

A novel allergen-encoding immunotherapeutic vaccine in the treatment of peanut allergy

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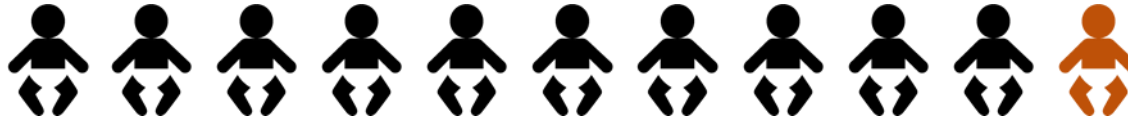


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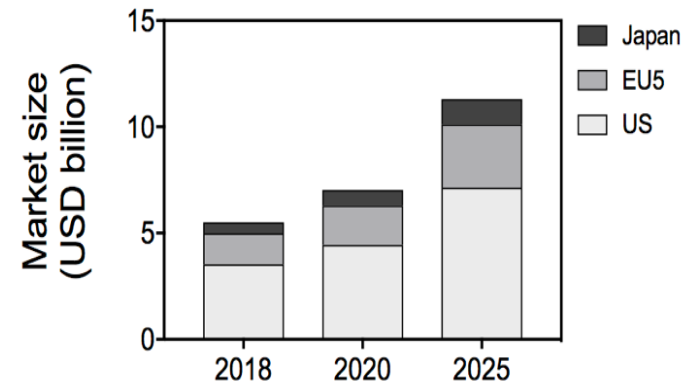
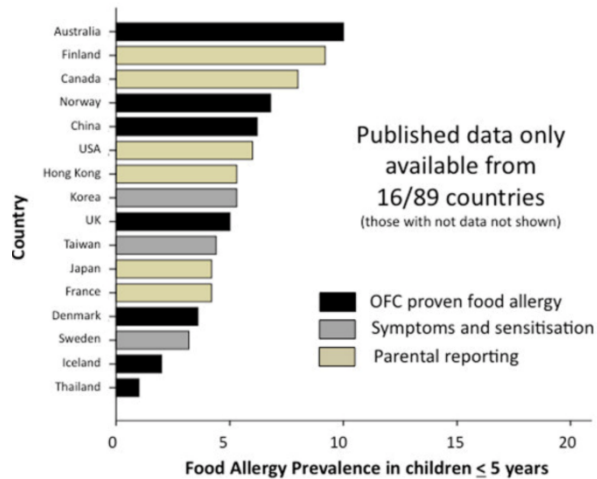
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Peanut allergy statistics



food allergy affects about 1 in 10 infants

Studies reporting Food Allergy Prevalence
in preschool children ≤ 5 years

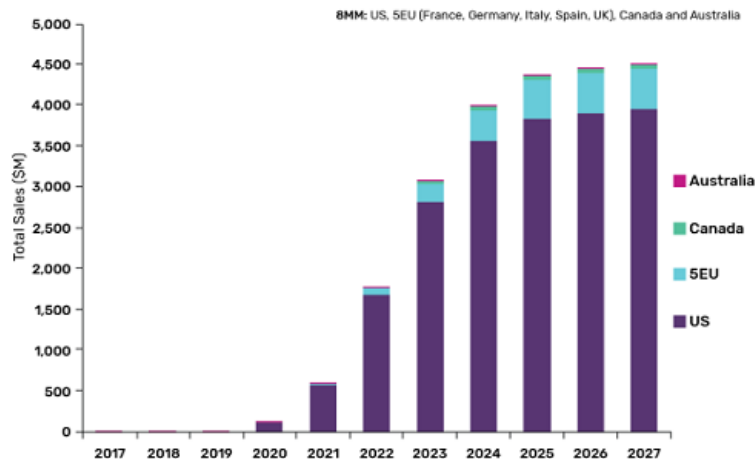


- ❖ Peanut allergy: high prevalence in Australia
- ❖ 3% of children are peanut allergic
- ❖ Of which, 80% remain allergic for life

By 2025:

- ❖ Projected 8 million peanut allergic individuals in the 7 major markets
- ❖ Projected market size of 11.3 billion USD

Sales forecast for peanut allergy in 8MM, 2017-2027



Source: GlobalData, Pharma Intelligence Centre

"This incredible growth stems from the projected entry of four new peanut immunotherapy products into a previously empty marketplace. These new therapies include three oral immunotherapy (OIT) products—Aimmune Therapeutics' AR-101, Prota Therapeutics' PPOIT, and Camallergy's CA-002—and one epicutaneous immunotherapy product—DBV Technologies' Viaskin Peanut."

Vaccine (company)	Technology	Mode of action	Route of administration	Stage
Viaskin® Peanut/ DBV-712 (DBV Technologies)	Epicutaneous immunotherapy	Desensitization	Transdermal	Phase III
Aimmune	CODIT-characterised oral desensitisation immunotherapy	Desensitization	Oral	Phase III
HAL-MPE-1 (HAL Allergy Group)	Hypoallergenic peanut extract	Desensitization	Subcutaneous	Phase I
Peanut allergen vaccine (Tunitas Therapeutics)	Ara h2-human FC gamma 1 chimeric fusion protein vaccine	IgE-Fc receptor 1 antagonist	Parenteral	Phase I
Ara-LAMP-vax (Immunomic Therapeutics/Astellas)	Lysosomal associated membrane protein DNA vaccine	Immuno-modulation	Parenteral	Phase I

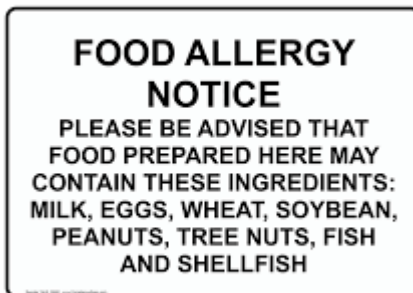
Current treatment: total avoidance



THIS SCHOOL IS
NUT FREE



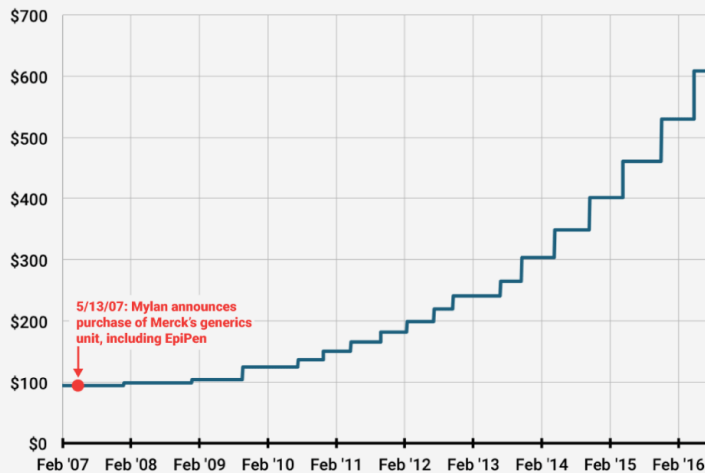
THANK YOU
for keeping our school safe!



If you are exposed: EpiPen adrenaline

Markets  Chart of the Day

EPIPEN PRICE UNDER MYLAN



SOURCE: Truven Health Analytics

BUSINESS INSIDER

BUSINESS INSIDER



Rx

PATIENT NAME _____

ADDRESS _____

Prescription:

*3 EpiPen 2-Pak cartons
2-Pak carton for home
2-Pak carton for school or gym bag
2-Pak carton for relative's house work

Write DAW
for 6 total EpiPen Auto-Injectors

Date _____ Signature _____

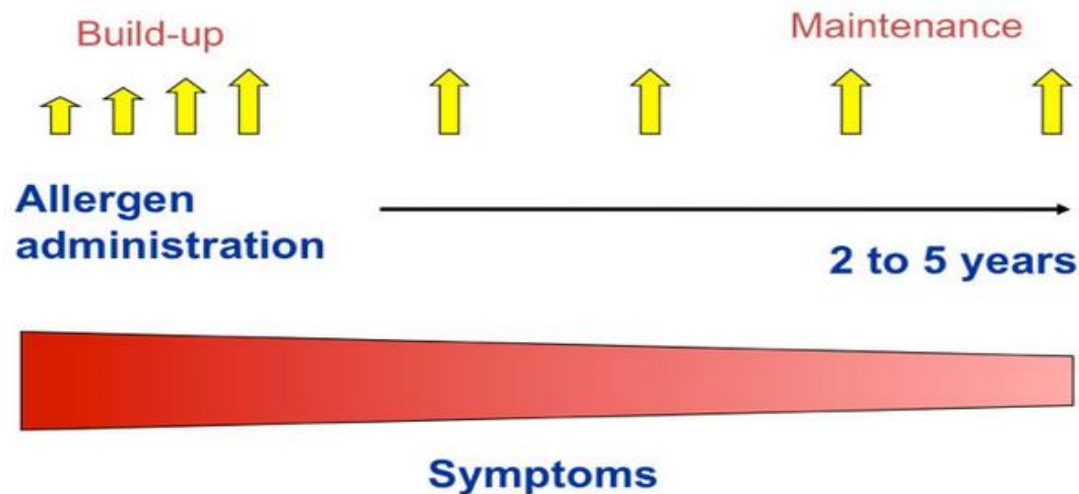
The more specific the prescription, the greater the likelihood the pharmacist will fill it as intended

Prescribe an EpiPen 2-Pak® for each location where your patient may need immediate access

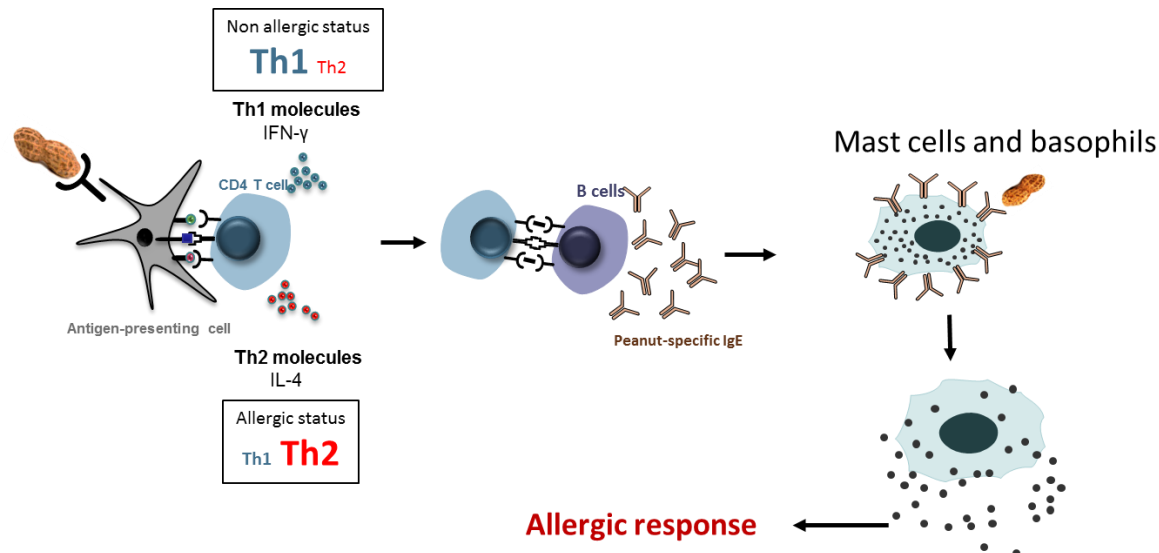
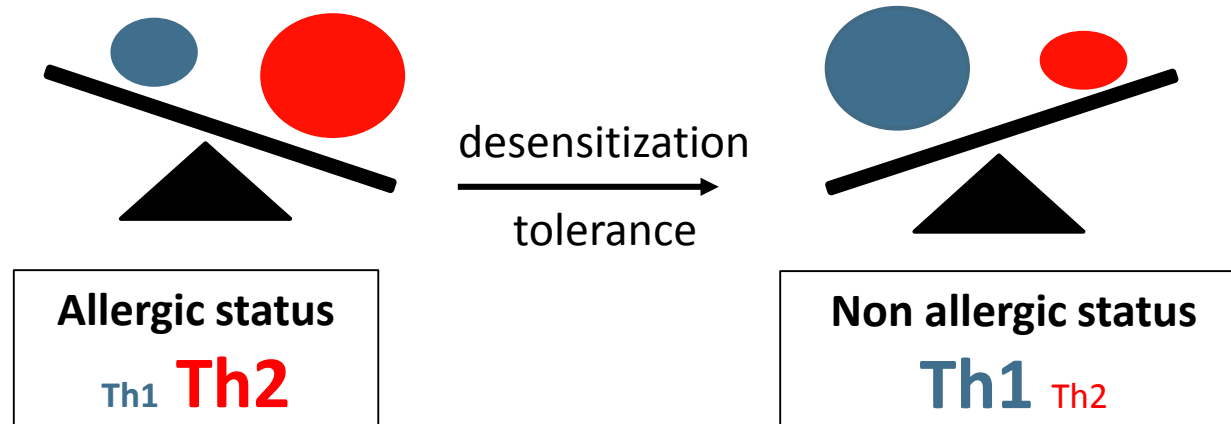
- ☒ "HOME"
- ☒ "SCHOOL"
- ☒ "WORK"
- ☒ "GYM BAG"

Desensitization-oral immune therapy

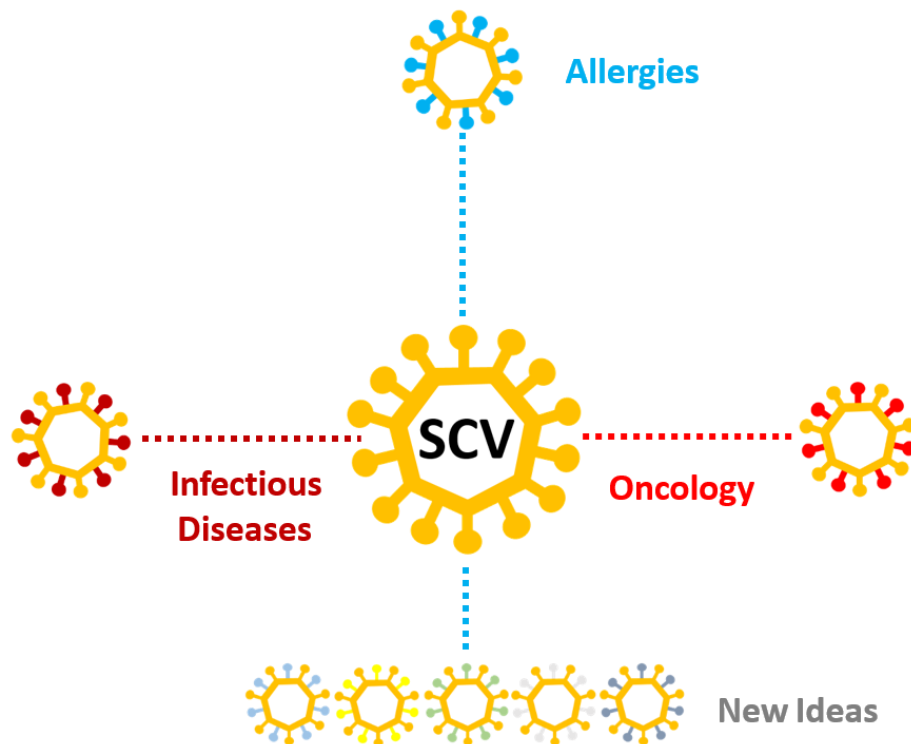
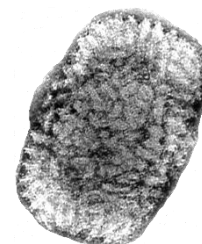
- Intense and costly administration of allergen
- Requires maintenance
- Benefit not a long term solution
- This treatment has safety concerns and is not approved by the FDA
- Sub lingual oral immunotherapy at home, 3 years duration (dust mite and pollen) compliance as low as 7%



Permanent desensitization by re-educating the allergic T cell response with a vaccine?



The propriety 'Sementis Copenhagen Vector' platform technology developed with Sementis Ltd.



Vaccine Delivery Vehicle (SCV Vector):

“Genetically crippled smallpox vaccine that can be engineered to make ANTIGENS from disease targets to raise immunity to that disease”

Totally attenuated vaccine vector system

Manufacturing Cell Substrate:

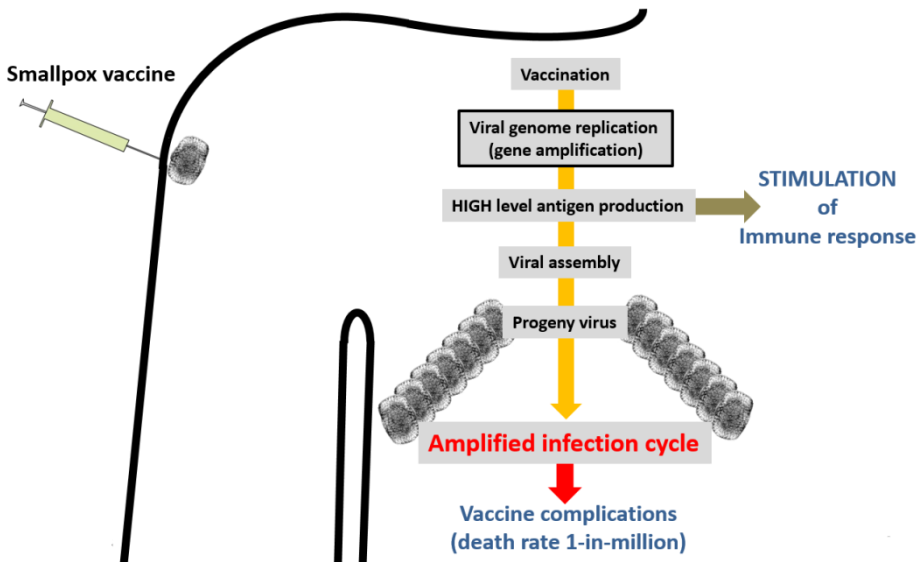
“The **CHO** biotechnology friendly cell substrate engineered to produce the SCV vector”

A first for the production of vectored vaccines!

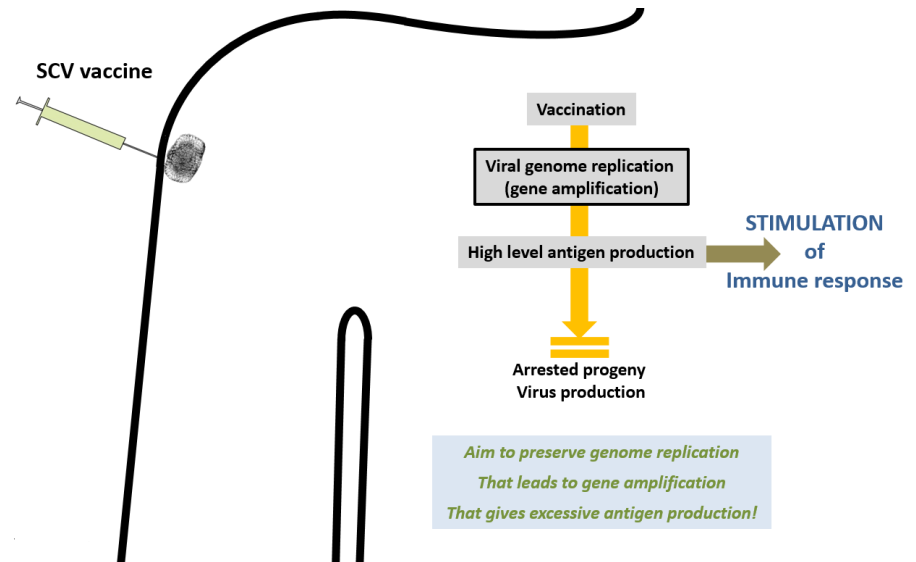
Declared COI: JD Hayball holds shares in Sementis Ltd and sits on the SciAdBrd

How does the SCV platform work?

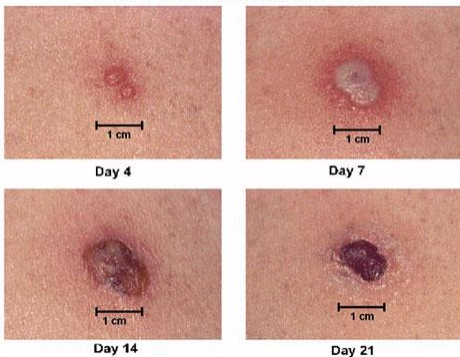
Smallpox Vaccine (Live replication competent)



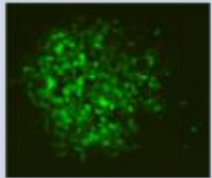

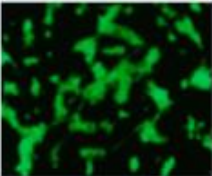
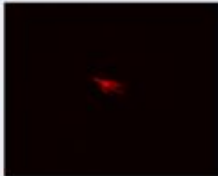
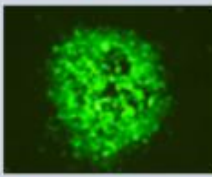

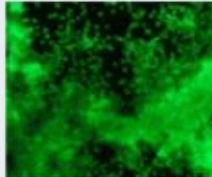

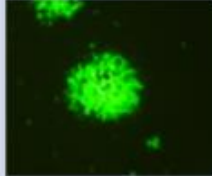

SCV Vaccine (Live NON-replication competent)



Primary Vaccination Site Reaction

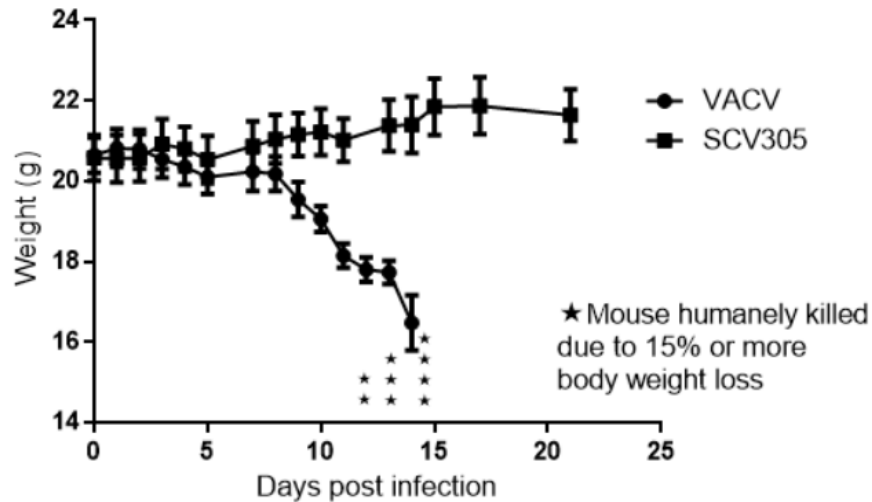


SCV does not multiply in human and mammalian cells lines

		Vaccinia	SCV
143B	Human Bone Cells		
MRC-5	Human Lung Cells		
HEK-293	Human Kidney Cells		
A431	Human Skin Cells		
HeLa	Human Cervical Cells		

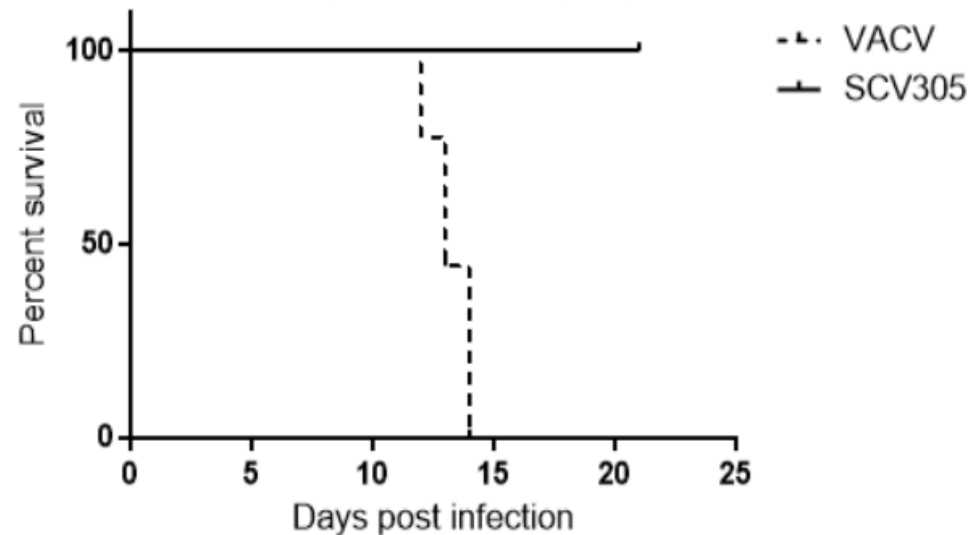
Safety and biodistribution of SCV in immunocompromised SCID mice

Average Body Weights \pm SEM
(n=9 per treatment group)



In the absence of an antiviral immune response SCV was unable to cause productive disease.

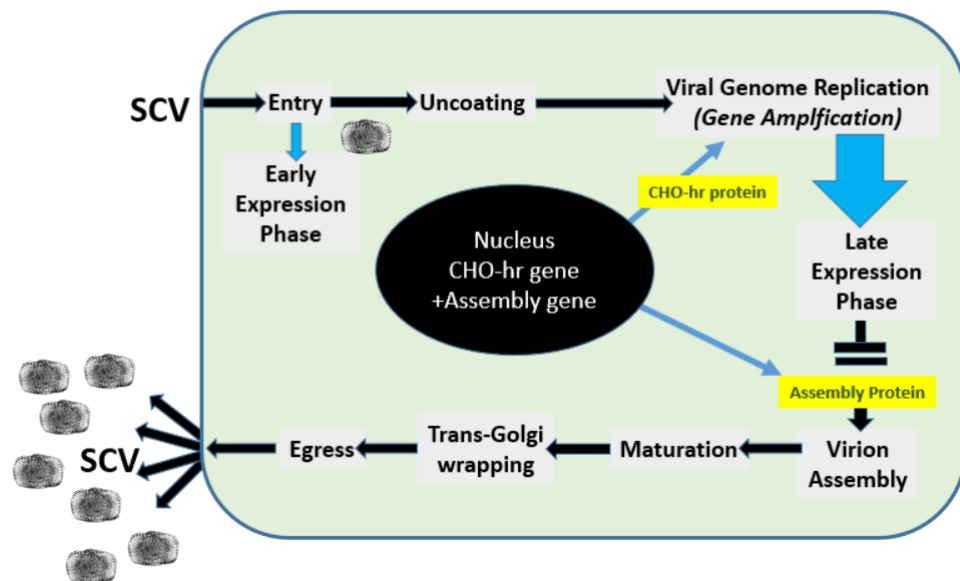
Survival Plot
(n=9 per treatment group)



In the absence of an antiviral immune response SCV is not pathogenic.

CHO-based SCV cell substrate for manufacturing

SCV Production CHO Cell Line

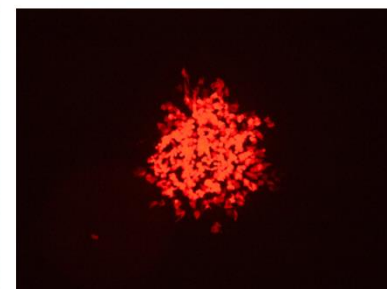


Infection with SCV

(Totally attenuated SCV expressing Red Fluorescent Protein)



CHO

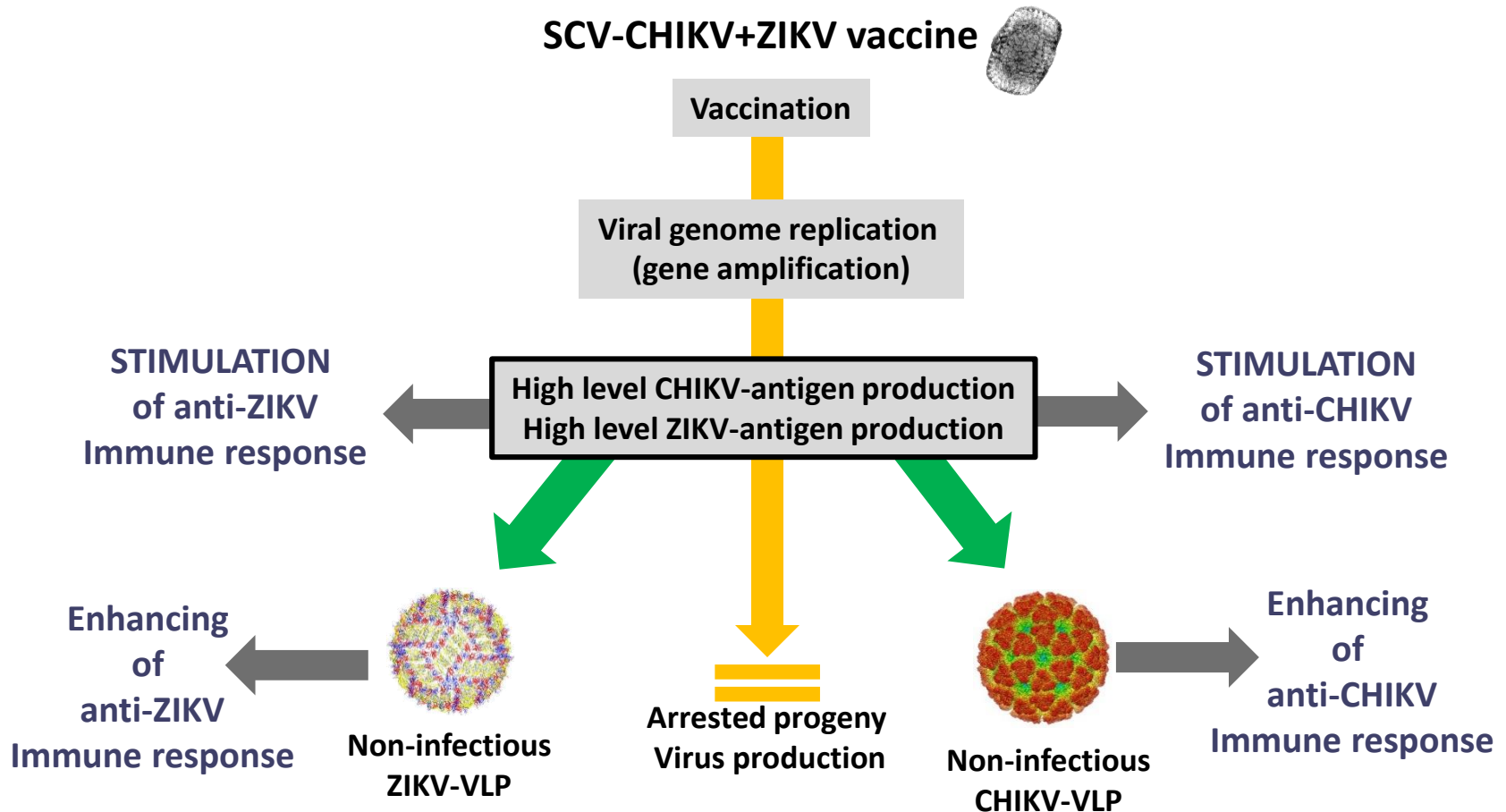


SCV Rescue cell line

Sementis' SCV-cell substrate for manufacturing was derived from GMP produced CHO-S cell line :

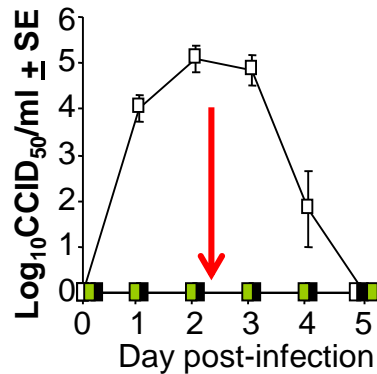
- Sourced as a GMP produced batch of CHO-S from Life Technologies (ThermoFisher Scientific), Cat # A1136401, royalty free, one off licence fee per field, ie, infectious diseases, immunotherapeutics
- Suspension cell line – suitable bioreactor production
- Cultured in serum-free chemically defined medium, eg, CD-CHO medium from Life Technologies, Cat # 10743029

An effective single shot SCV-CHIKV+ZIKV vaccine

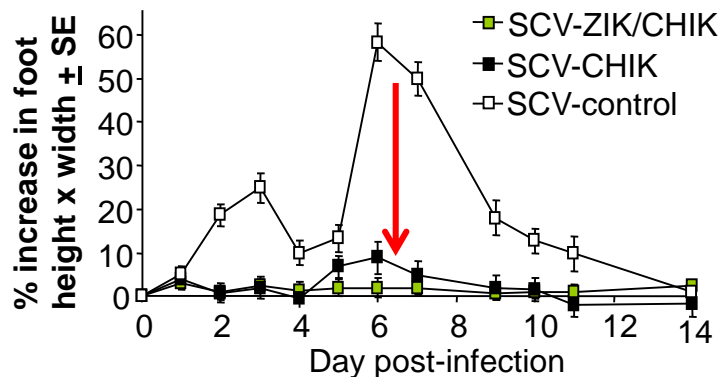


Single-shot SCV-CHIKV+ZIKV vaccination protects against infection with both diseases

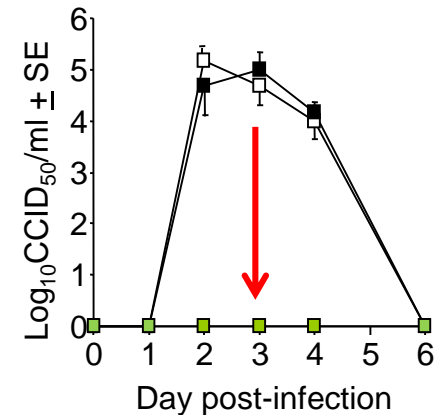
- C57BL/6 mice
Protection against viraemia



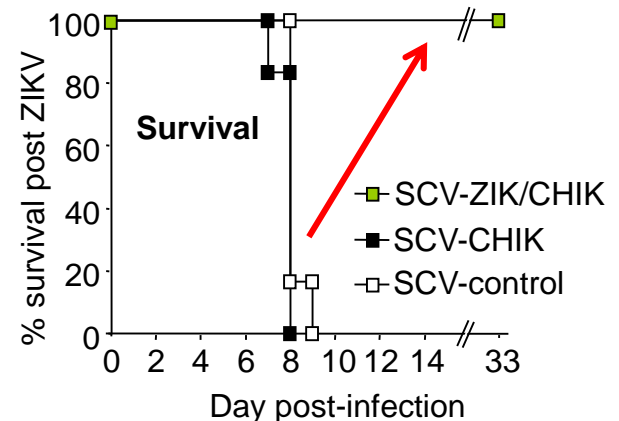
Protection against
CHIKV arthritis



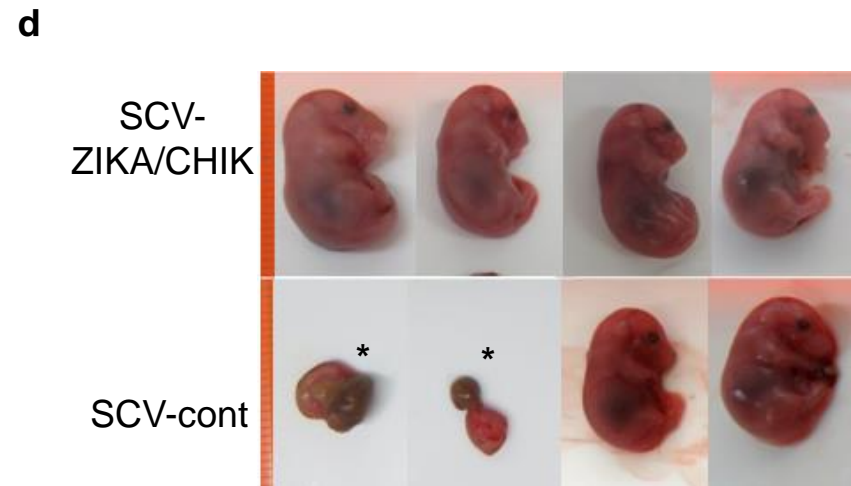
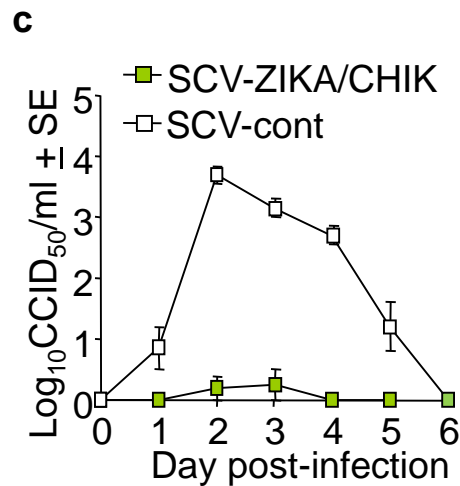
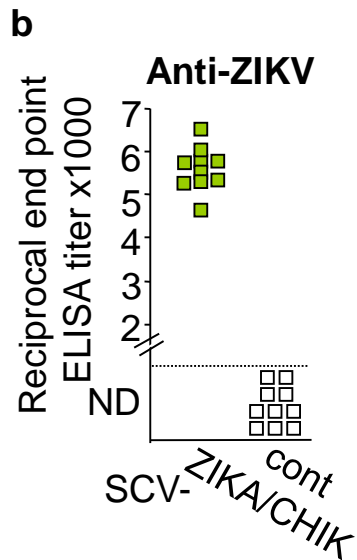
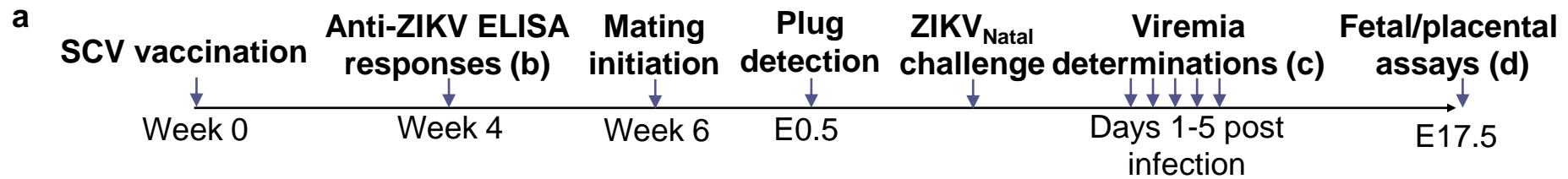
- IFNAR mice
Protection against viraemia



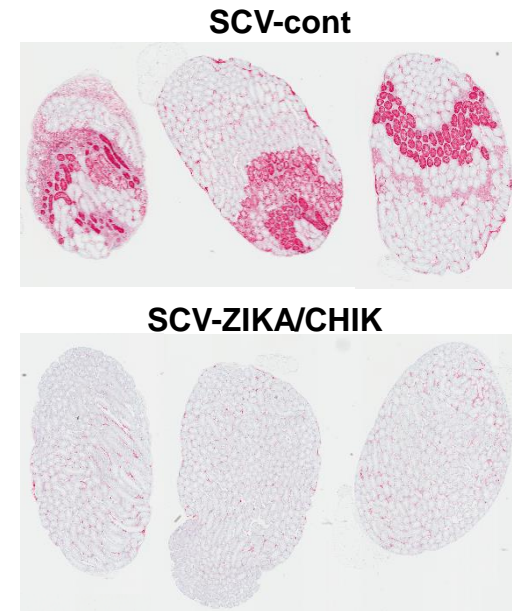
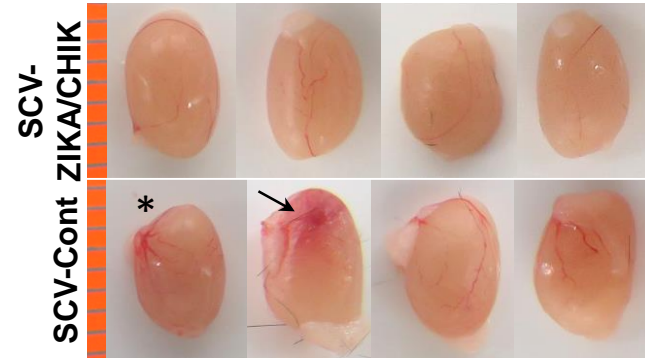
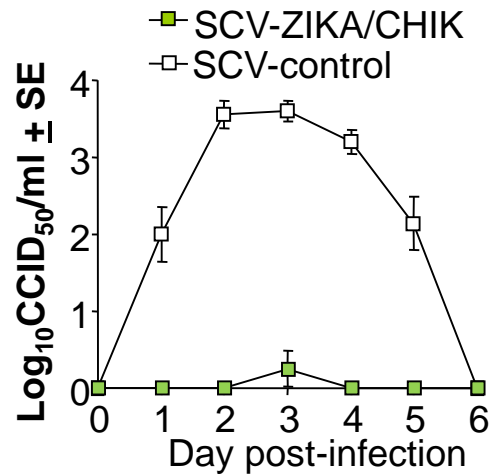
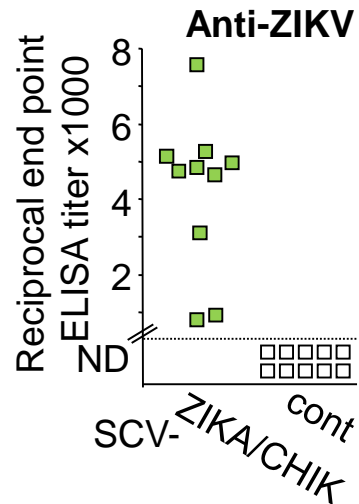
Protection against
lethal ZIKV_{MR766}



A single shot vaccination protects against ZIKV detrimental foetal outcomes



A single shot vaccination protects against ZIKV testicular damage





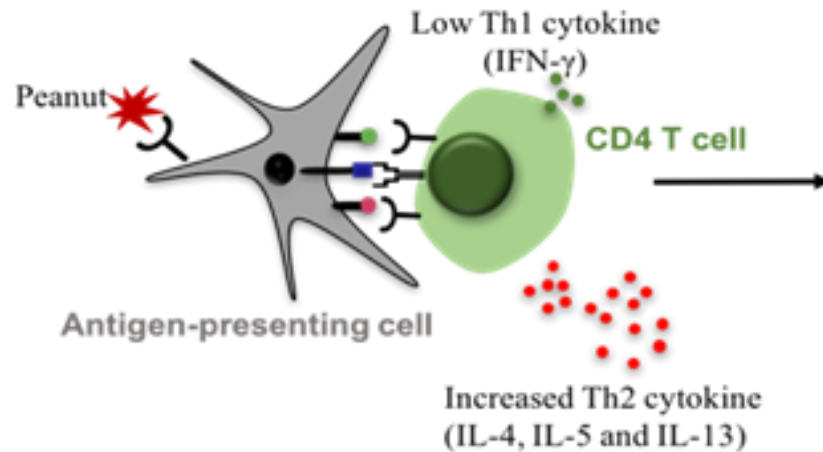
- Implavax technology for SCV delivery
 - Enhanced stability?
 - Enhanced immune responses?
- Stage 1: Formulation of SCV into solid doses (Enesi)
- Stage 2: Immunogenicity study (Sementis)
 - CHIKV/ZIKV vaccine
 - Peanut vaccine

Summary I

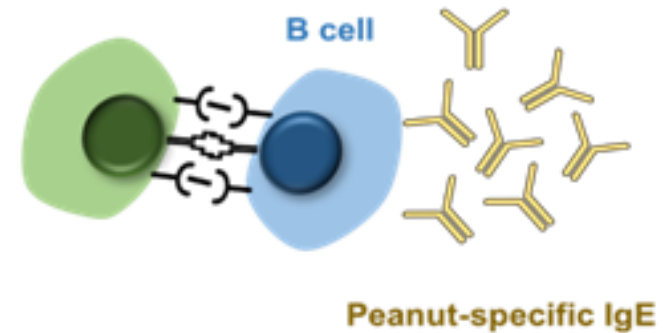
- SCV is replication-defective *in vitro* and safe *in vivo*
- Commercially-proven CHO cells for scalable vaccine production
- SCV-CHIKV+ZIKAV vaccination elicits single shot and long term protective immune responses
 - Protects pregnant mice and their offspring from ZIKAV infection
 - Protects testis of male mice from ZIKAV mediated damage
 - No immune interference between CHIKV and ZIKV vaccine antigen expression nor booster responses (**data not shown**)
- Liu *et al*, BioTechniques, 2017.
- Eldi *et al*, Molecular Therapy, 2017
- Prow *et al*, Nature Communications, 2018.
- Prow *et al*, Expert Review Vaccines, 2019
- US NIH/NIAID-sponsored NHP challenge study completed, 2018.

Permanent desensitization by re-educating the allergic T cell response with a vaccine?

1. Induction of Th2 biased peanut-specific T cells

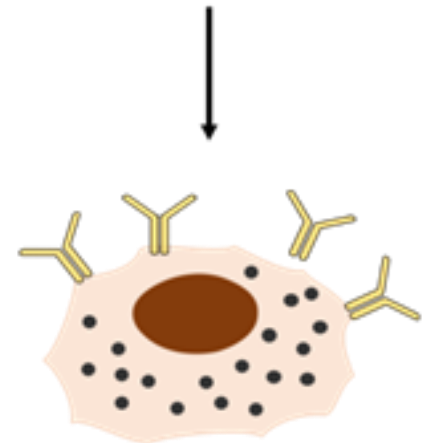


2. IgE production

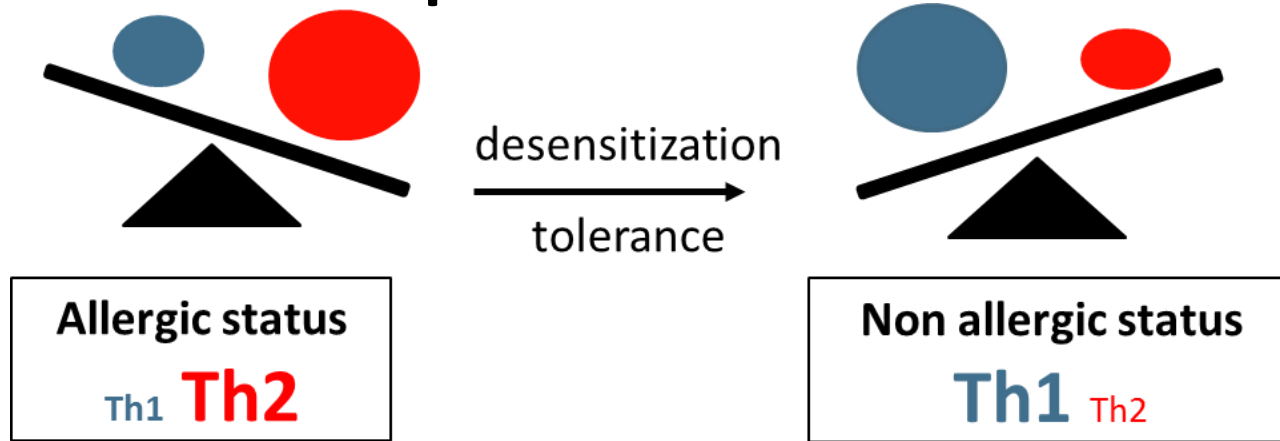


4. Mediator release leading to allergic symptoms

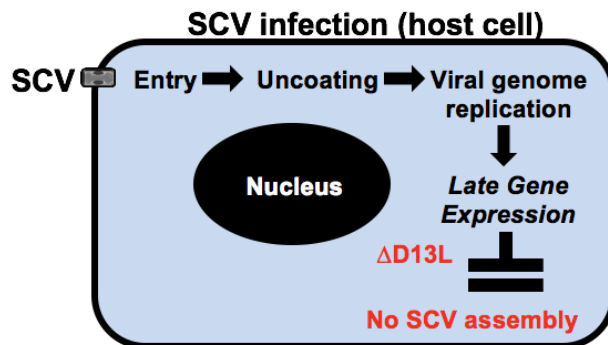
3. Mast cell priming with IgE



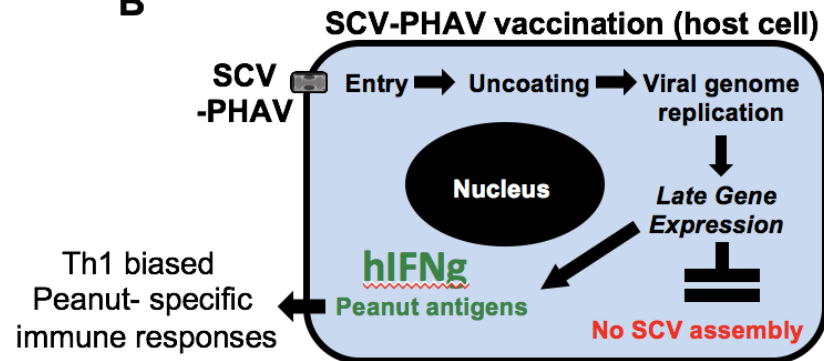
Can an SCV-based vaccine skew a peanut allergy-specific Th2 responses to a Th1 bias?



A

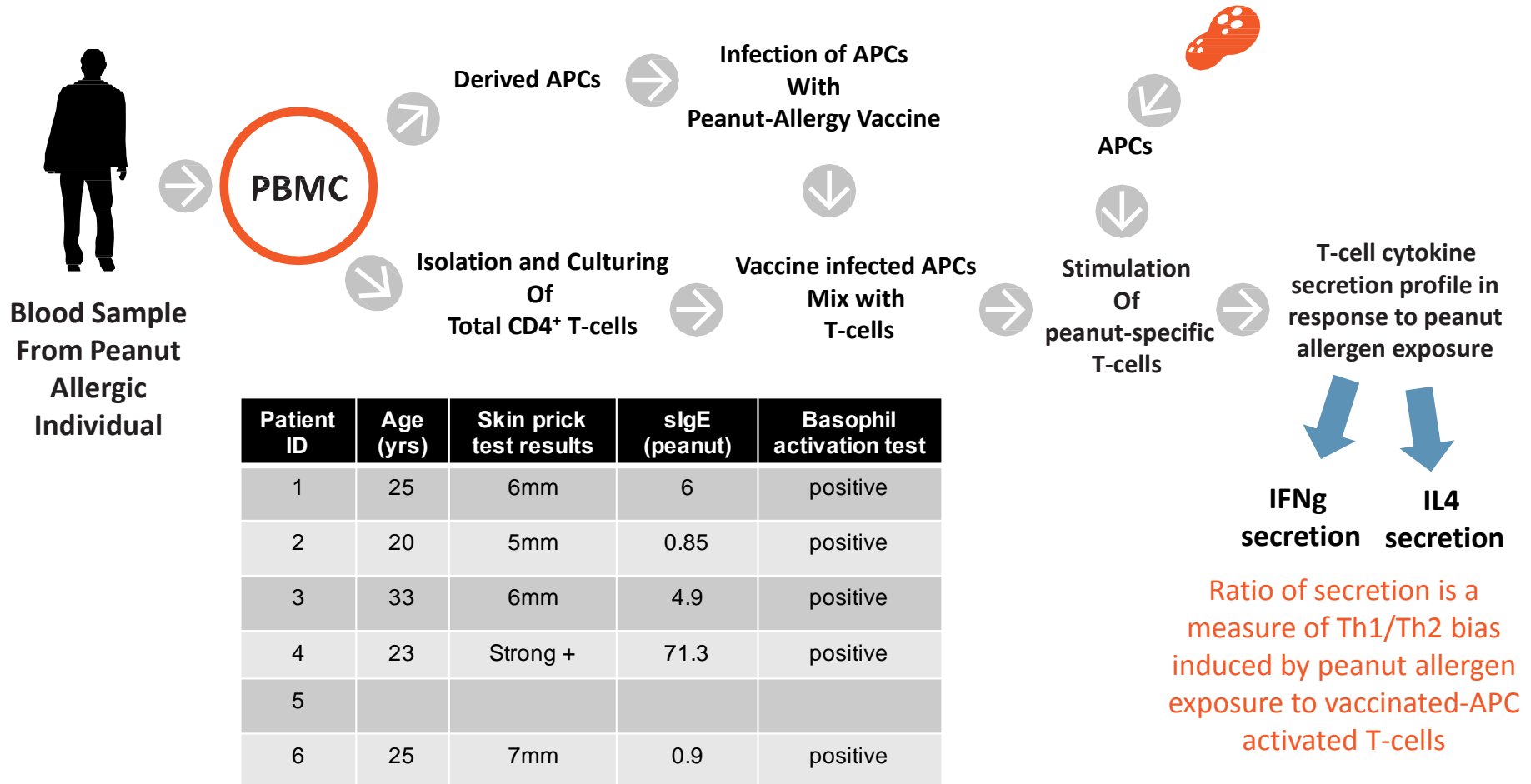


B



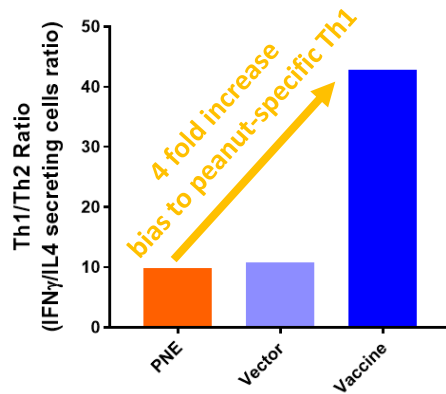
SCV-PHAV expresses a ubiquitinated, multi-peanut antigen fusion protein expressing:
Ara h 1, 2, 3, 5, 6, 7, 8, 8.1, 9, 10, 11

Confirming vaccine mechanism of action using APC and total T-cells from blood of a peanut allergic individual

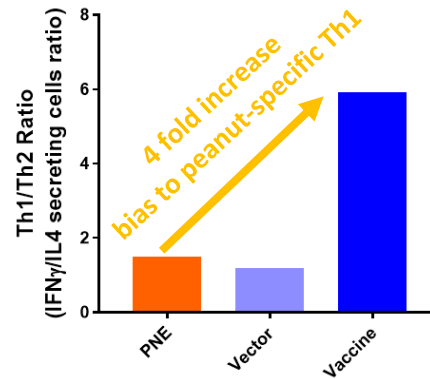


Th1/Th2 profiles for SIX peanut allergic volunteers

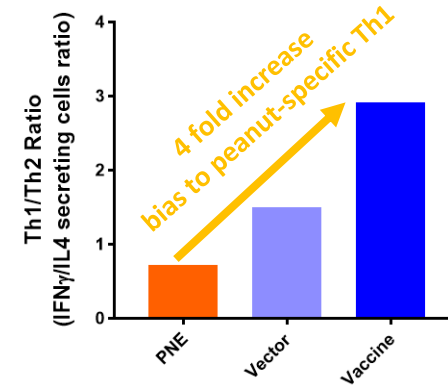
Peanut Allergic Volunteer: MD (female)
Ex Vivo Th1/Th2 Profile



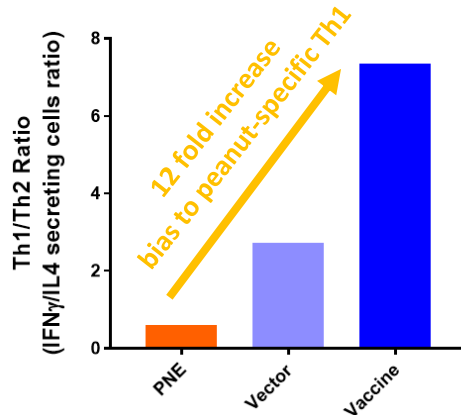
Peanut Allergic Volunteer: JD (female)
Ex Vivo Th1/Th2 Profile



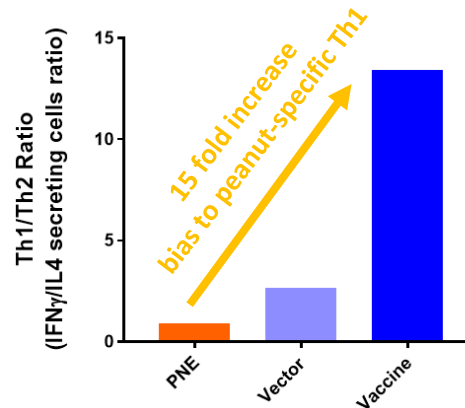
Peanut Allergic Volunteer: AB (female)
Ex Vivo Th1/Th2 Profile



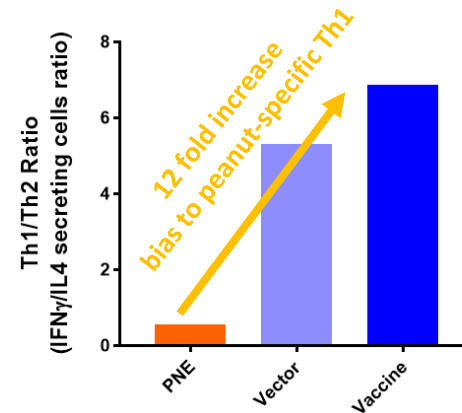
Peanut Allergic Volunteer: MA (male)
Ex Vivo Th1/Th2 Profile



Peanut Allergic Volunteer: SN (male)
Ex Vivo Th1/Th2 Profile

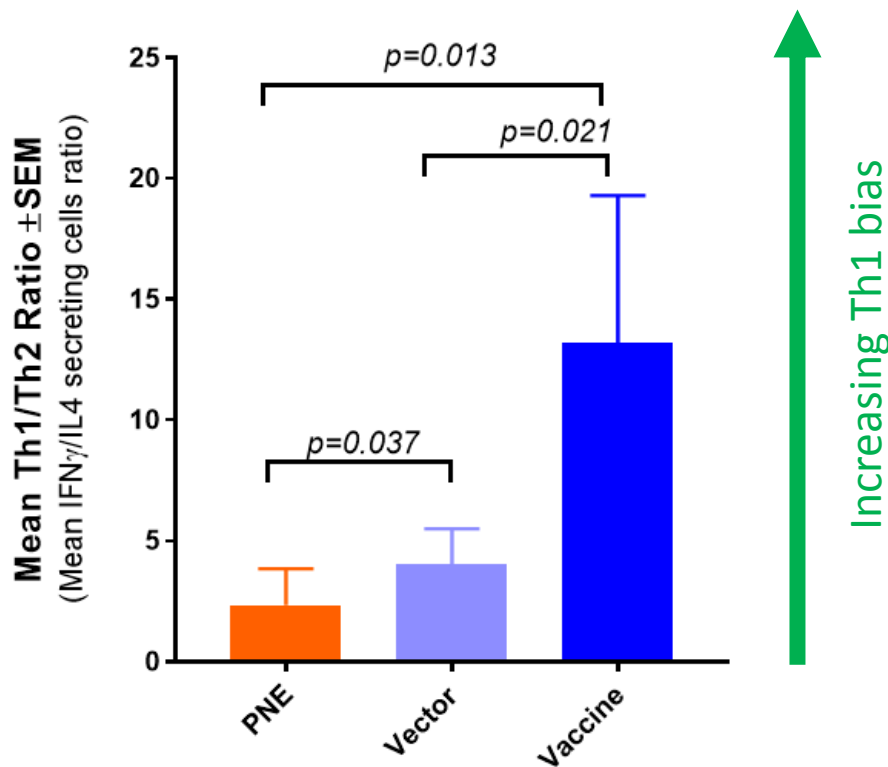


Peanut Allergic Volunteer: KD (female)
Ex Vivo Th1/Th2 Profile



Vaccine inducing Th1 efficiency in a sample population of 6 peanut allergic volunteers

The Mean Ex Vivo Vaccination Induced Th1/Th2 Profile of 6 peanut allergic Volunteers

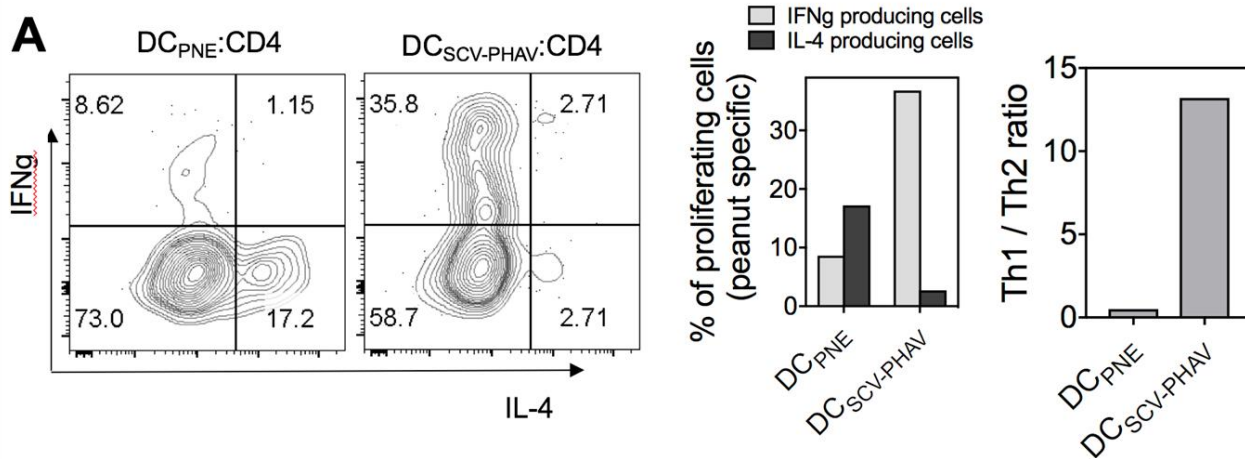


Significance was determined using one-tailed Mann-Whitney T-test
Significance = $p < 0.05$

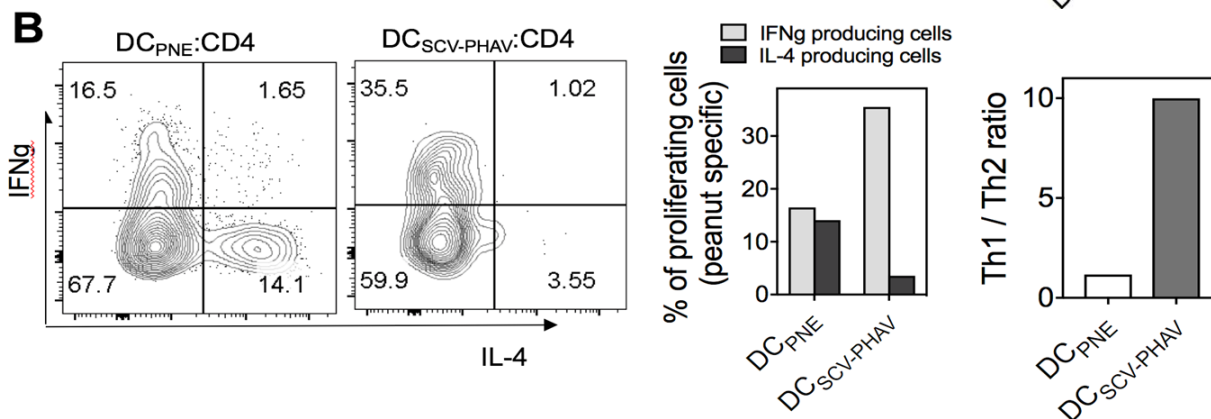
Conclusion:

1. The **peanut hypoallergy vaccine** treated DCs induces a significant increase in a peanut-specific Th1 response over and above the T-cells treated with **PNE-treated DCs** (peanut protein extract).
2. The **peanut hypoallergy vaccine** treated DCs also induced a significant increase in a peanut-specific Th1 response over and above the T-cells treated with **SCV-vector only DC**.

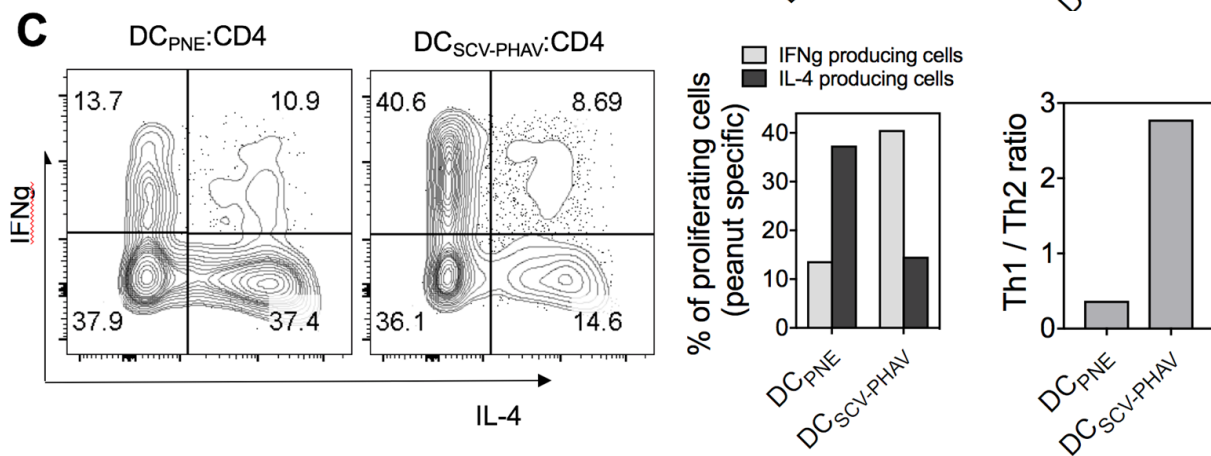
Assay done in 2016



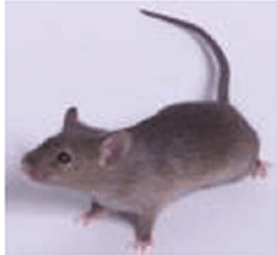
Assay done in Jan 2017



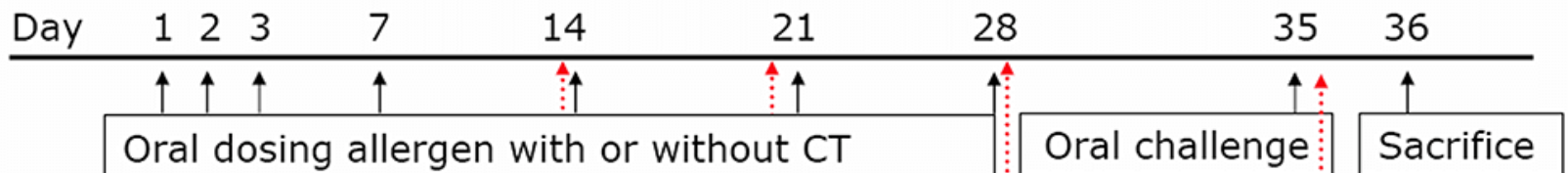
Assay done in Aug 2017



A mouse model for food allergy



- C3H/HeOuJ mice
- Oral (gavage) dosing of allergen: Peanut, casein or whey with the mucosal adjuvant cholera toxin (CT)

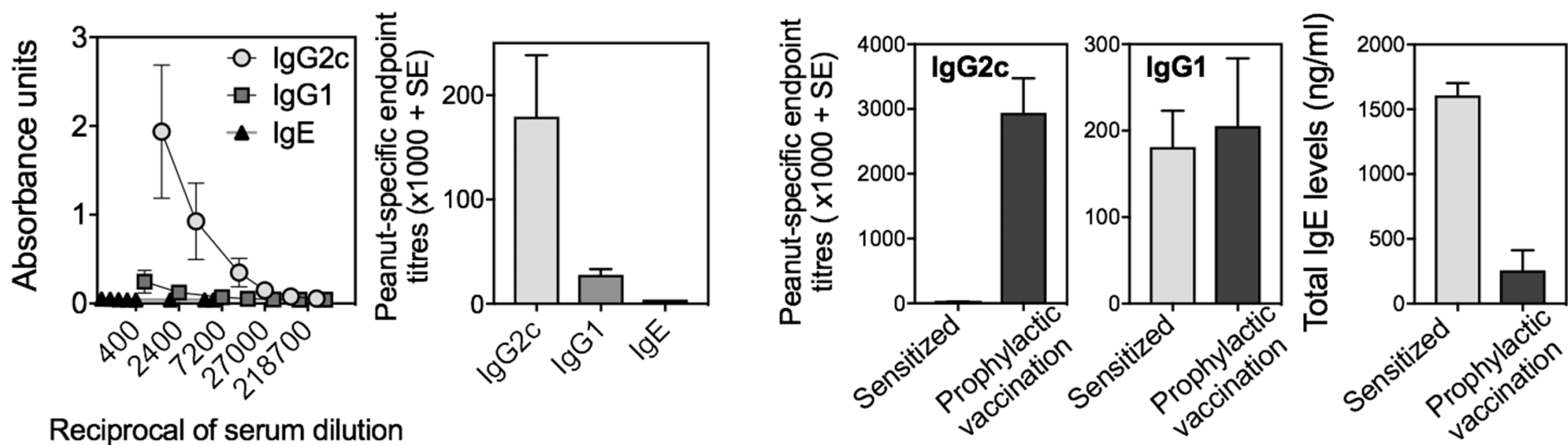
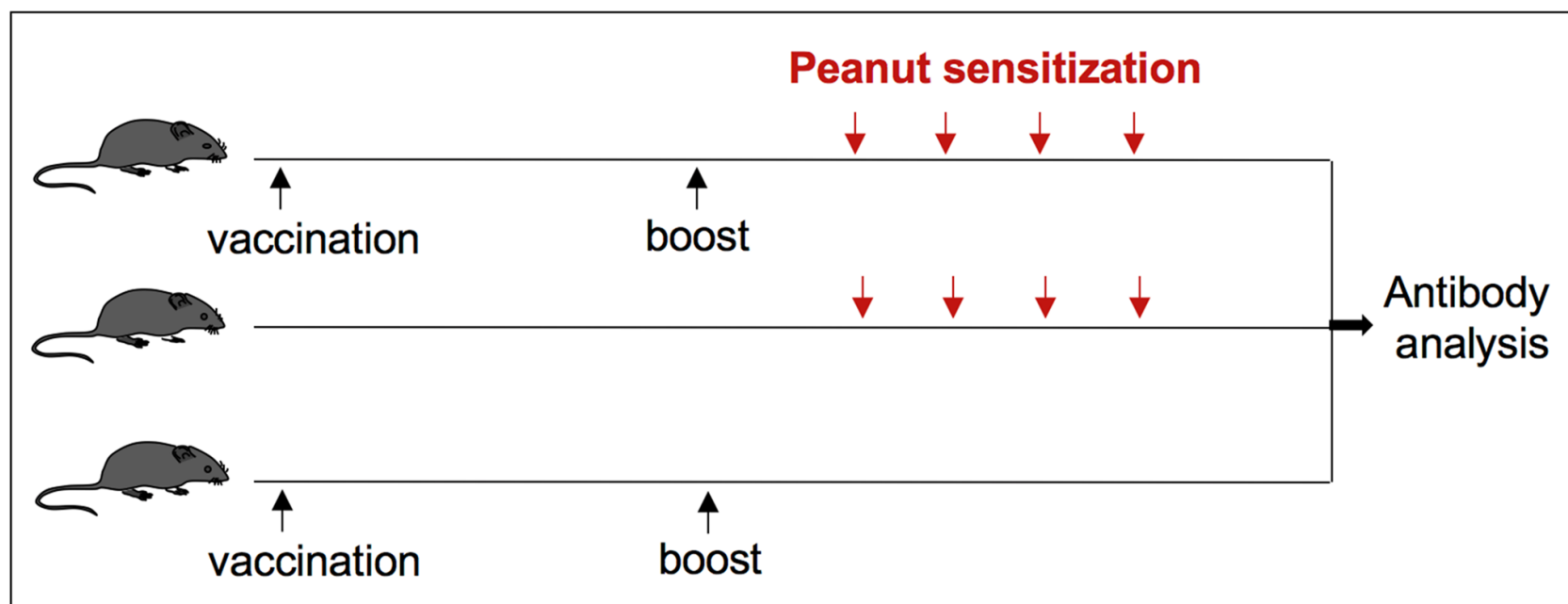


- Early parameters like allergen-specific cytokine production by spleen

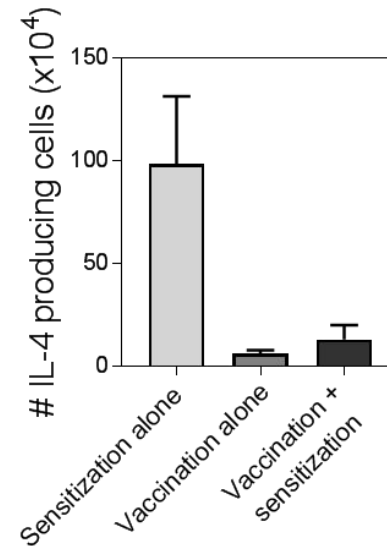
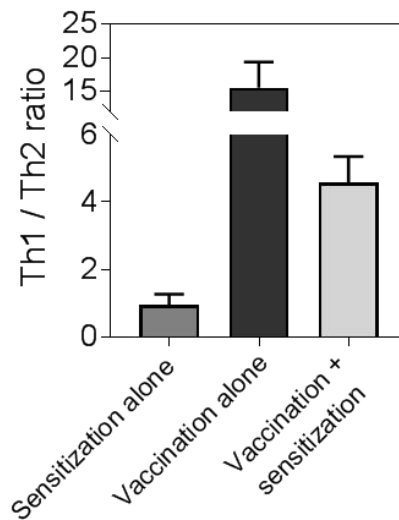
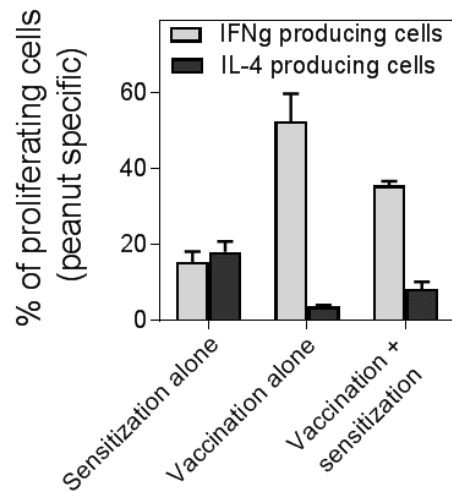
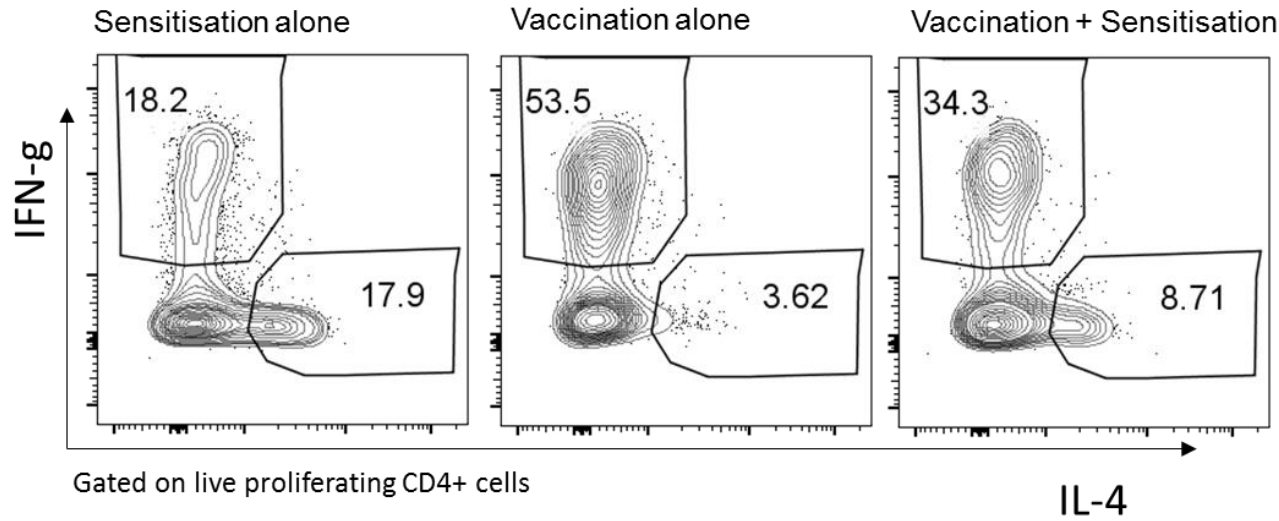
- Weekly blood collection, serum ELISA's (antibodies against allergen)
- Allergen-specific cytokine production in the spleen

Clinical parameters upon oral challenge with allergen:

- Acute allergic skin response
- Intestinal permeability
- Mast cell degranulation
- Diarrhea
- Intestinal motility



Ex-vivo stimulation antigen specific CD4 T cell cytokine analysis



Summary II

- SCV-PHA *ex vivo* vaccination induces Th1-skewed response in a sample population of 6 peanut allergic volunteers
- The same Th1-skewed response pattern is observed in the same donor when tested three times over a 12month period
- SCV-PHA *in vivo* vaccination delivers a skewed Th1 vsTh2 response in peanut allergic mice
- Eldi *et al*, manuscript in preparation.

Experimental Therapeutics Laboratory



sementis

Dr Paul Howley, *Sementis Ltd., Vic.*

Prof Andreas Suhrbier, *QIMR Berghofer, Qld.*

Dr William Smith, *Royal Adelaide Hospital, SA.*

Dr George Lovrecz. *CSIRO, Clayton, Vic.*

In collaboration with

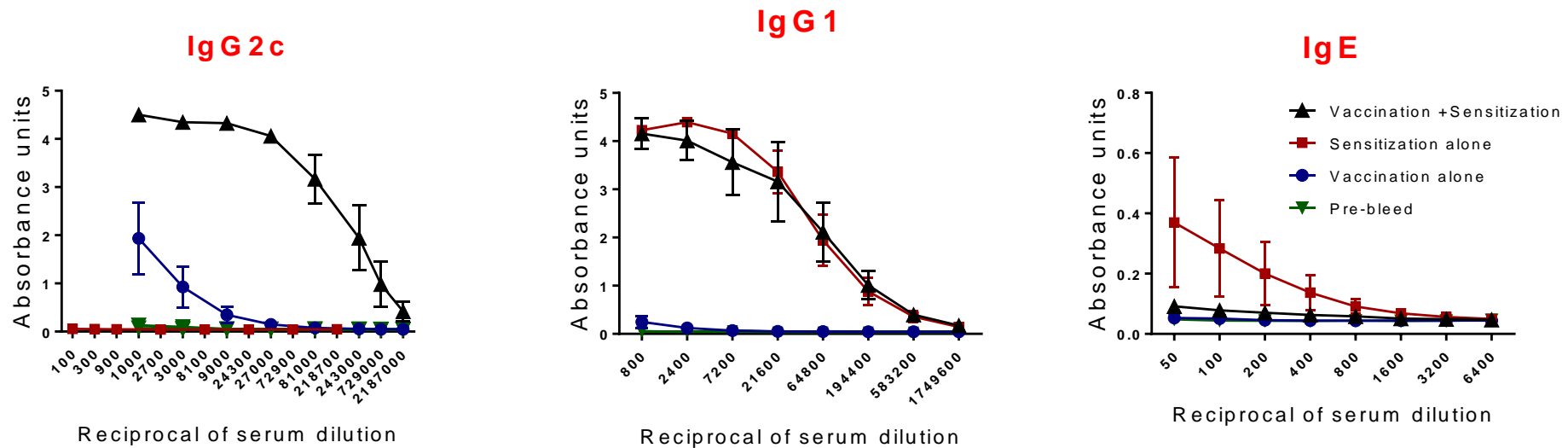


University of
South Australia



Australian Government
Australian Research Council

What happens to the peanut-specific antibody levels post-sensitization in vaccinated mice?



Th1 response: Sensitization boosts Th1 response in vaccinated mice

Th2 response: Sensitization does not induce IgE in vaccinated mice
IgG1 response similar to sensitized mice

Does vaccination prevent mast cell degranulation following peanut exposure?

