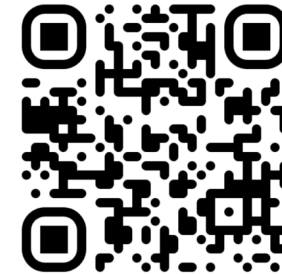
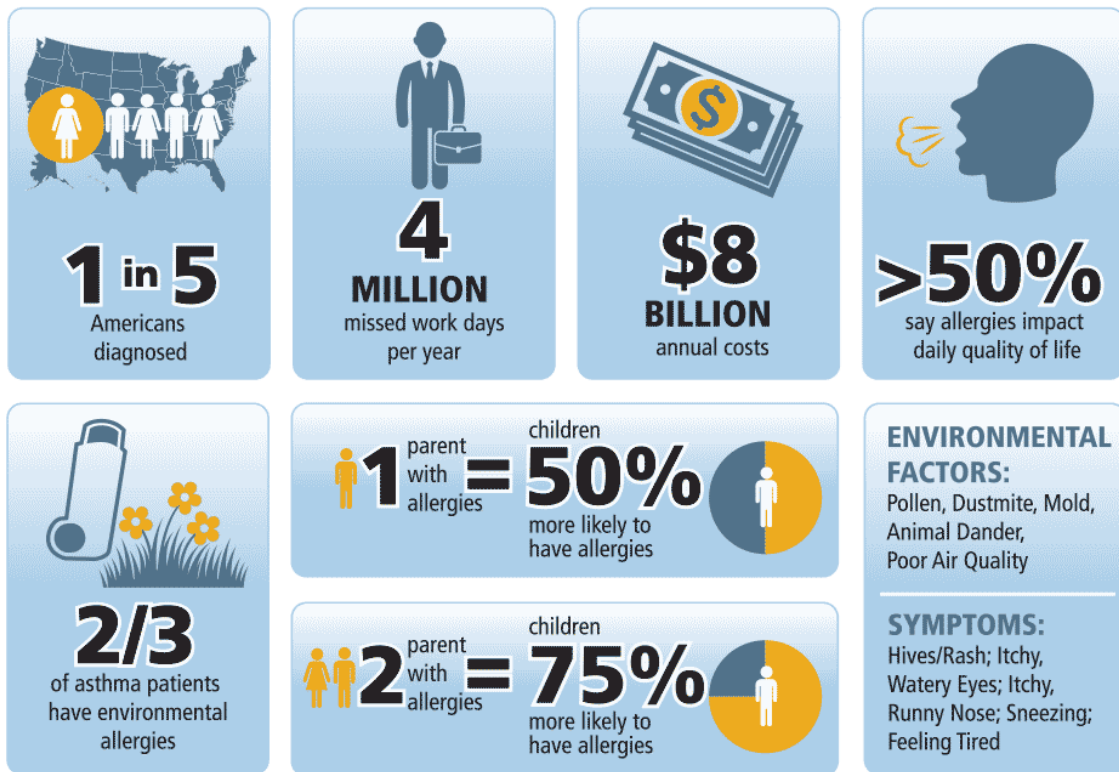




Nanoparticle-based immunometabolism approach to mitigate allergic airway inflammation

Shruti Dharmaraj, MS
Dr. Ryan Pearson Laboratory
Department of Pharmaceutical Sciences
University of Maryland School of Pharmacy



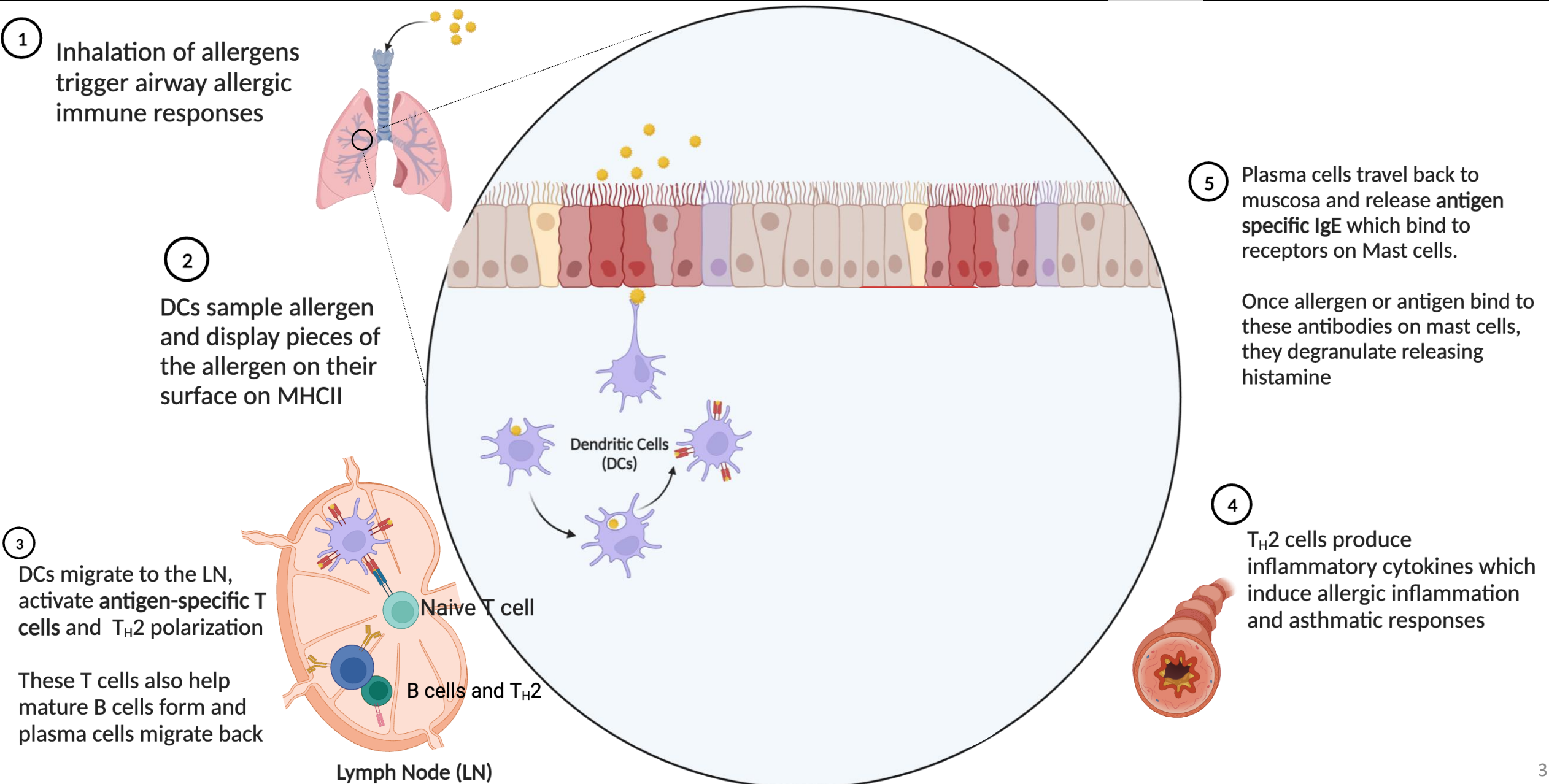


AllergyAsthmaNetwork.org

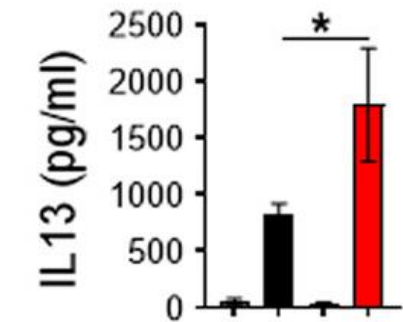
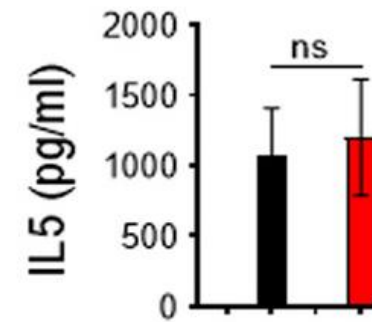
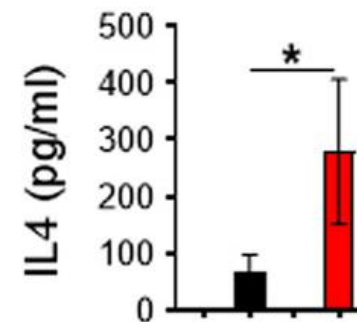
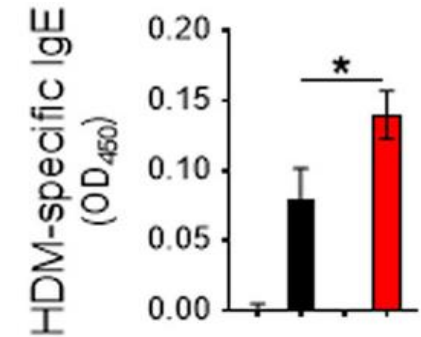
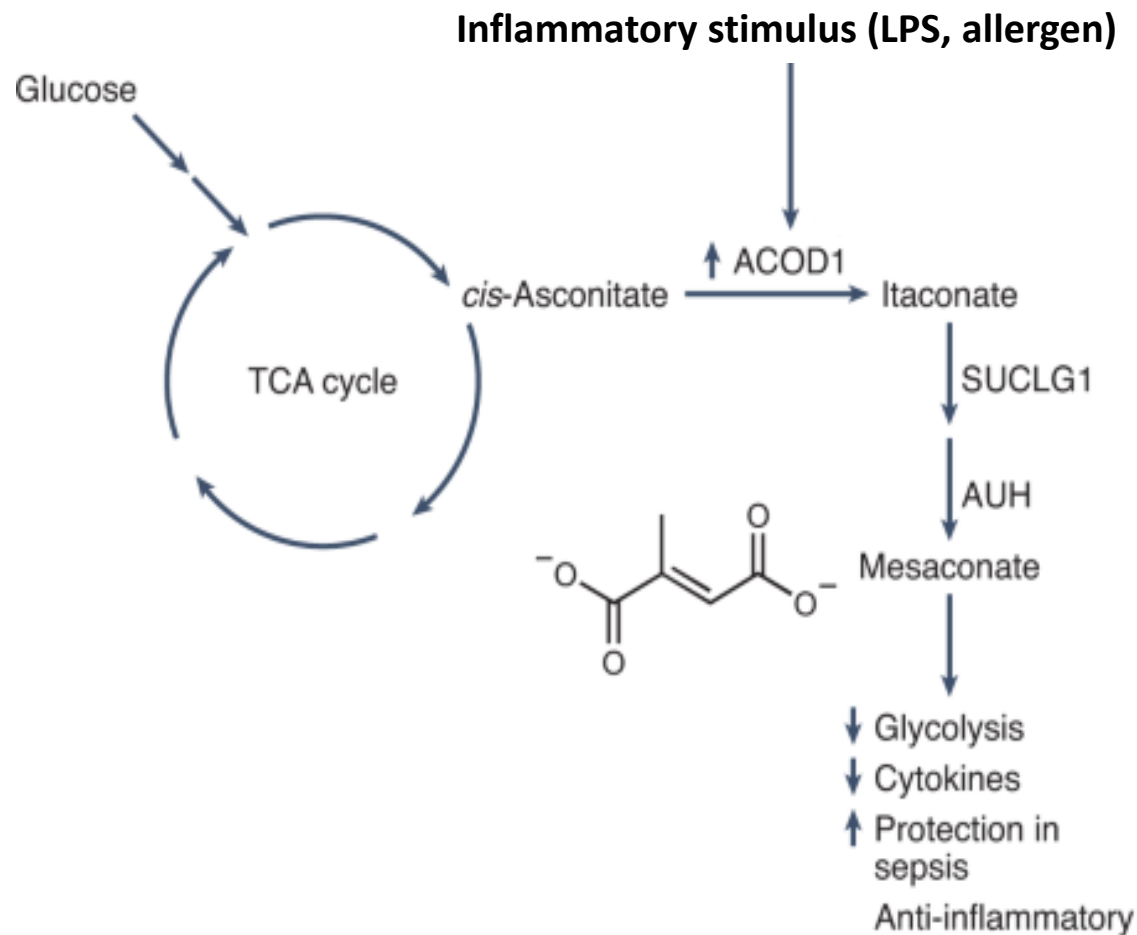


First line treatments only focus on symptom management

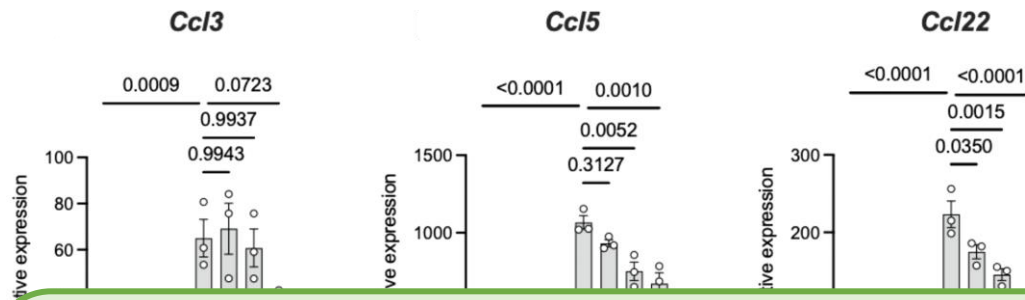




Irg1/ itaconate pathway is a promising target for treating allergies



Modified from: Jaiswal Mucosal Immunology 2022

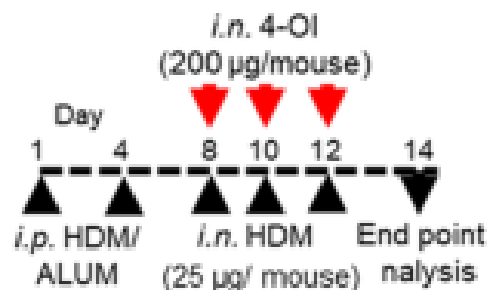


1. Poorly soluble – limiting

Goal: To address the underlying metabolic dysfunction in allergy using a more clinically translatable approach

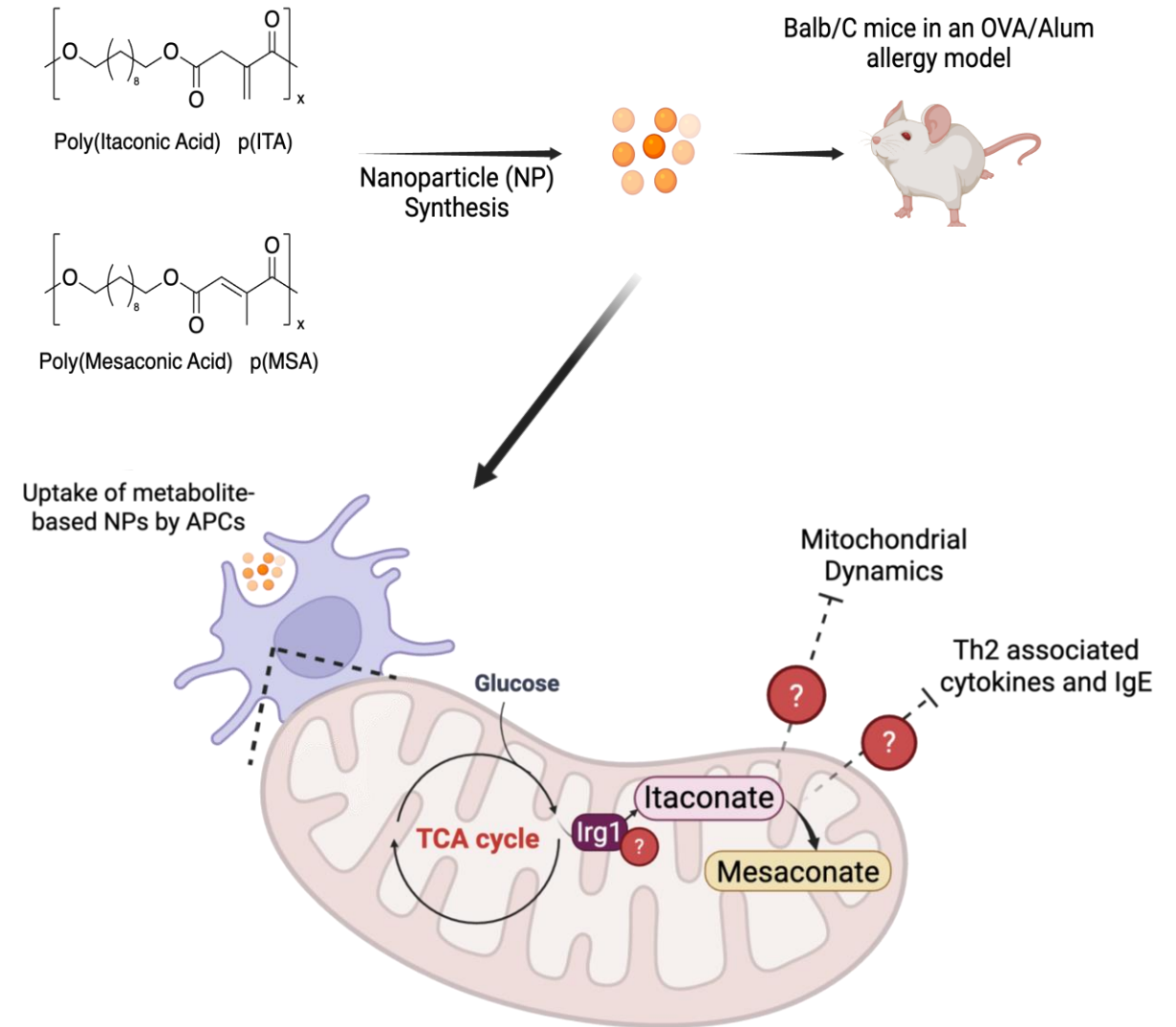
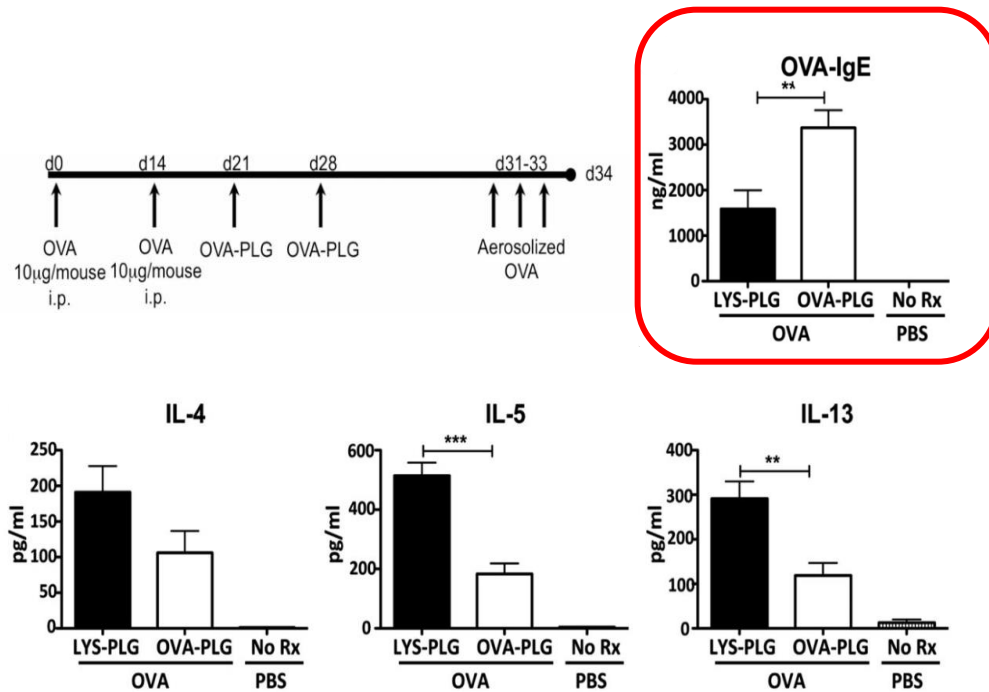
inflammatory properties.

3. Frequent and repeated doses



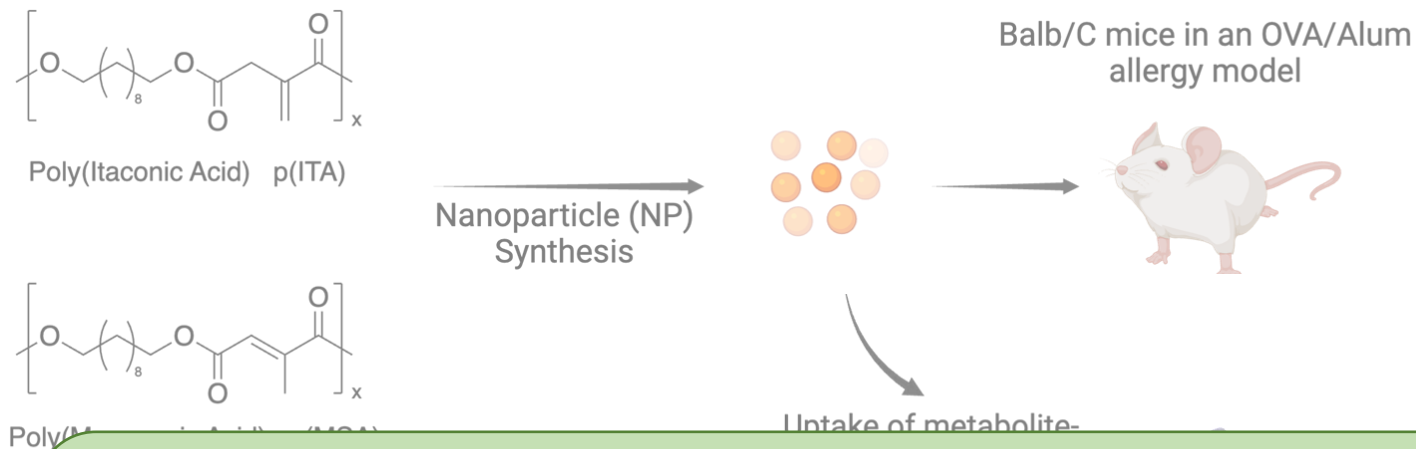
Modified: Jaiswal, A. et. al (2022). *Mucosal immunology*, 15(2), 301–313. <https://doi.org/10.1038/s41385-021-00462-y>

Using itaconate-based polymeric nanoparticles to treat allergic disease

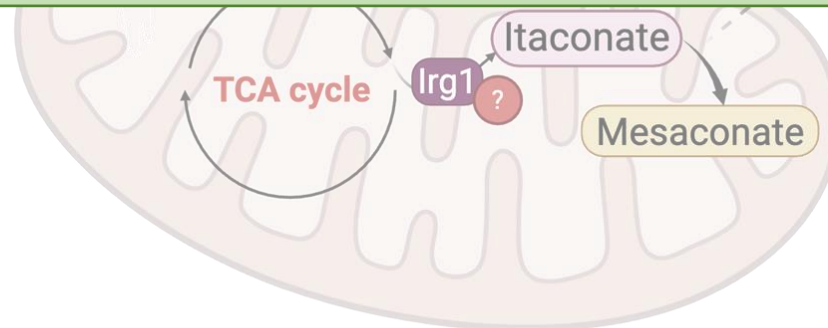


C.B. Smarr, et al Proc. Natl. Acad. Sci. U.S.A. 113 (18) 5059-5064, <https://doi.org/10.1073/pnas.1505782113> (2016).

Using itaconate-based polymeric nanoparticles to treat allergic disease

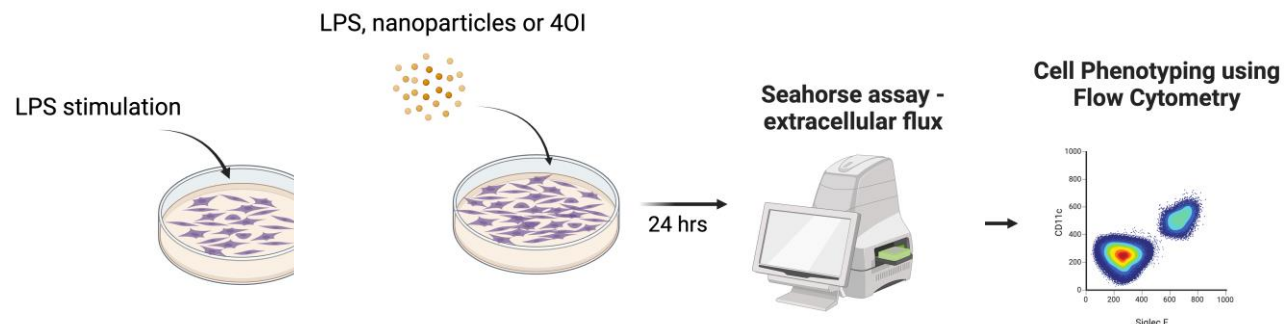


Overall, we hypothesize these metabolite-based NPs will be a safe and effective platform in mitigating allergy through modulation of mitochondrial dynamics and **reduction in Th2 cytokines**.

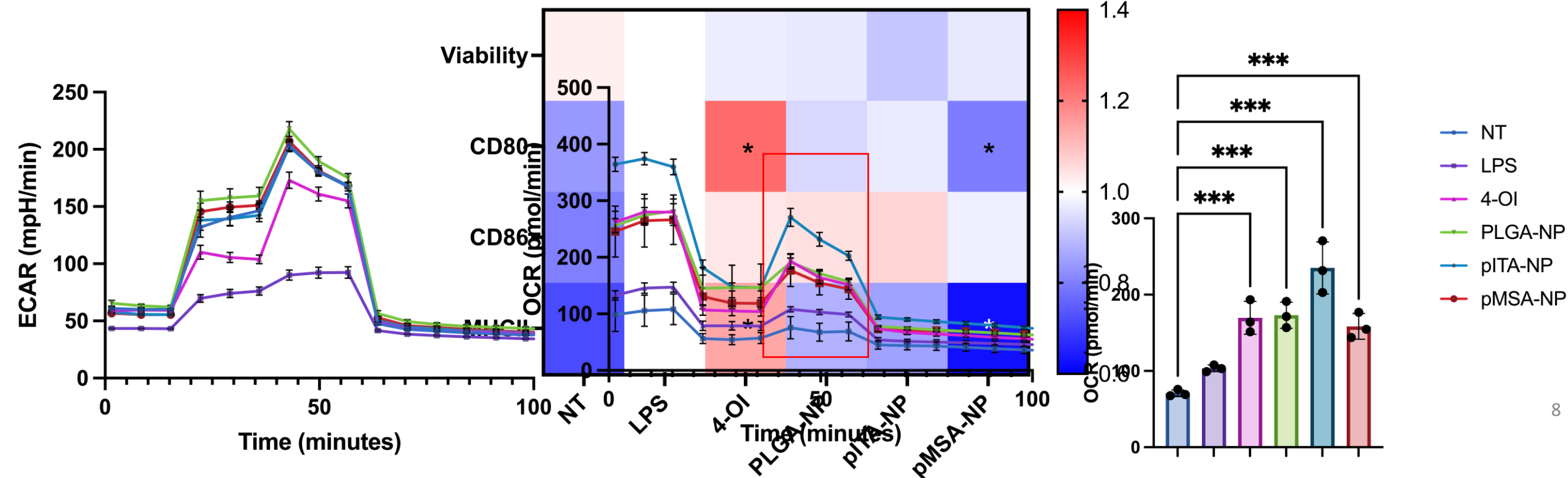


Metabolite- based NPs significantly increase oxidative phosphorylation in MH-S cells

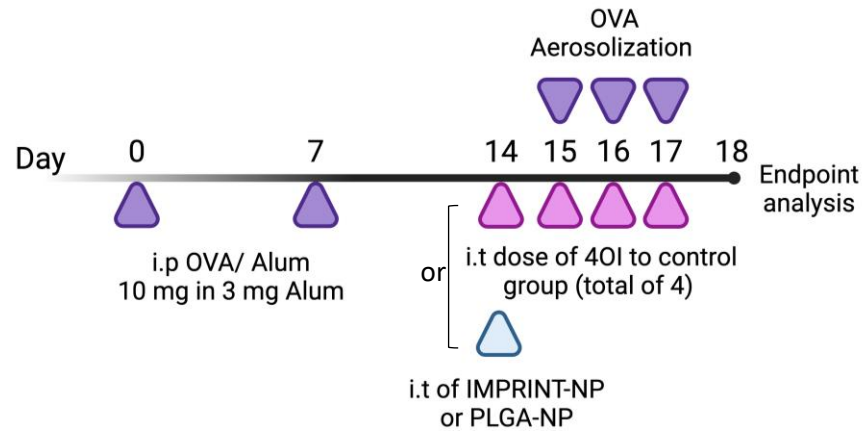
Nanoparticle	Size (nm)	PDI	Zeta (mV)
PLGA	258.3 ± 52.0	0.104 ± 0.069	-27.1 ± 5.28
pITA	496.0 ± 63.9	0.146 ± 0.059	-23.4 ± 1.86
pMSA	449.7 ± 89.1	0.145 ± 0.044	-23.5 ± 1.67



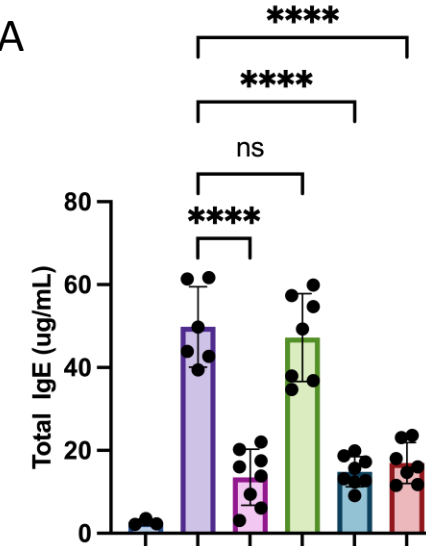
In collaboration with Dr. Abhinav Acharya Lab



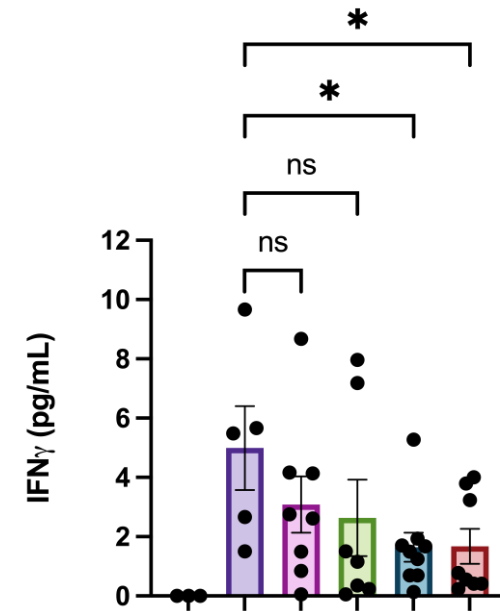
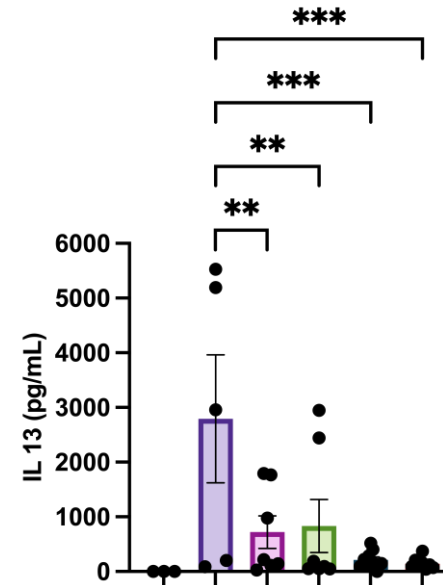
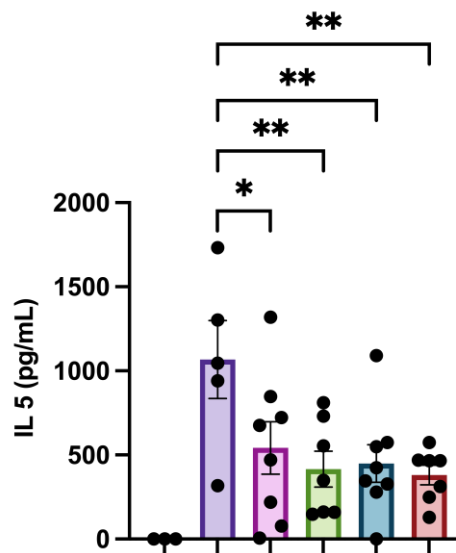
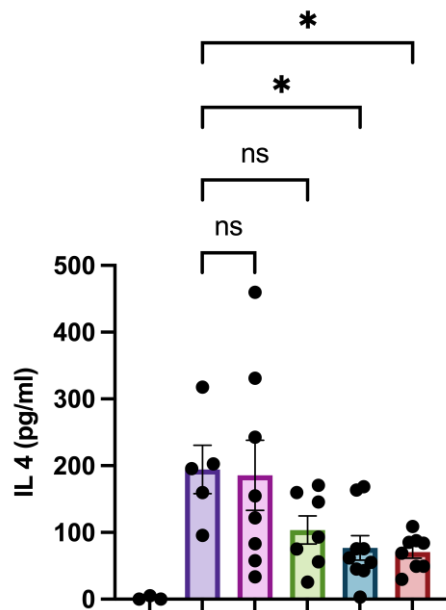
Metabolite-based NPs suppress total IgE and Th2 associated cytokines



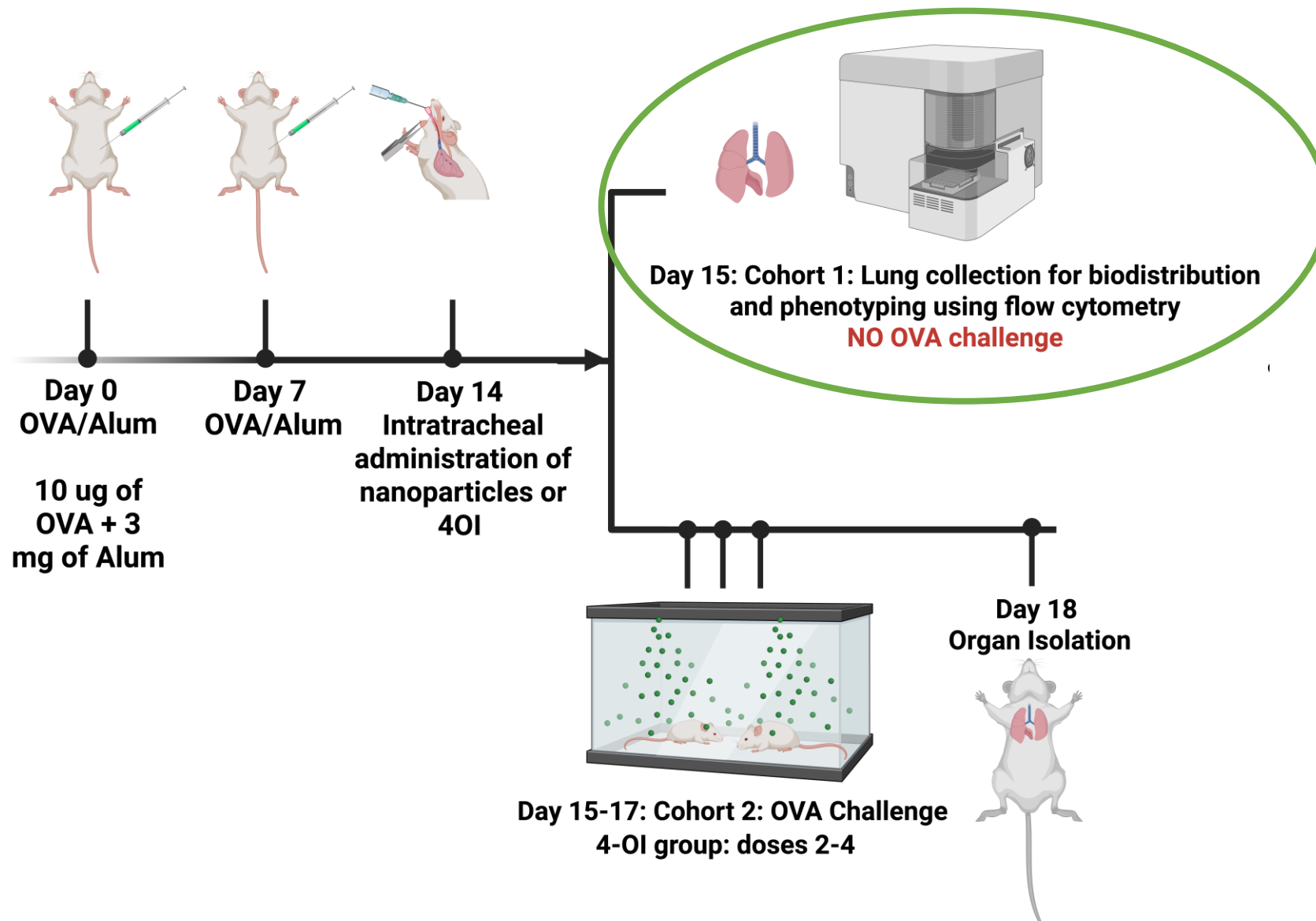
PLASMA



BAL



How are immune cell populations modulated by the metabolite-based NPs?



pITA and pMSA treatment significantly increase suppressor cells in the lung

Polymorphonuclear myeloid-derived suppressor cells attenuate allergic airway inflammation by negatively regulating group 2 innate lymphoid cells

Yingjiao Cao, Yumei He, Xiangyang Wang, Yongdong Liu, Kun Shi, Zheng Zheng, Xue Su, Aihua Lei, Juan He, Jie Zhou

First published: 21 December 2018 |

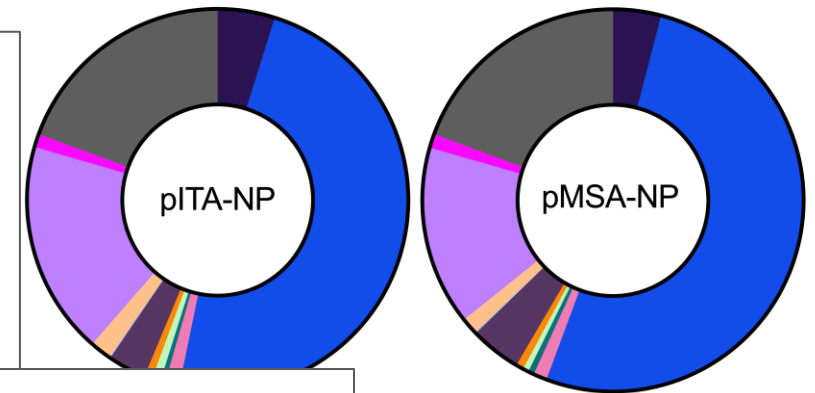
Front Immunol. 2021 Jul 12;12:695933. doi: [10.3389/fimmu.2021.695933](https://doi.org/10.3389/fimmu.2021.695933)

Myeloid-Derived Suppressor Cells Dampen Airway Inflammation Through Prostaglandin E2 Receptor 4

Chiel van Geffen^{1,2,3}, Astrid Deißler¹, Sandra Beer-Hammer⁴, Bernd Nürnberg^{4,†}, Rupert Handgretinger⁵, Harald Renz^{2,3}, Dominik Hartl^{6,7}, Saeed Kolahian^{1,2,3,*}

Author information Article notes Copyright and License information

PMCID: PMC8311661 PMID: [34322123](https://pubmed.ncbi.nlm.nih.gov/34322123/)



- Dendritic Cells
- Alveolar Macrophages
- MonocyteDerivedAMs
- Interstitial Macrophages
- Eosinophils
- Ly6Chi monocytes
- Ly6Cint Mo
- B cells
- T cells
- Other Cells

IN-MDSCs



Journal of Allergy and Clinical Immunology: Global

Volume 2, Issue 4, November 2023, 100163



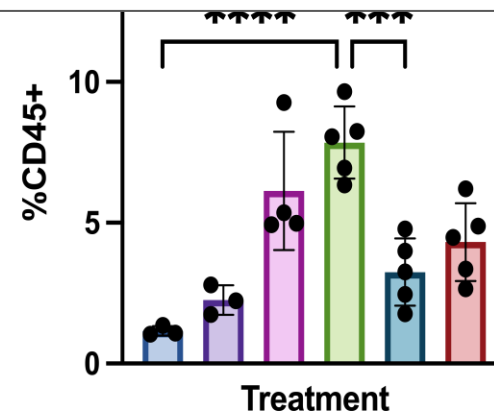
Original article

Short-chain fatty acids ameliorate allergic airway inflammation via sequential induction of PMN-MDSCs and Treg cells

Min-Ting Huang MSc^a, Chiao-Juno Chiu PhD^b, Ching-Yi Tsai MSc^a, Yue-Ru Lee PhD^a, Wei-Liang Liu PhD^c, Hsiao-Li Chuang PhD^d, Miao-Tzu Huang MD, PhD^{a,b,e}

BS/Alum
VA/Alum
OI
GA-NP
TA-NP
MSA-NP

11



Treatment

- Metabolite-based NPs significantly reduced Th2 cytokines and total IgE in an therapeutic OVA/Alum allergy model
- Modulation of key immune cell populations within the lung 24 hours after NP administration
 - PMN-MDSCs specifically has been implicated in mitigating allergic inflammation

Establishing a promising platform to safely and effectively treat allergic airway disease

- *Further characterization of mitochondrial dynamics*
- *Antigen specific approach – loading NP with proteins like house dust mite*
- *Elucidating mechanisms behind the reduction in IgE*



Pearson's Particle People

Ryan M. Pearson, PhD

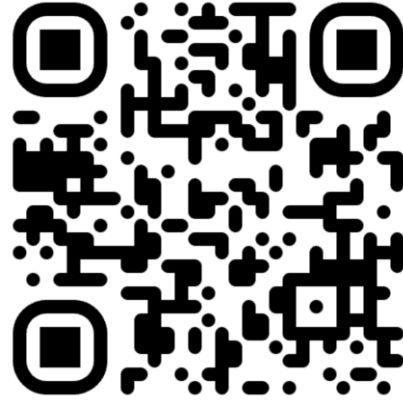
Jason Sung, PhD

Jacob Shaw, PhD

Andrea Cottingham

Fanny Xu

Sara Kolhatkar, MS



Collaborators

Abhinav Acharya, PhD (CWRU, OH)

Achsah Keegan, PhD (UMB SOM)

Svetlana Chapoval, PhD (UMB SOM)

UMB Cores

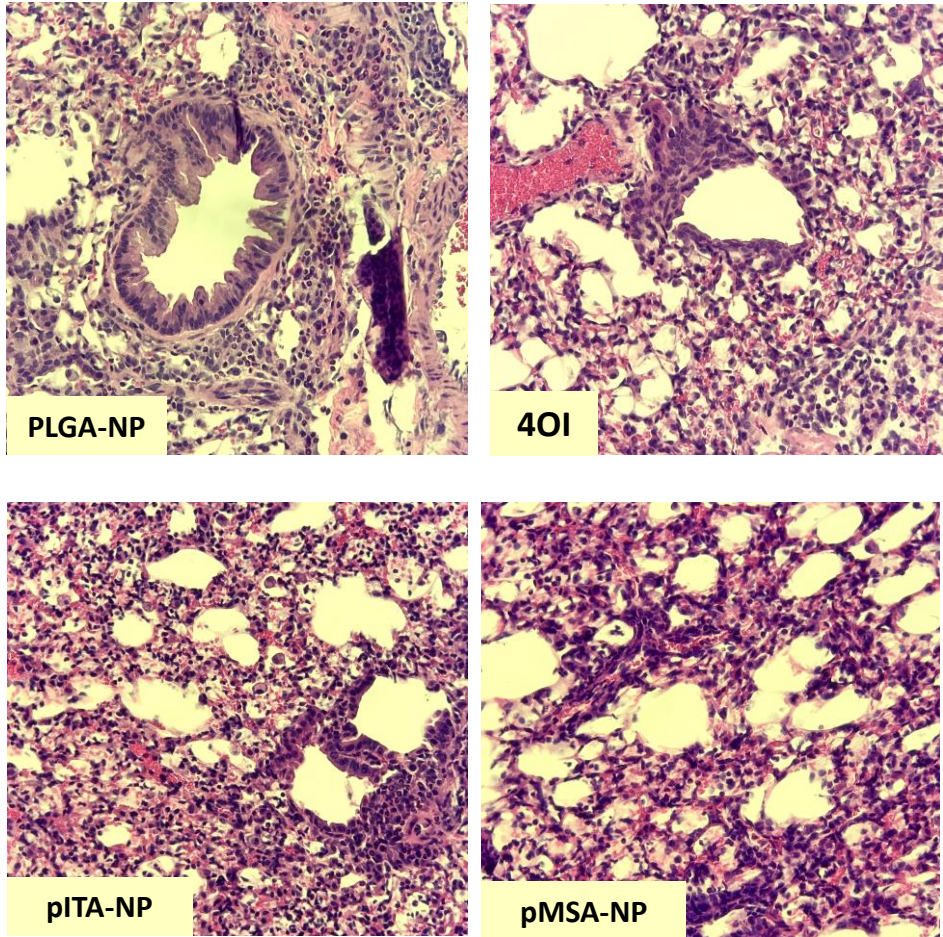
Flow and Mass Cytometry Facility

Funding Sources



Bronchial narrowing of the lungs reduced with metabolite- based NP treatment

H&E staining of the lungs – reduction in bronchial narrowing



Differential staining of cells from the bronchoalveolar lavage

