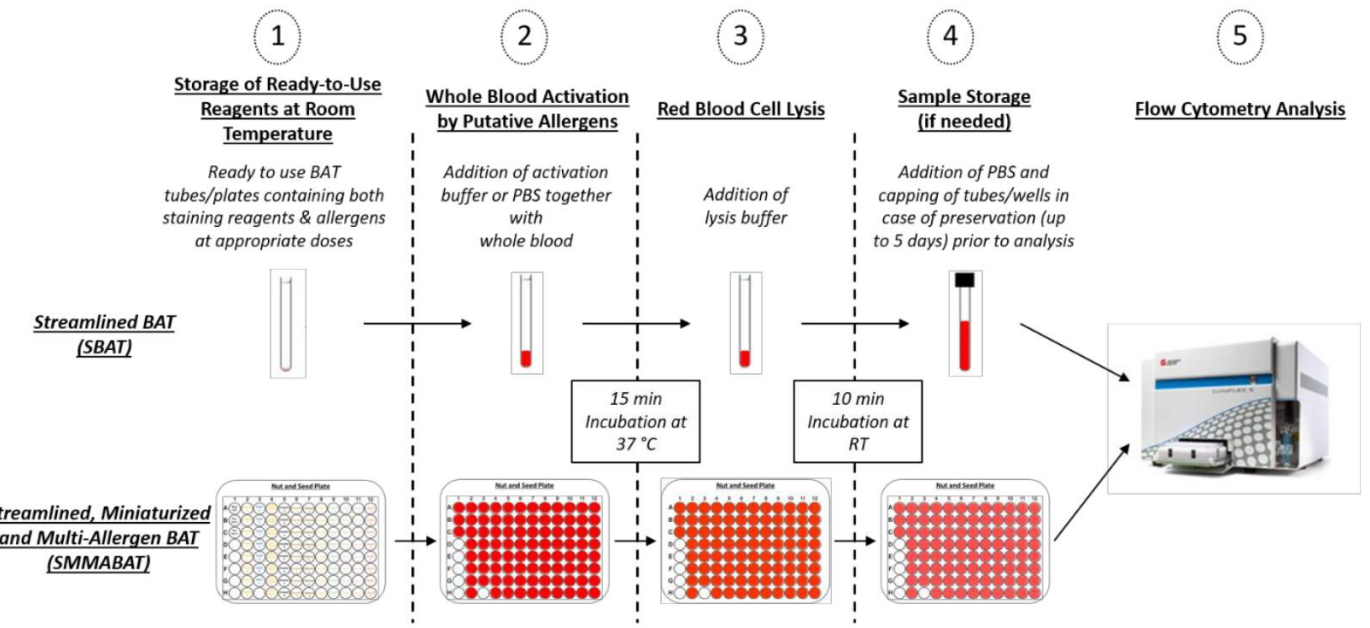
Do allergy blood tests ever deliver false-positive results?

About 50% to 60% of all allergy blood tests give false-positive results. False-positive results show you have an allergy even when you don't. Sometimes false positives happen if your body is reacting slightly to substances in certain foods you've eaten recently.

A note from Cleveland Clinic



Opportunities to Automate From Sample Preparation...

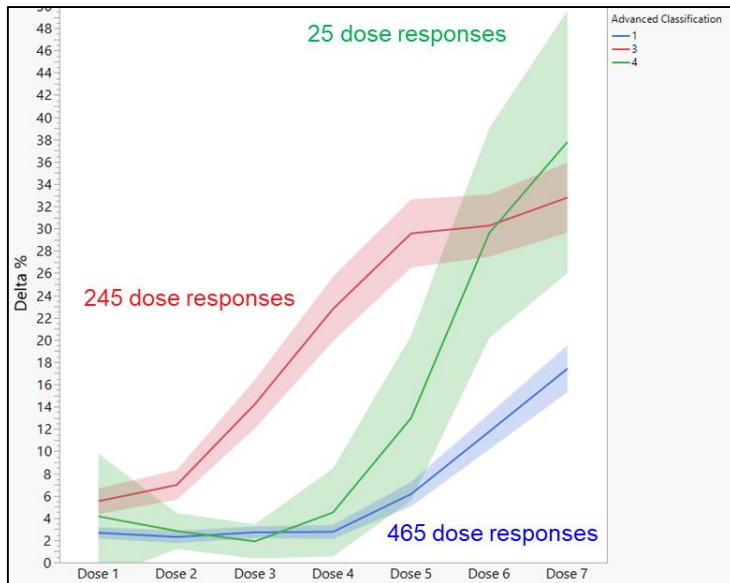


- Higher throughput can be achieved leveraging plate-based assay and sample prep automation

Early Assessment of the Clinical Relevance of Tested Prototype Workflow

Demographics considering pairs of allergen & individuals

1. Eats the food (n=465)
2. Avoid the food w/o in vivo evidence for allergy (n=151)
3. Allergic (n=245)
4. Allergic under OIT (n=25)
5. Avoiding food to manage another conditions i.e. EoE/FPIES (n=5)



* SMMABAT PPV and NPV based on data from 245 allergic and 465 tolerant status

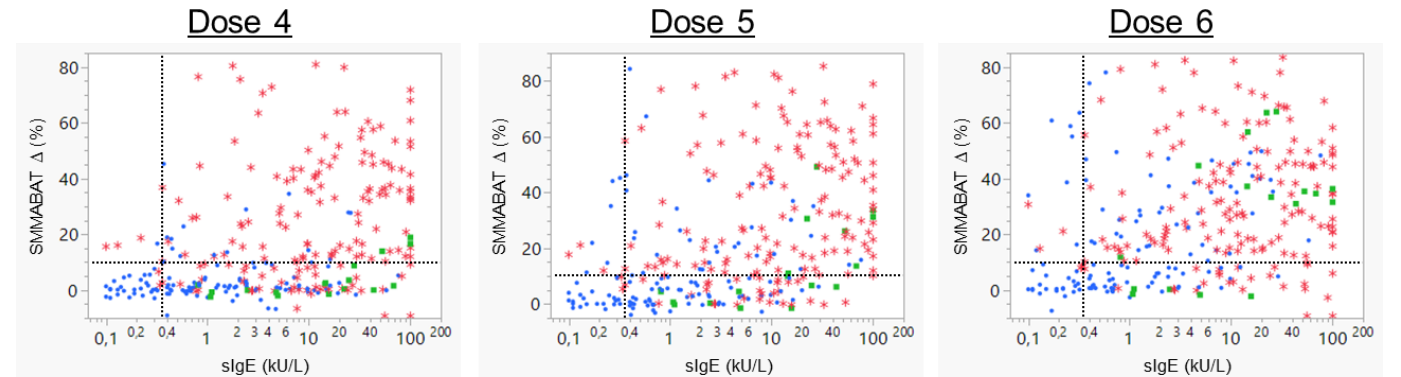
** sIgE PPV and NPV based on data from 162 allergic and 89 tolerant status

	PPV	All Allergens		All allergens but sesame, brazil & almond	
		$\Delta > 10\%$	$\Delta > 15\%$	$\Delta > 10\%$	$\Delta > 15\%$
		S	Dose 1	52,9	63,3
M	Dose 2	67,5	76,4	75,6	87,5
M	Dose 3	75,3	88,3	83,2	93,3
A	Dose 4	75,7	85,5	83,4	92,1
B	Dose 5	67,0	72,2	76,1	80,6
A	Dose 6	55,3	57,5	63,8	66,4
T	Dose 7	49,5	50,4	56,8	58,7

	NPV	All Allergens		All allergens but sesame, brazil & almond	
		$\Delta > 10\%$	$\Delta > 15\%$	$\Delta > 10\%$	$\Delta > 15\%$
		S	Dose 1	68,6	67,6
M	Dose 2	71,8	69,0	67,6	64,8
M	Dose 3	77,2	74,6	74,6	71,9
A	Dose 4	81,9	78,6	80,8	77,6
B	Dose 5	86,5	82,0	86,1	81,6
A	Dose 6	86,9	82,9	86,0	81,4
T	Dose 7	83,5	80,1	81,9	78,3

PPV	sIgE<0,35 kU/L	sIgE>1 kU/L	sIgE>5 kU/L
sIgE	65,0	73,0	82,0

NPV	sIgE<0,35 kU/L	sIgE<1 kU/L	sIgE<5 kU/L
sIgE	92,0	82,0	71,0



As expected, BAT provides higher PPV than sIgE, thereby representing a complementary & useful technique to improve individual characterization

Thank you! Questions?

