Johns Hopkins Engineering

Immunoengineering

Immunoengineering—Allergy and Autoimmunity

Delivery of Allergy Immunotherapy

JOHNS HOPKINS
WHITING SCHOOL
of ENGINEERING

Biomaterial Case Studies to Illustrate Design Principles

- Replicating tolerance at the cellular level - particles
- Replicating tolerance at the organ level - scaffolds
- **Delivery of allergen immunotherapy**

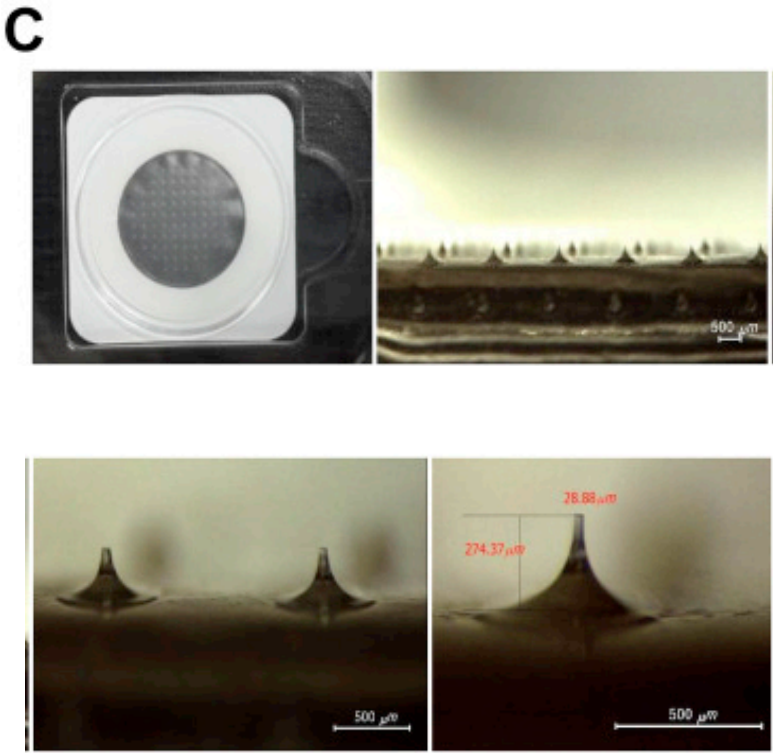
Current Allergen Immunotherapy

- SCIT – Subcutaneous Allergen Immunotherapy
- SLIT – Sublingual Allergen Immunotherapy

- Requires frequent visit to the hospital
- Administration may not represent physiological allergen exposure

Microneedles for Allergen Immunotherapy

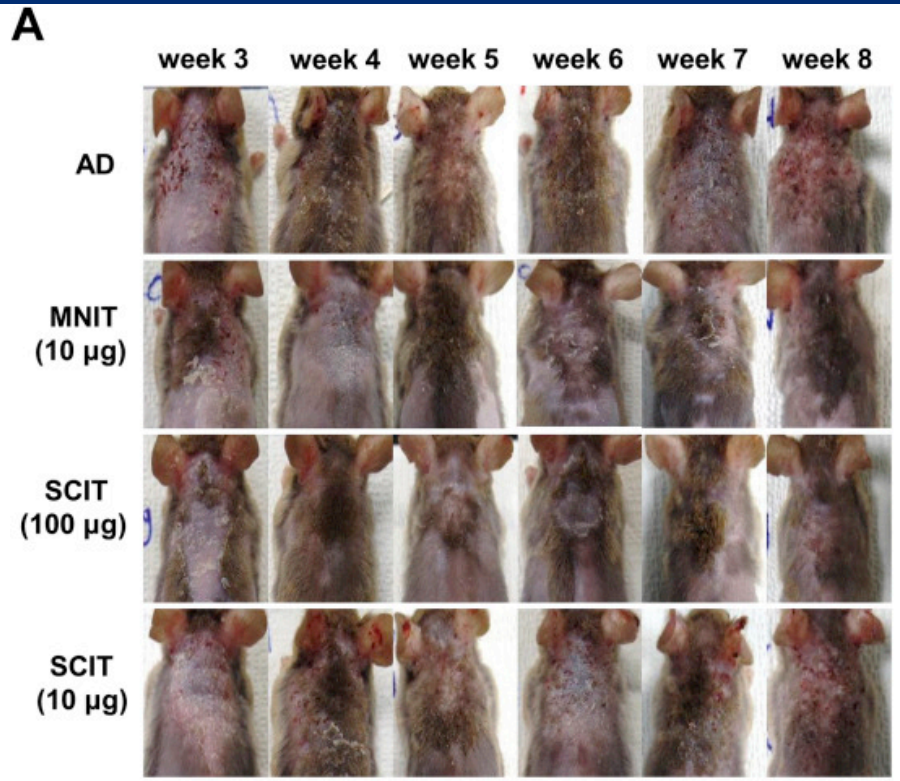
- Adhesive and microneedle patch
- Biodegradable polymer needles with allergen pierce skin to deliver antigen
- Allows controlled and sustained release
- Decrease the number of patches needed



Kim, Ji Hye, et al. "Successful transdermal allergen delivery and allergen-specific immunotherapy using biodegradable microneedle patches." *Biomaterials* 150 (2018): 38-48.

Microneedles for Allergen Immunotherapy

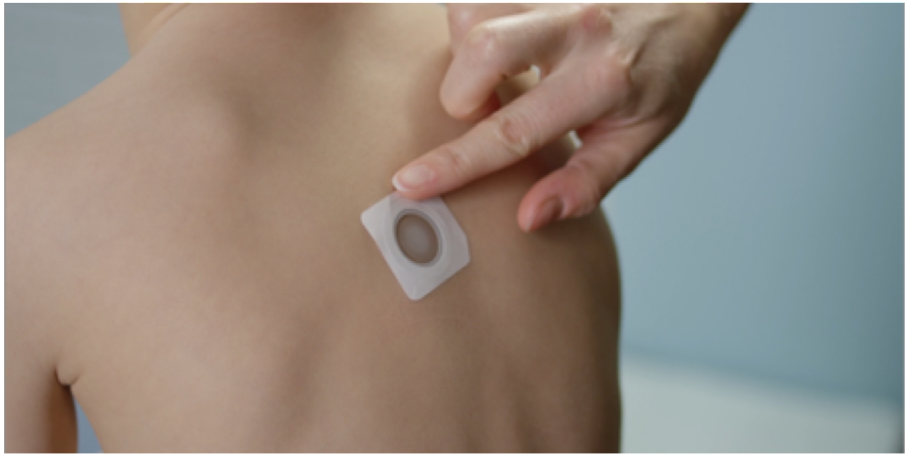
- Effective in mouse models at reducing allergic dermatitis
  - Not tested in other forms or locations of allergy
- Allows dose sparing compared to SCIT



Kim, Ji Hye, et al. "Successful transdermal allergen delivery and allergen-specific immunotherapy using biodegradable microneedle patches." *Biomaterials* 150 (2018): 38-48.

Epicutaneous Delivery of Allergen Immunotherapy

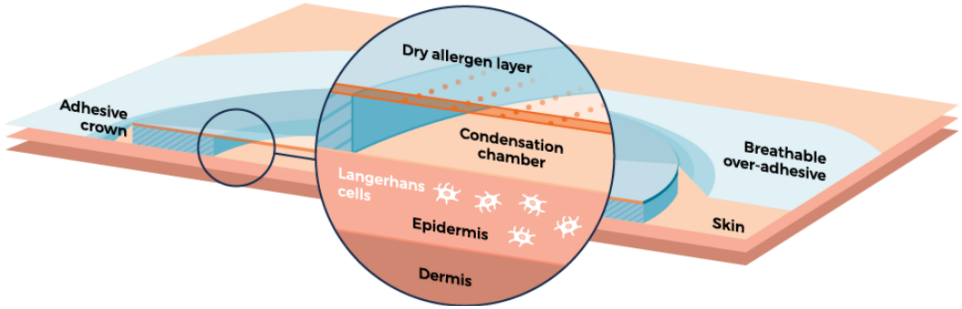
- Self and easily administered
- Decrease access to circulatory system limiting systemic effects
- Sustained release of antigen



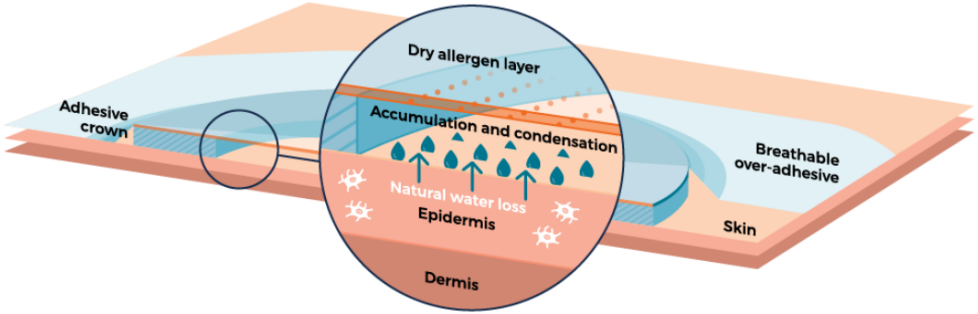
https://www.dbv-technologies.com/

Epicutaneous Delivery of Allergen Immunotherapy

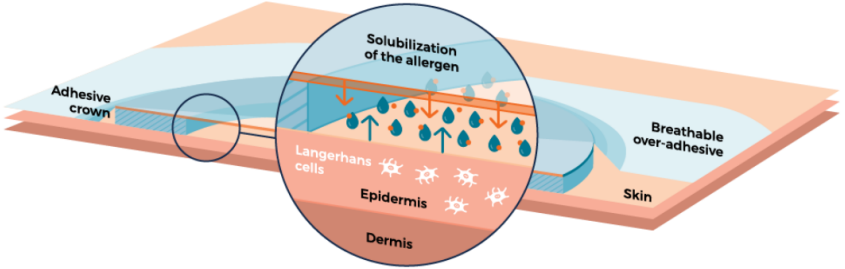
Containing a dry layer of allergen in its center, the patch is positioned on intact skin, without prior preparation.



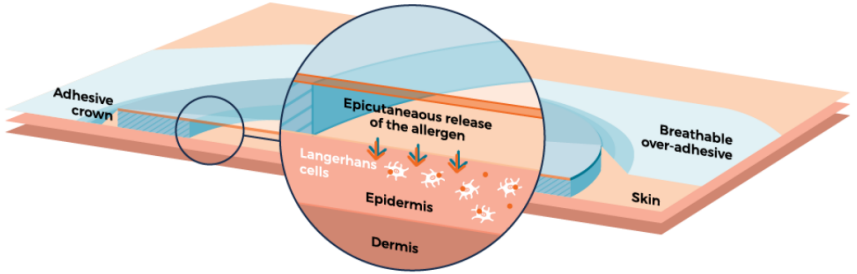
The condensation chamber formed between the skin and the center of the patch creates hyperhydration of the skin and an accumulation of water.



The accumulation of water solubilizes the allergen. Due to this condensation chamber, the epidermis becomes more permeable allowing passage of the allergen into the epidermis.



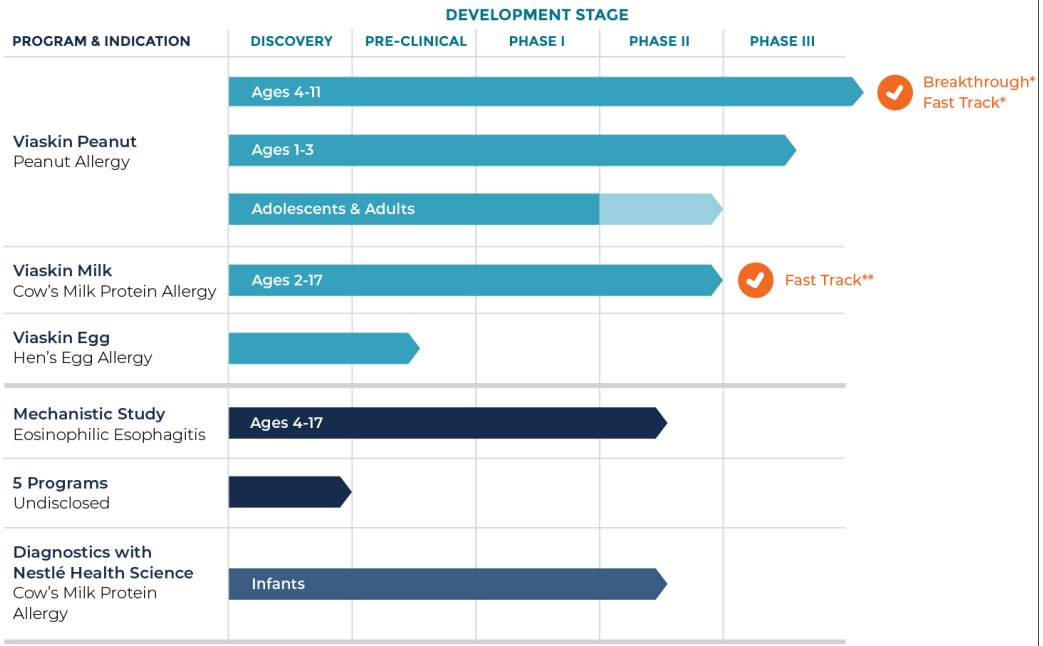
Once in the epidermis, the allergen is captured by a population of highly specialized cells: Langerhans cells. These cells can take the protein at the surface of the skin, process it and present its epitopes to the lymphocytes in the lymph nodes.



https://www.dbv-technologies.com/viaskin-platform/

Epicutaneous Delivery of Allergen Immunotherapy

Development Pipeline



*US FDA Breakthrough Therapy and Fast Track designation in children
**US FDA Fast Track designation in pediatric patients two and older

https://www.dbv-technologies.com/

Allergen Immunotherapy with Thin Dissolving Films

- Improved allergen delivery and efficacy
- Smaller dose while prolonging the contact time between the allergen and oral APCs
- Minimize the risk of systemic side effects
- Easier to standardize by removing need for measuring allergen doses at the physician's office

Study Description Go to

Brief Summary:
The purpose of this study is to determine if a new method of administration of **peanut** sublingual immunotherapy, a dissolving **peanut film**, is effective.

Condition or disease	Intervention/treatment	Phase
Peanut Allergy	Drug: **Peanut** Dissolving **Film**	Phase 1 Phase 2

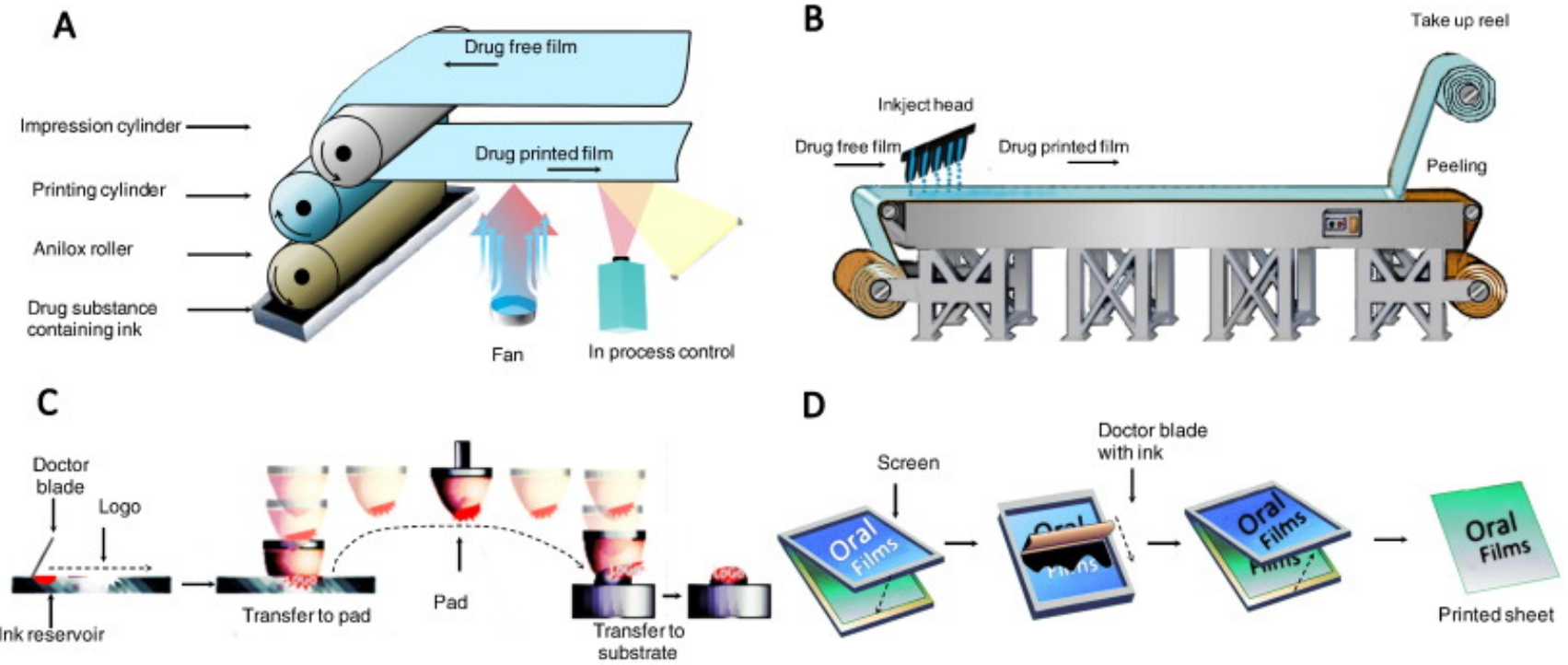
Detailed Description:
Peanut allergy is a common problem with no current treatment. Recent studies have shown some success with oral or sublingual immunotherapy for the treatment of food allergy. Oral treatment, which requires very high doses, is associated with a small but appreciable risk of systemic reactions. Sublingual immunotherapy, which utilizes much smaller doses, is safer but constraints inherent in the available methods of sublingual administration have limited the utility of this method. Typically sublingual immunotherapy for food allergy has used either fresh foods or a simple liquid extract. These methods are not optimized for practicality or dwell duration in the mouth, and, thus far, dosing has been limited by the ability to make concentrated extracts and by the volume of extract that can be applied to the sublingual space. This study is being conducted to determine if a dissolving peanut extract film, will improve efficacy for immunotherapy for peanut allergy.

Study Design Go to

Study Type:	Interventional (Clinical Trial)
Estimated Enrollment:	15 participants
Allocation:	Non-Randomized
Intervention Model:	Single Group Assignment
Masking:	None (Open Label)
Primary Purpose:	Treatment
Official Title:	The Safety and Efficacy of a **Peanut** Immunotherapy Dissolving **Film** for **Peanut** Allergy
Actual Study Start Date:	November 2012
Estimated Primary Completion Date:	March 31, 2018
Estimated Study Completion Date:	March 31, 2018

https://clinicaltrials.gov/ct2/show/NCT01897077?term=peanut+film&rank=1

Methods to Generate Orally Dissolvable Patches



Borges, Ana Filipa, et al. "Oral films: current status and future perspectives: I—galenical development and quality attributes." *Journal of Controlled Release* 206 (2015): 1-19.

Delivery of Oral Immunotherapy

Oral Mucosal Immunotherapy

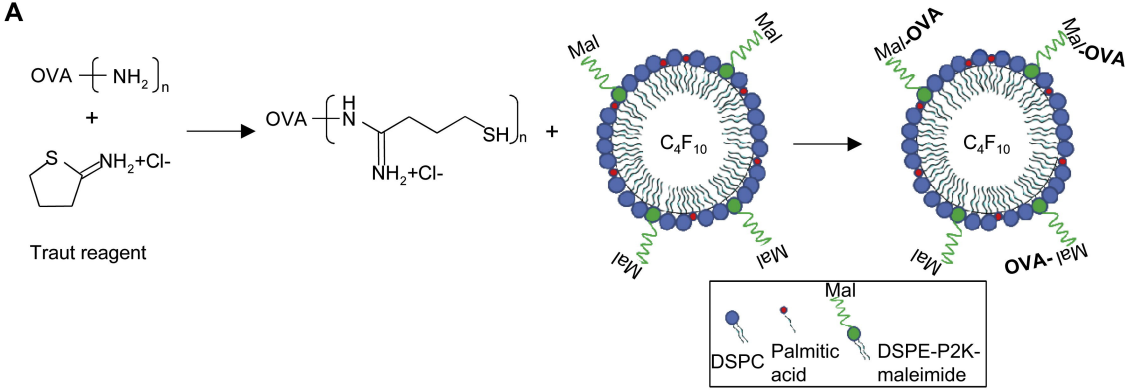
Oral mucosal immunotherapy (OMIT) is a novel form of allergen-specific immunotherapy. Immunotherapy has a 100-year track record of use for respiratory allergies. OMIT improves upon this approach by delivering immunotherapeutic agents to the areas of the oral cavity with the highest likelihood of decreasing allergy symptoms.

http://www.intrommune.com/

Intranasal Delivery with Microbubbles

- Skin or oral exposure may not recapitulate many allergies including seasonal allergies
- Microbubbles to deliver allergens to mucosa and lung
- Allow targeting to APCs to ameliorate features of allergic asthma

A



B

	Structure	DV (μm)	DN (μm)	Conc. (MB/ml)[a]	Zeta potential (mV)	OVA density (molec./μm²)[b]	OVA/MB (μg/mg)
P-MB	DSPC/PA/DSPE-P2K-mal	3.05	1.36	$2.80x10^9$	-12.8	0	0
Cy3:OVA-MB	DSPC/PA/DSPE-P2K-mal-OVA:Cy3	2.71	1.32	$3.06x10^9$	-20.7	16'289	165.6
Cy3:OVA_{low}-MB	DSPC/PA/DSPE-P2K-mal-OVA:Cy3	2.94	1.33	$2.69x10^9$	-14.2	8'256	69.8
Cy3:OVA-LB	LB-OVA:Cy3	1.86	1.85	$1.17x10^9$	n.d.[c]	50'302	38.3
DQ:OVA-MB	DSPC/PA/DSPE-P2K-mal-OVA:DQ	2.90	1.35	$3.24x10^9$	-22.8	9'611	131.9
OVA-LB	LB-OVA	1.92	1.94	$1.03x10^9$	n.d.[c]	43'761	46.3
OVA-MB (A)	DSPC/PA/DSPE-P2K-mal-OVA	3.04	1.35	$2.54x10^9$	-21.7	33'414	160.3
OVA-MB (B)	DSPC/PA/DSPE-P2K-mal-OVA	2.62	1.24	$3.48x10^9$	-26.5	23'743	214.0

Bioley, Gilles, et al. "Gas-filled microbubble-mediated delivery of antigen and the induction of immune responses." *Biomaterials* 33.25 (2012): 5935-5946.

Summary

- Biomaterials can be utilized to overcome challenges with current allergen immunotherapy delivery
  - E.g. Decrease costs while increasing efficacy

- Important considerations for allergen immunotherapy delivery
  - Administration route
  - Dose
  - Sustained release
  - Safety
  - Patient compliance
  - Ease and standardization of application