

Dupilumab vs. Abrocitinib:

Distinct Impacts on Basophil Modulation in AD

Wenjing Jiang^{1*}, Xinyang Xie^{1*}, Sai Yang³, Xiaobao Huang^{1,2#}, Fang Wang^{3#}

¹ Department of Dermatology, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, Guangdong, China

² Institute of Precision Medicine, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, Guangdong, China

³ Department of Dermatology, Dermatology Hospital, Southern Medical University, Guangzhou, Guangdong, China



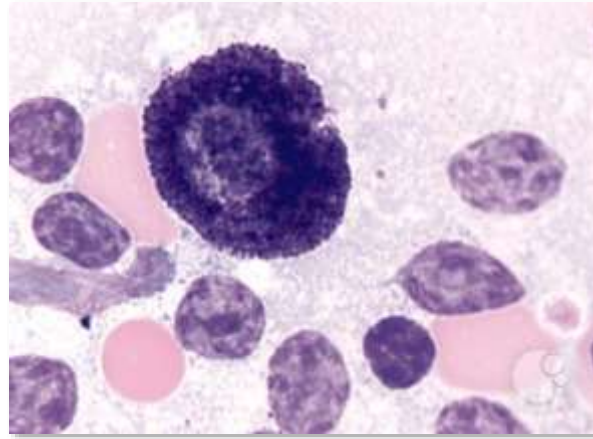
1

BASOPHILS BIOLOGY

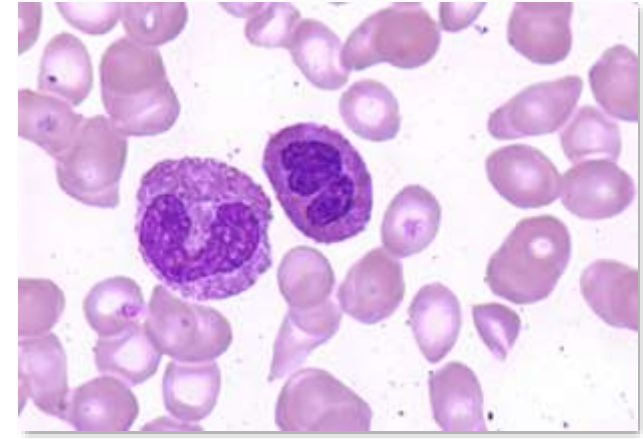
Basophils, Mast cells, Eosinophils



Basophils



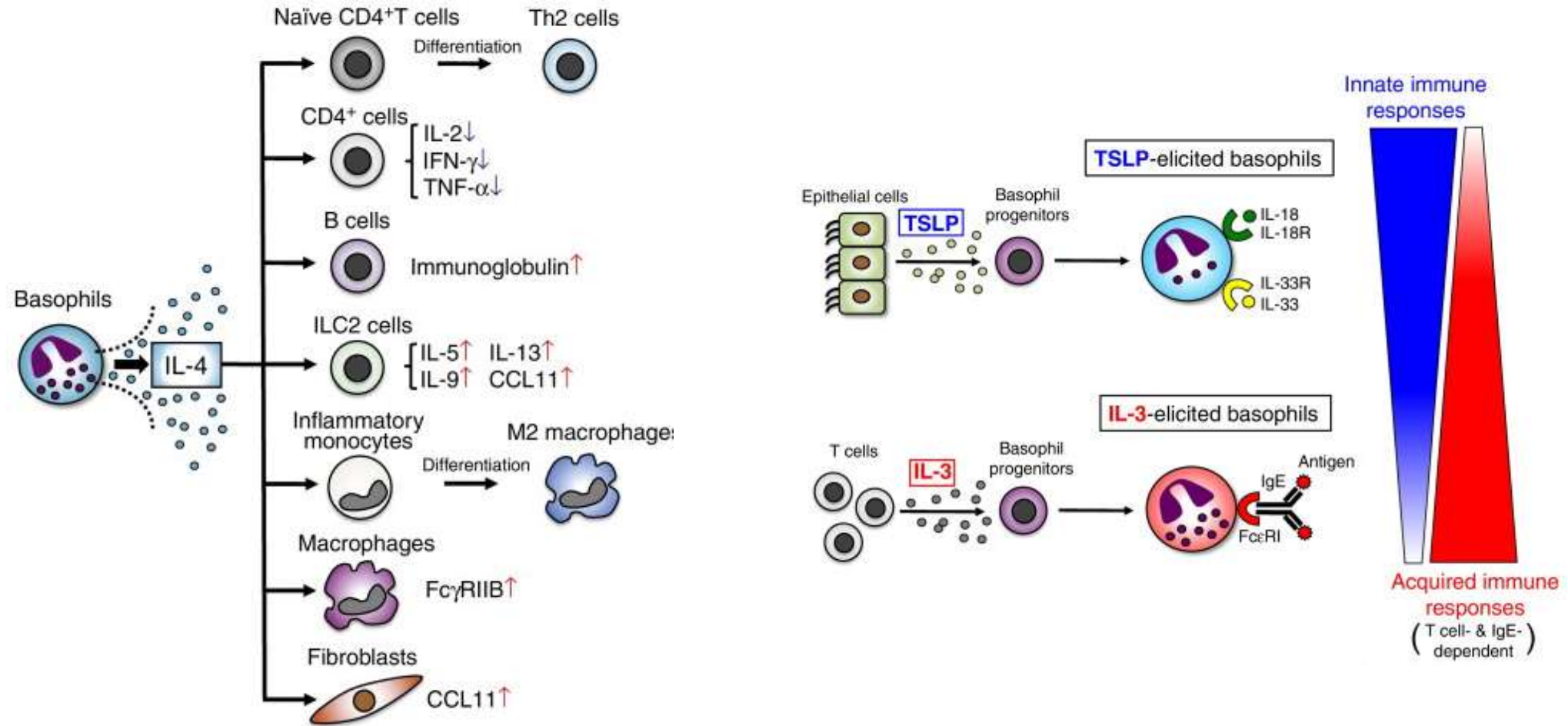
Mast cells



Eosinophils

- Basophils, eosinophils and mast cells were first recognized by Paul Ehrlich in the late 19th century.
- These cells have common, but non-redundant roles, in the pathogenesis of allergic diseases and in the protection against parasites.
- These cells exert different effector functions beside the expression of very similar receptors and cytokines.

Biological Function of Basophils





2

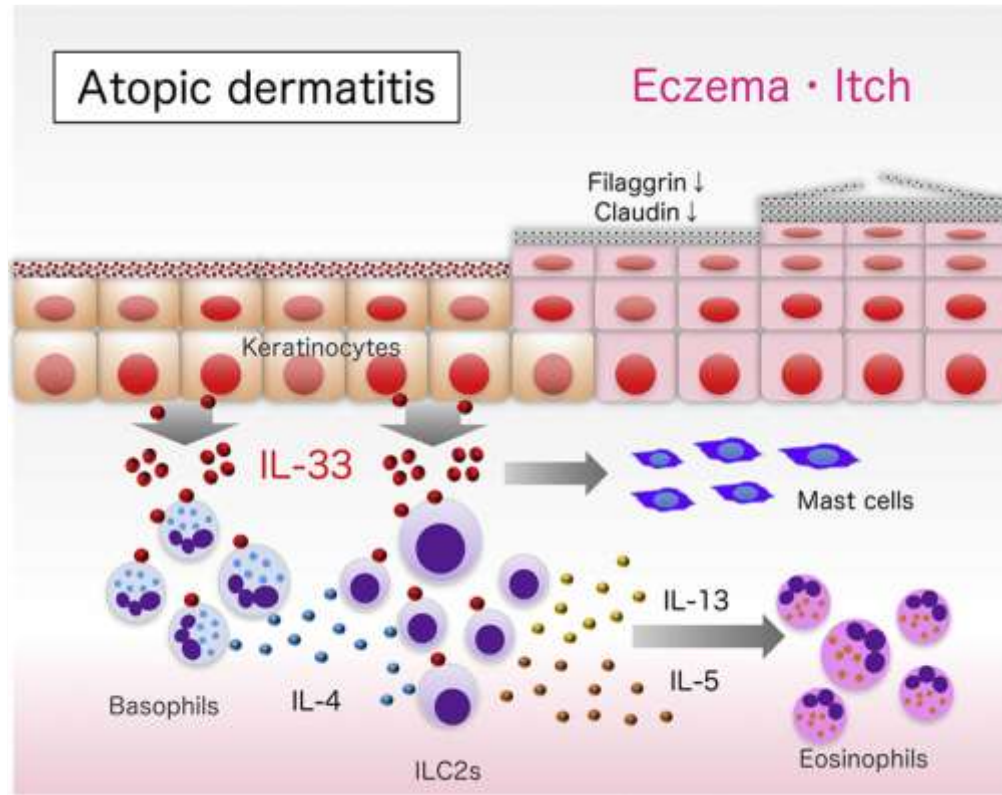
BASOPHILS IN ATOPIC DERMATITIS

AD: a common chronic skin disease

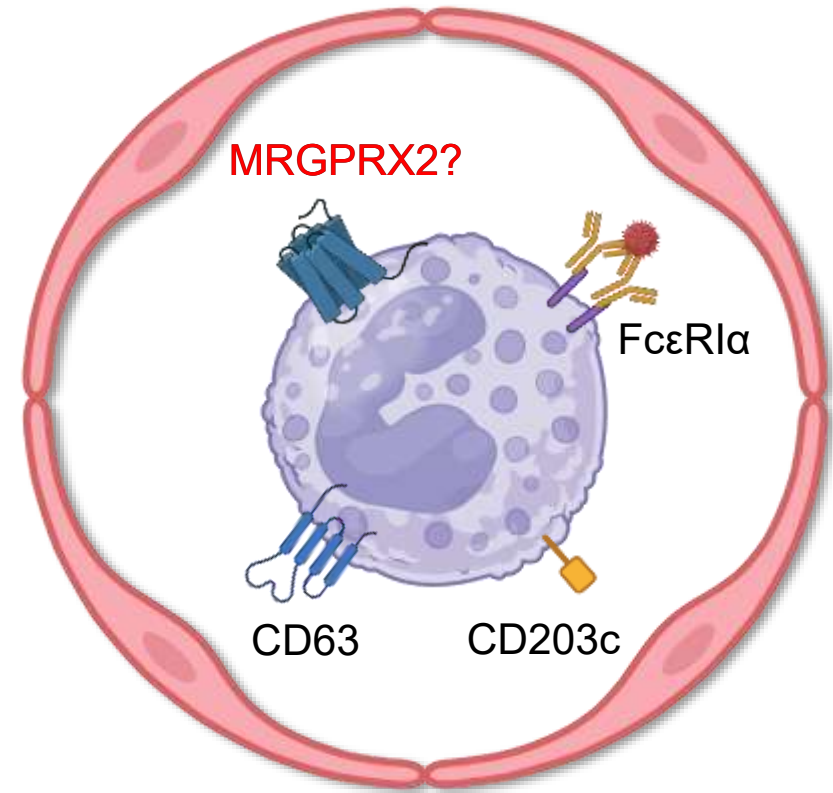


Basophil: an important player in AD pathogenesis

AD Mechanisms



Basophil Characteristic



EVO756, an oral MRGPRX2 inhibitor, in a clinical trial

A Novel MRGPRX2 Inhibitor in Chronic Inducible Urticaria (CIndU)

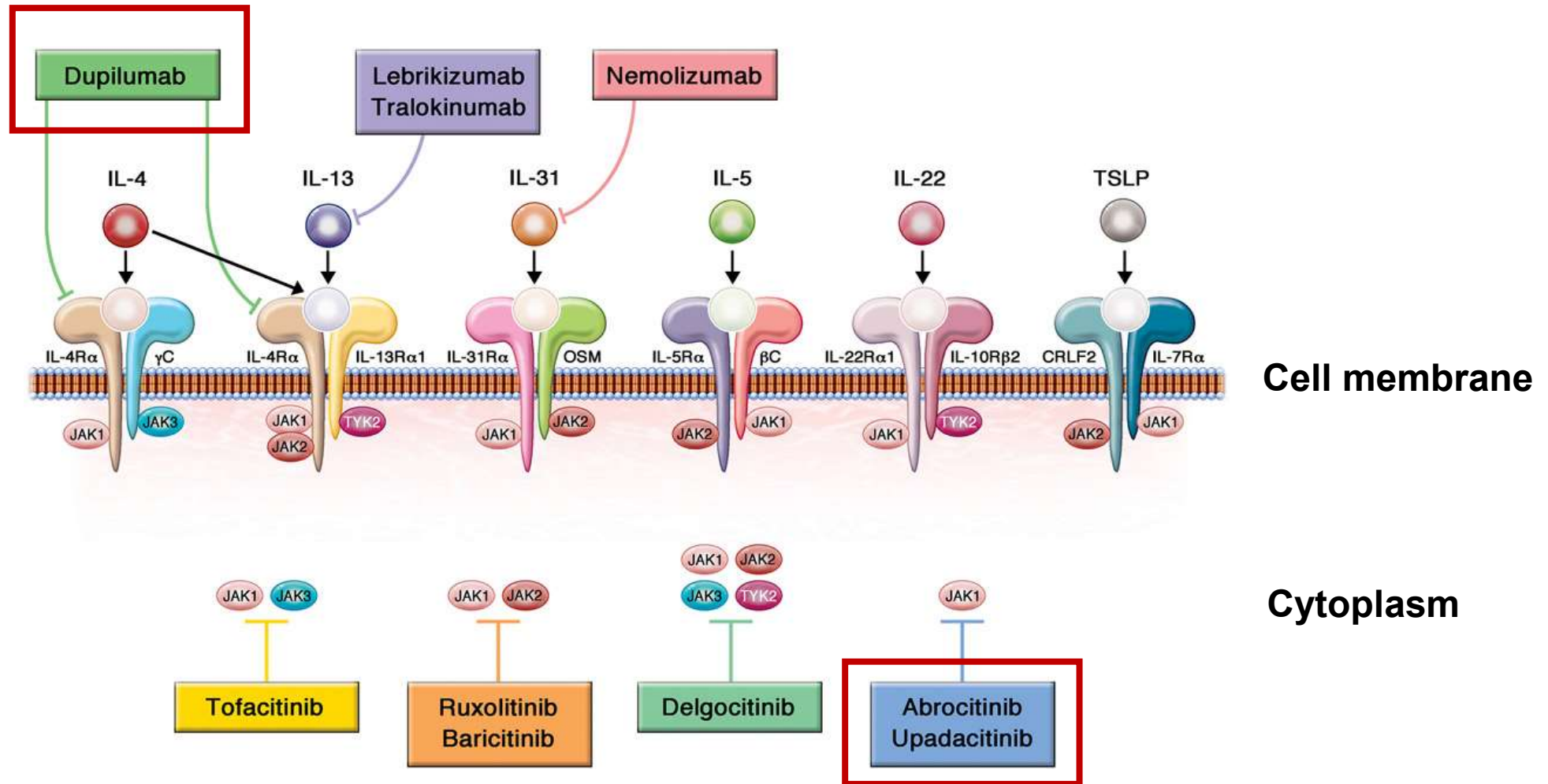
Ted Lain, M.D.
Austin, TX



Edward (Ted) Lain

EVO756, an Oral MRGPRX2 Inhibitor,
Demonstrates Robust Treatment
Effect in Chronic Inducible Urticaria

Impact of dupilumab vs. abrocitinib on basophils?



Two scientific questions

01

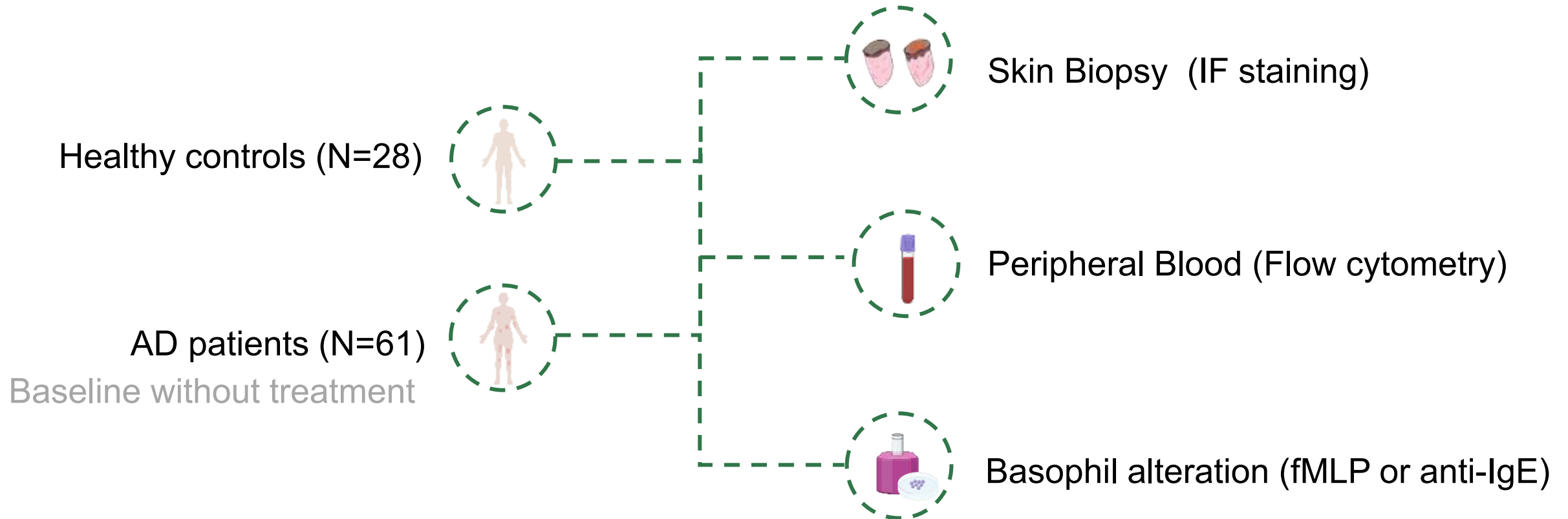
Comparative phenotype of basophils in AD patients and HCs.

02

Basophil alterations in AD following different medications.

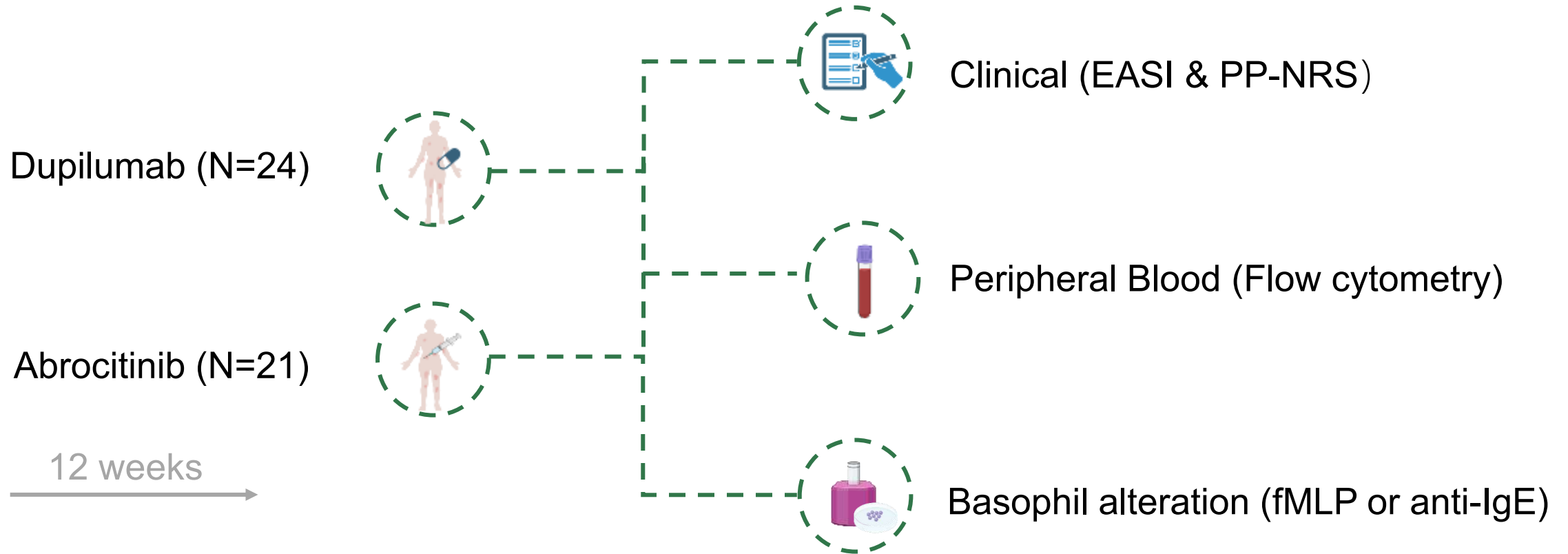
Study design

Q1: Comparative phenotype of basophils in AD patients and HCs.

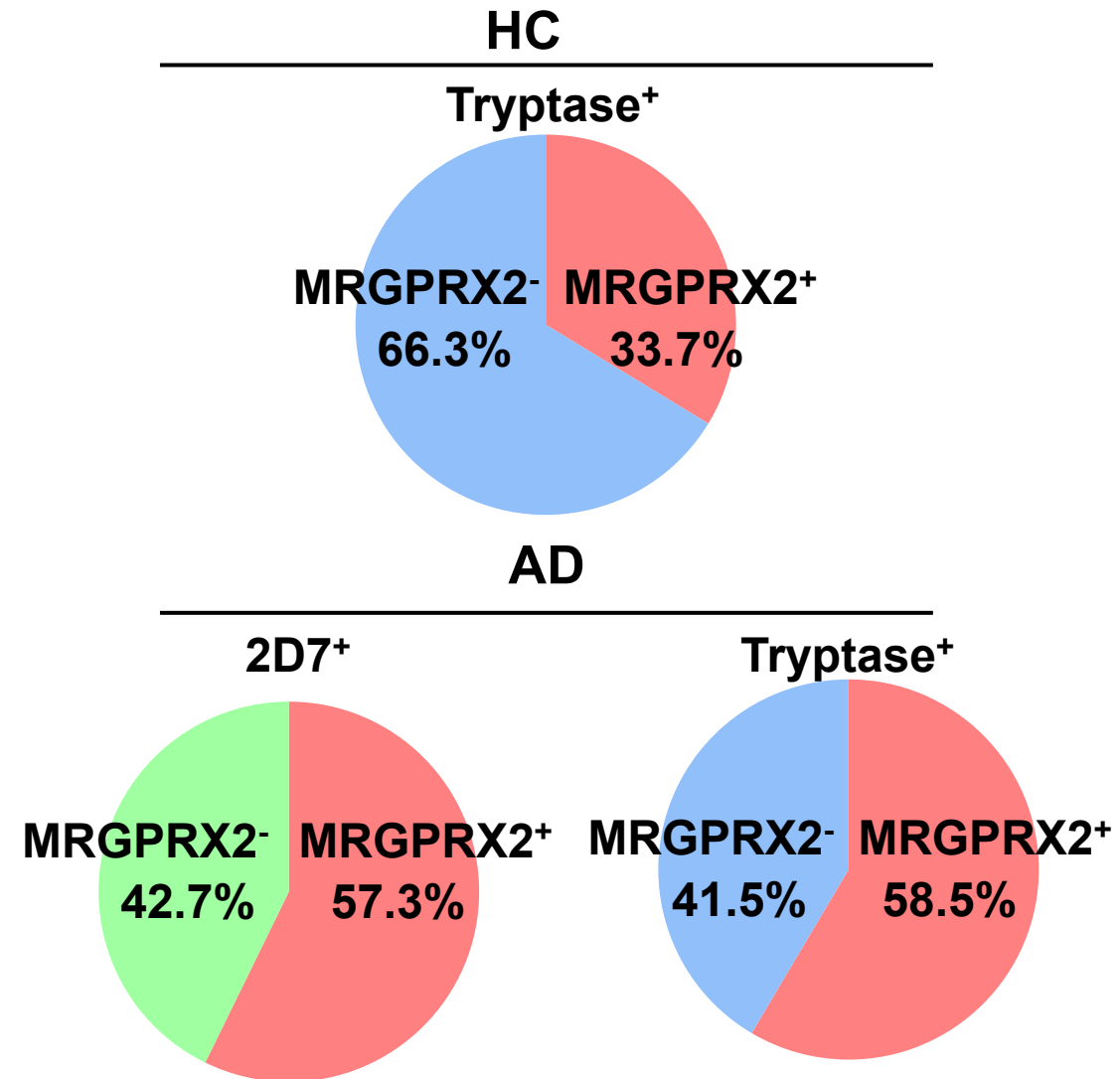
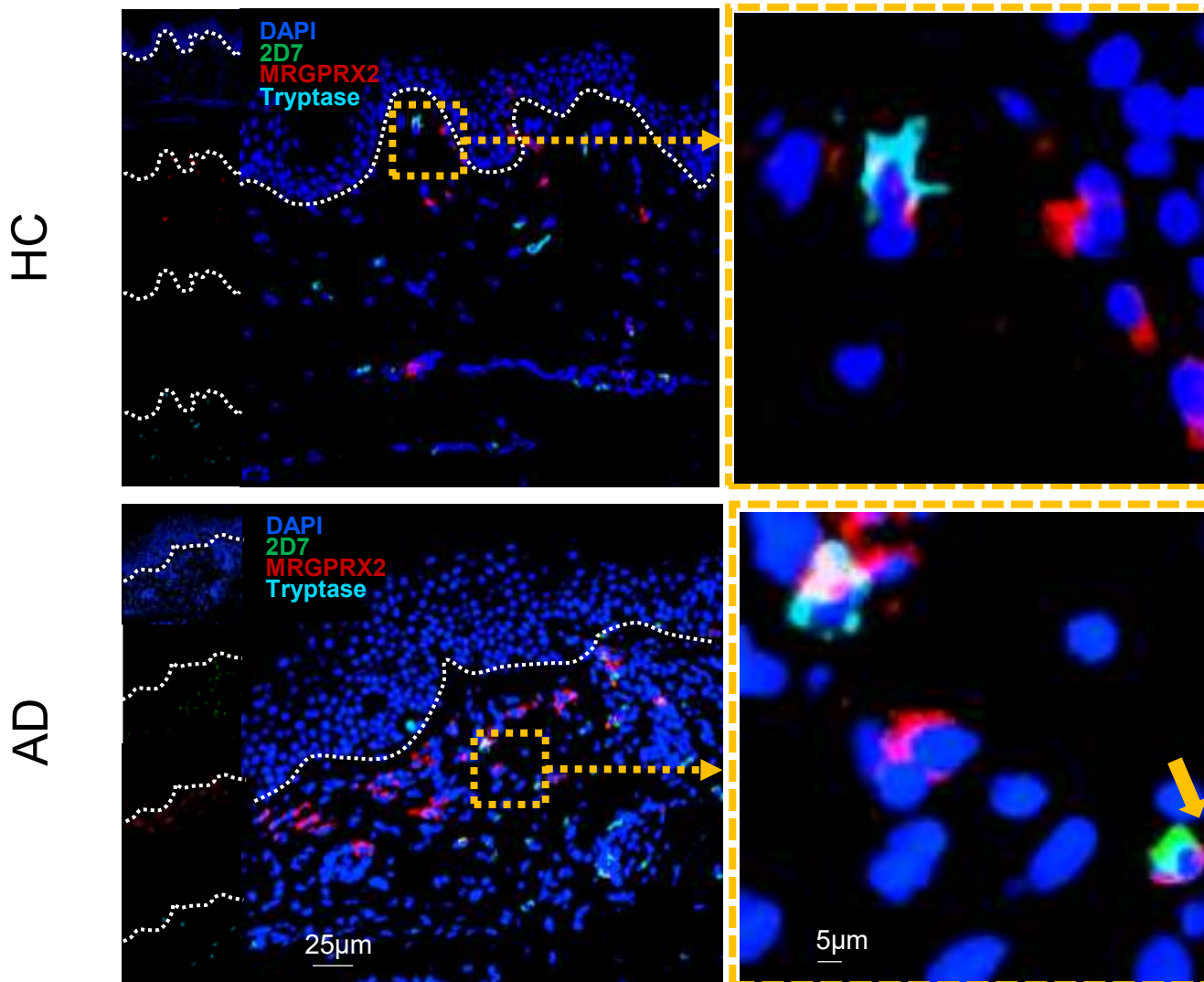


Study design

Q2: Basophil alterations in AD following different medications.



MRGPRX2⁺ basophils infiltrate in AD lesional skin

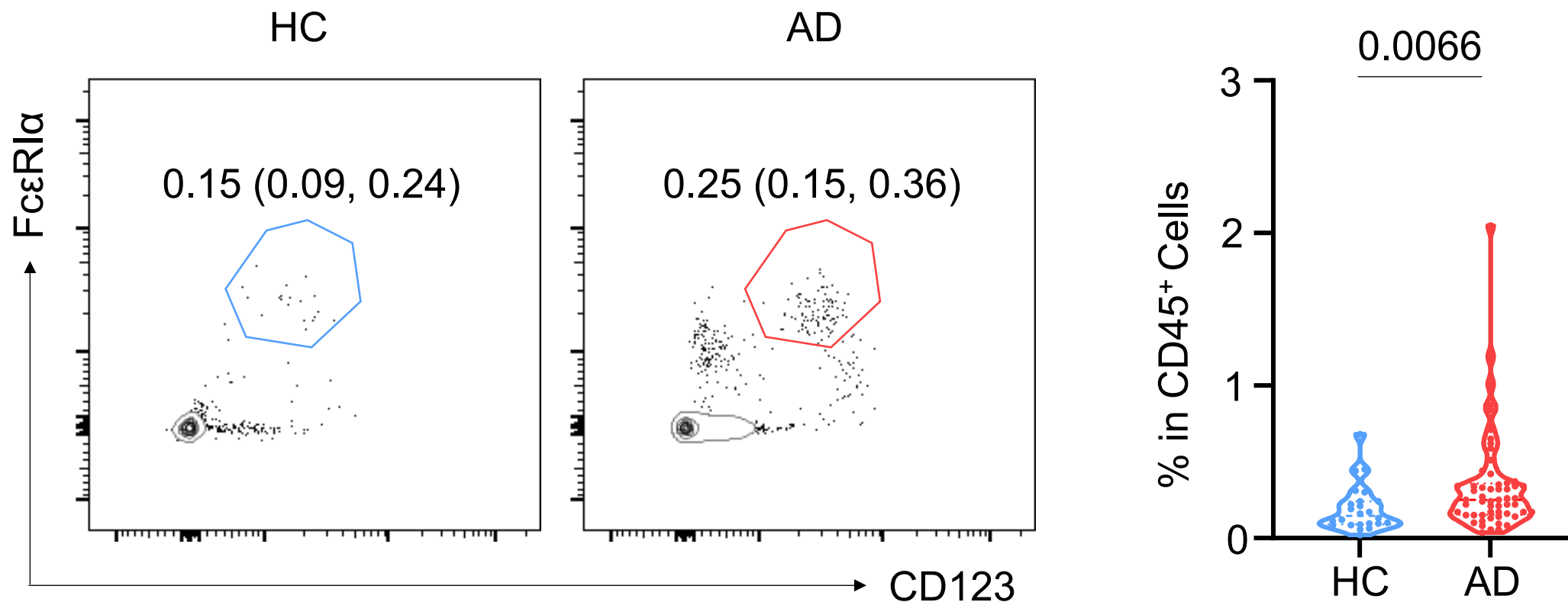


2D7: basophil biomarker

Unpublished

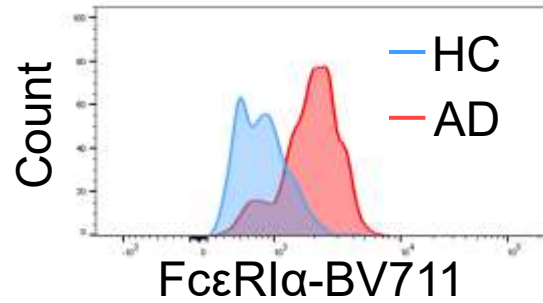
Circulating basophils are increased in AD

Basophil Percentage

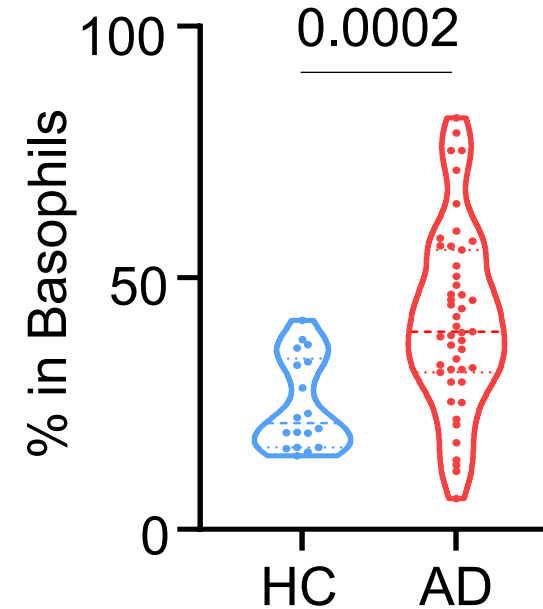
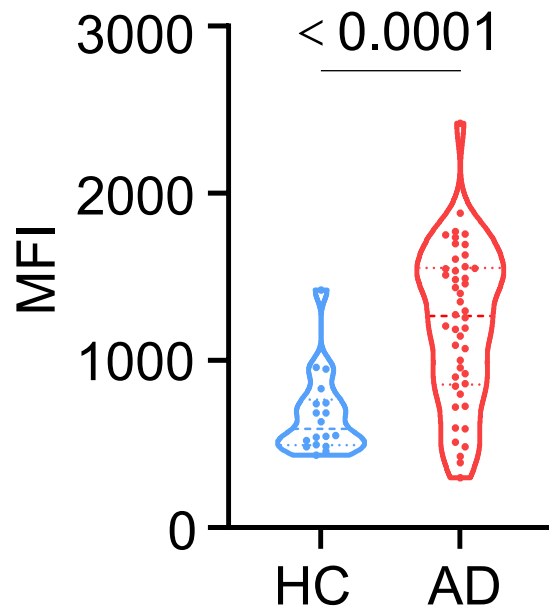
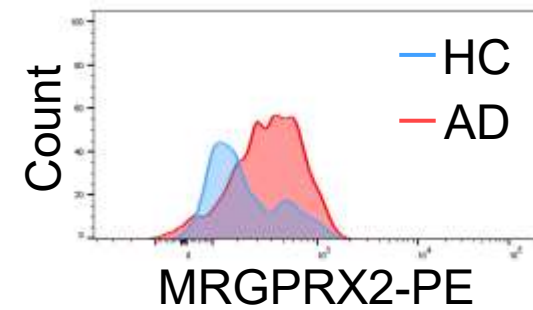


Both IgE and non-IgE pathways are upregulated in basophils

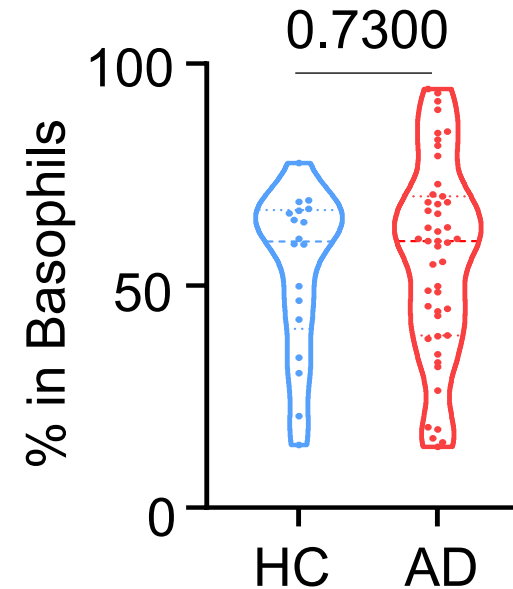
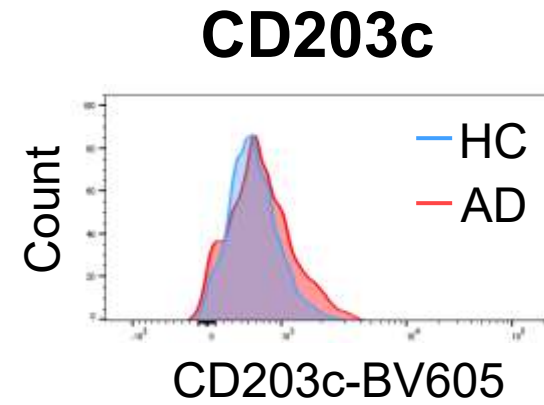
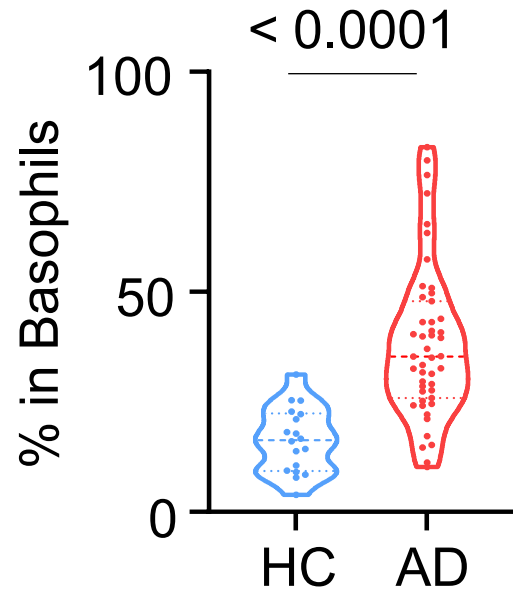
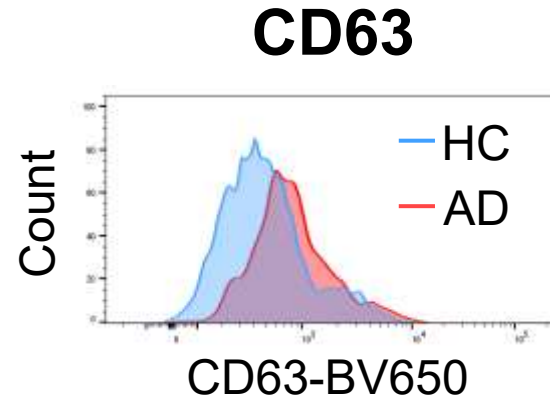
FcεR1α



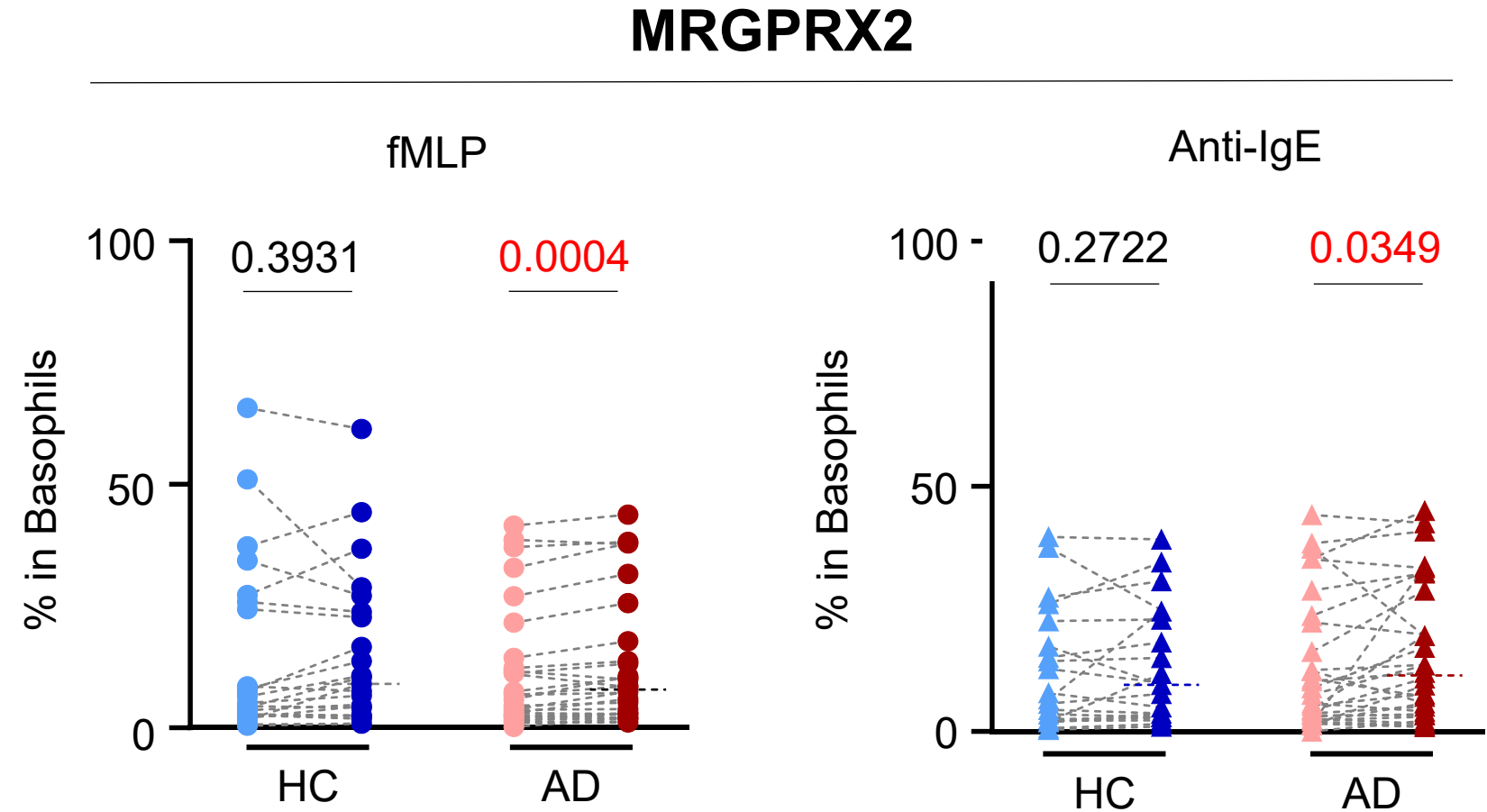
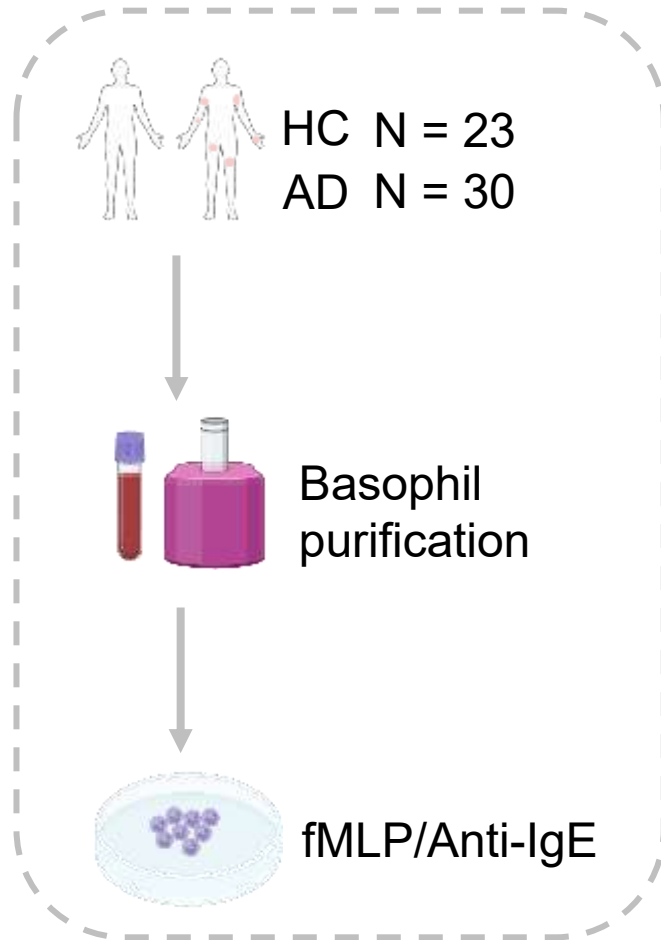
MRGPRX2



Basophils are partially activated in AD

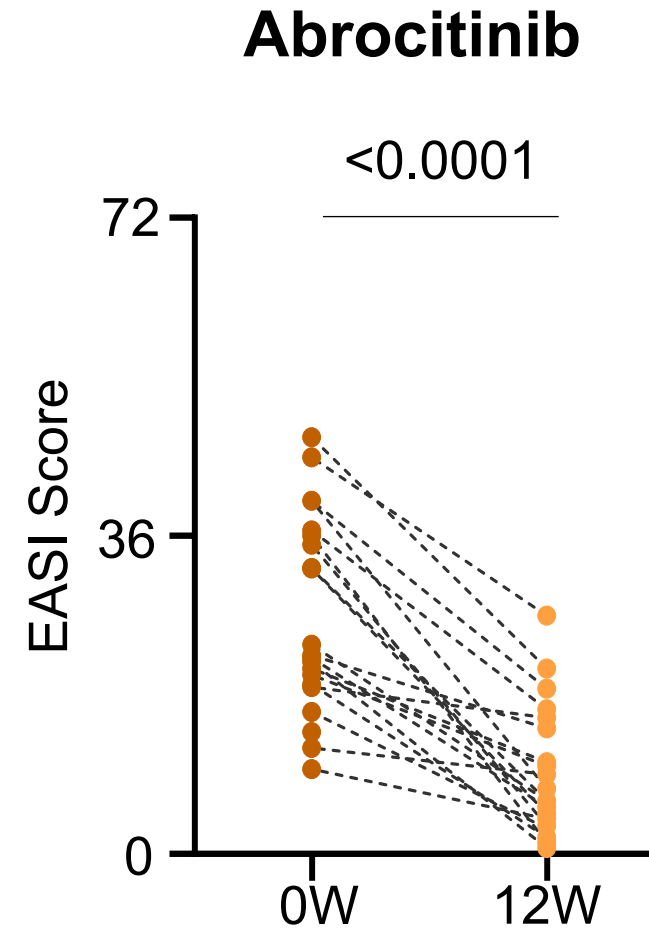
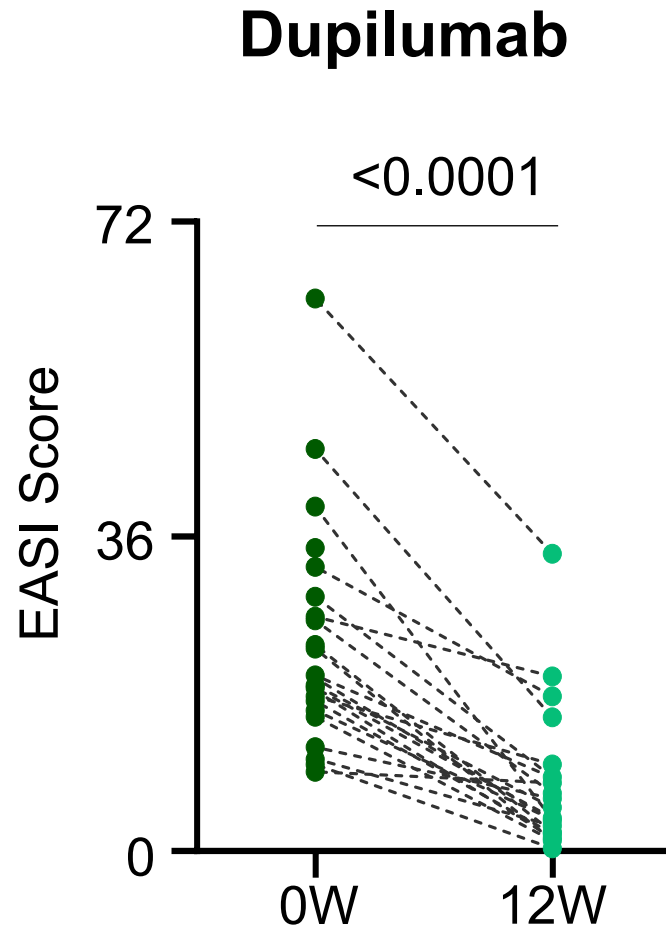


MRGPRX2 can be upregulated through stimulation in AD patients

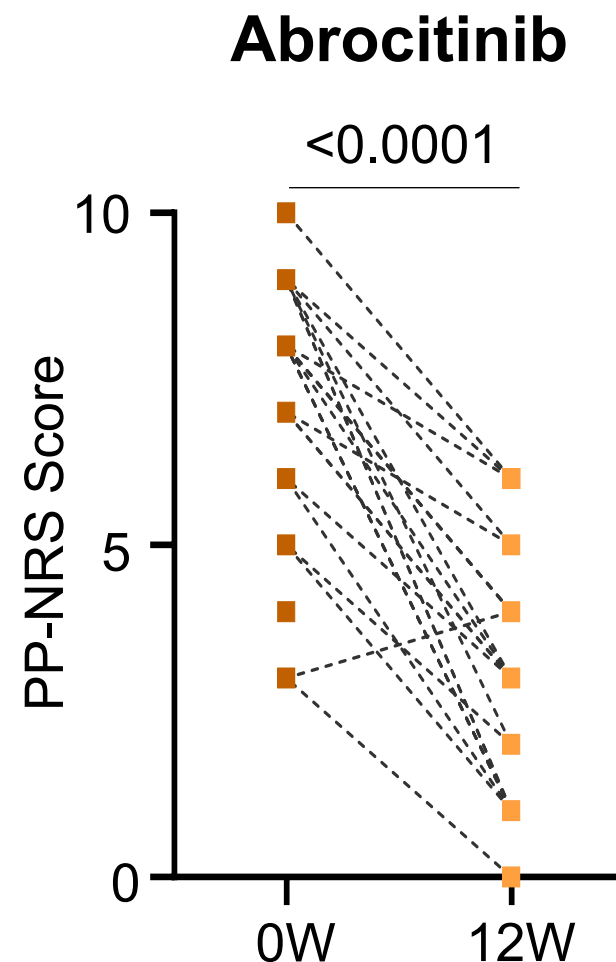
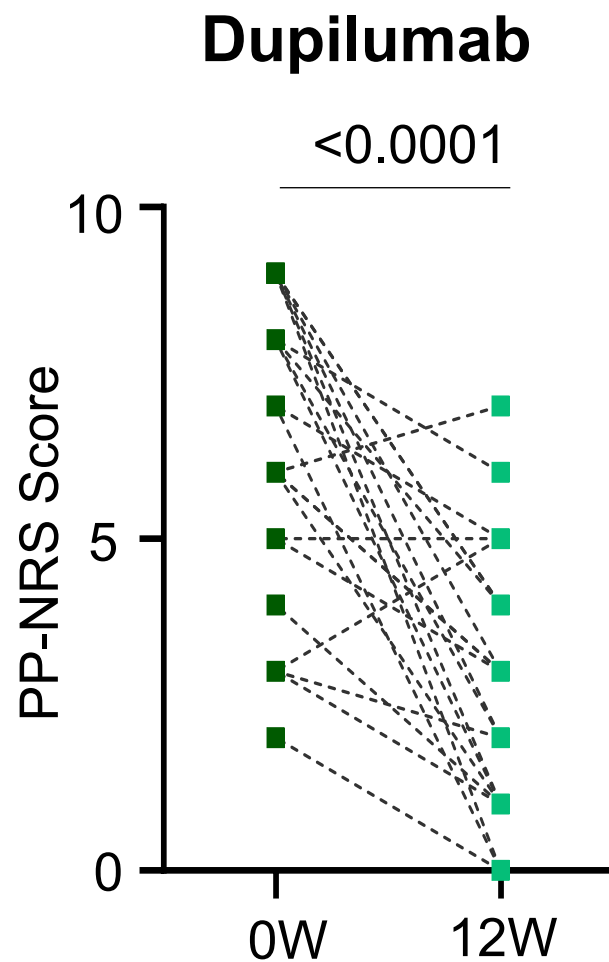


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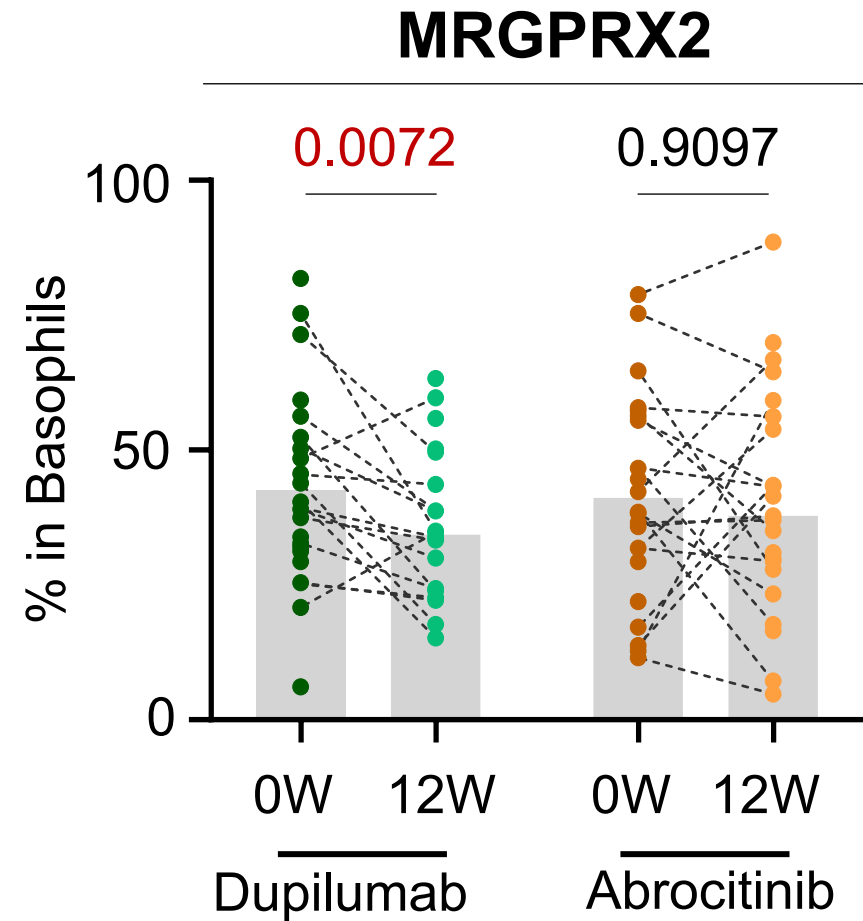
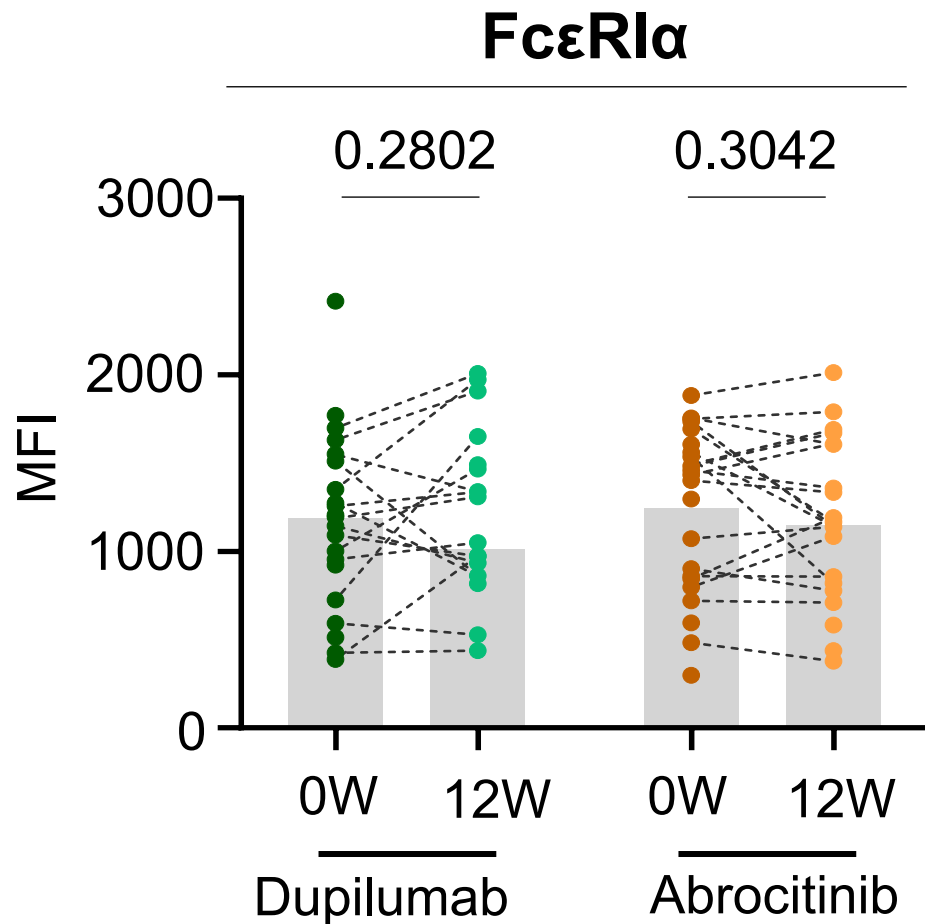
Skin inflammation is improved following treatment



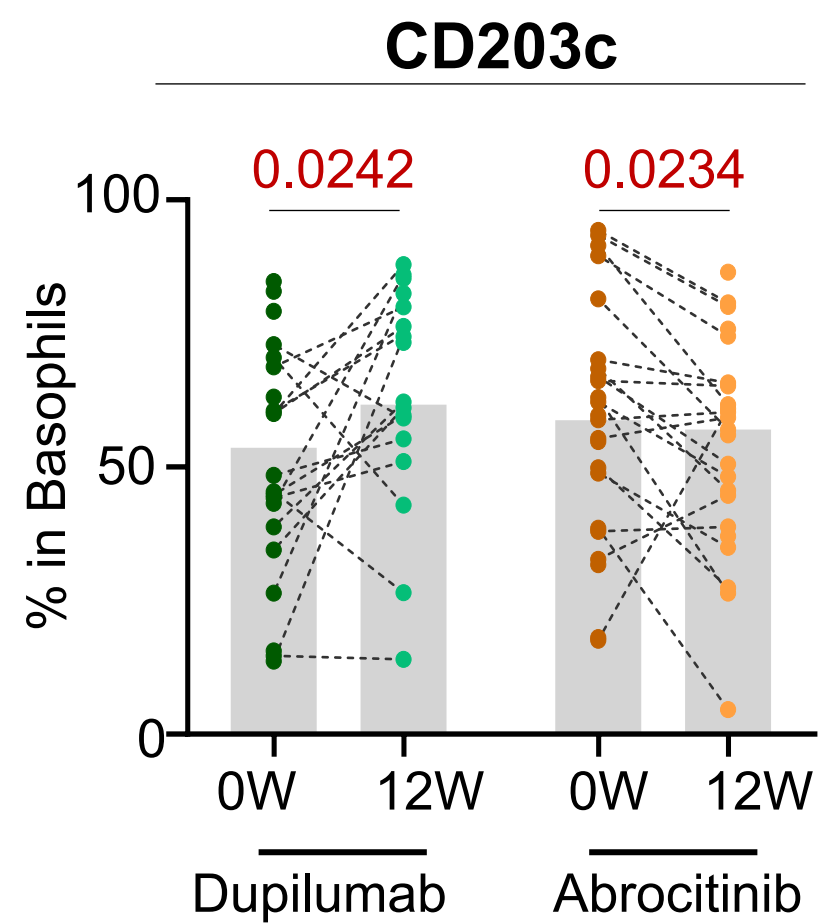
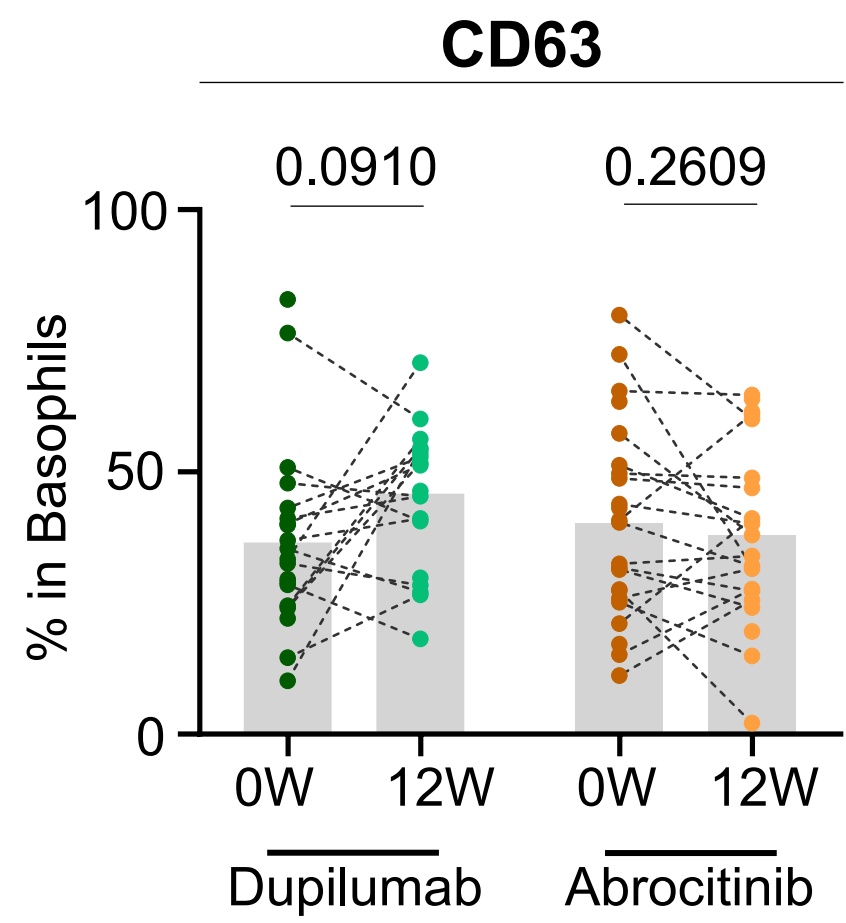
Pruritus is alleviated following treatment



Dupilumab suppresses the non-IgE-mediated pathway

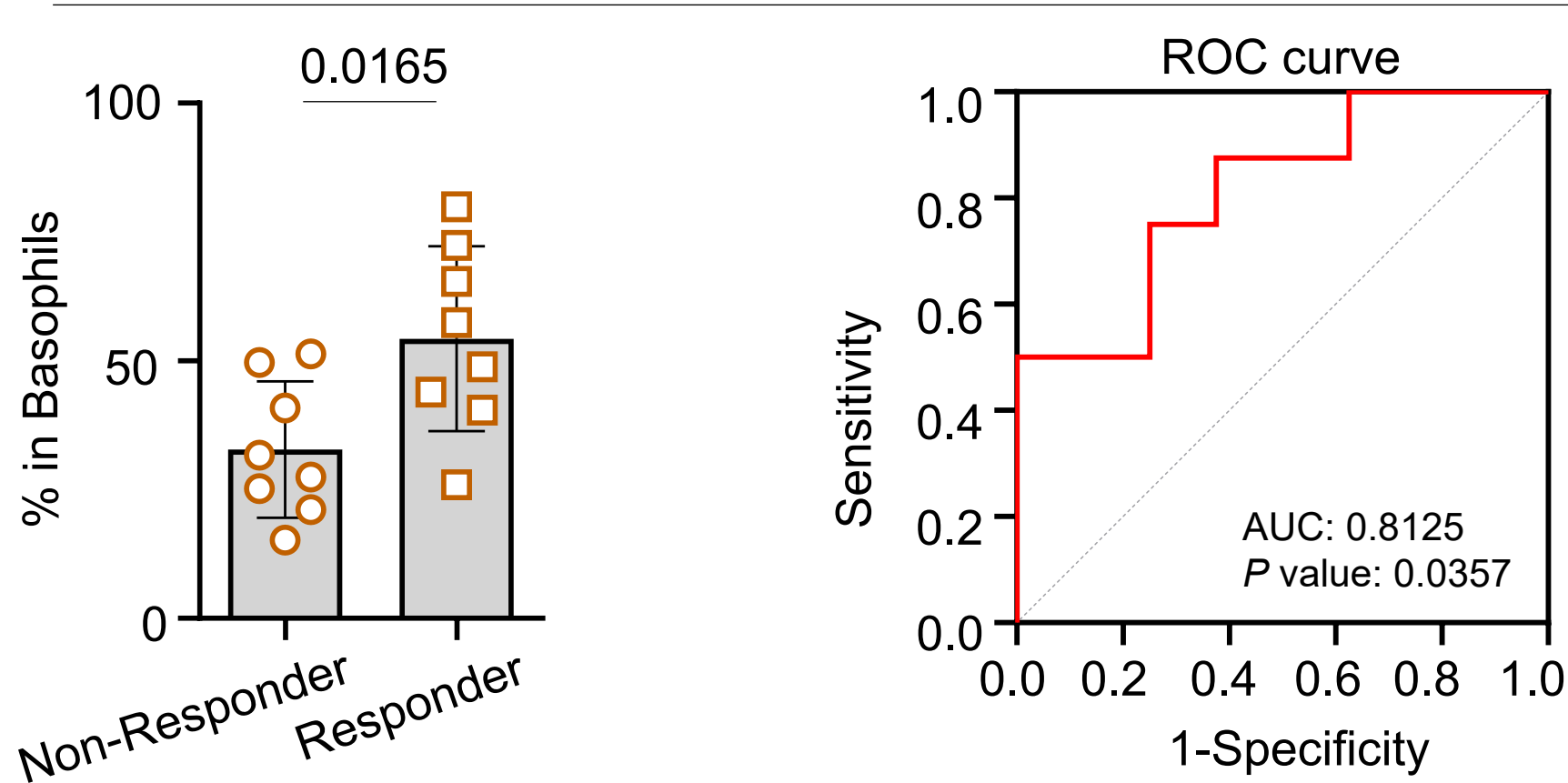


Dupilumab and abrocitinib exert distinct effects on basophil activation



Baseline CD63 predicts clinical response to abrocitinib

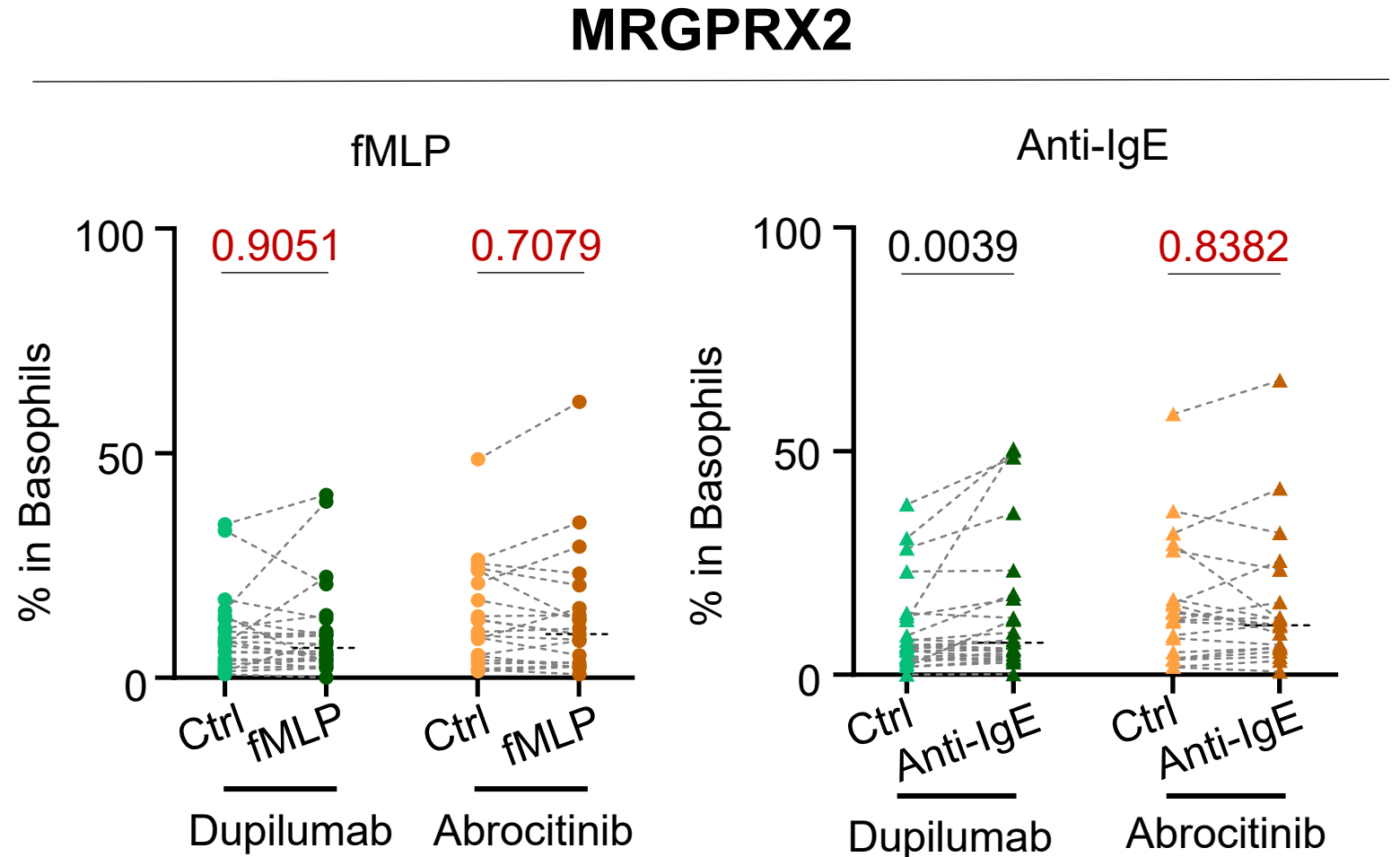
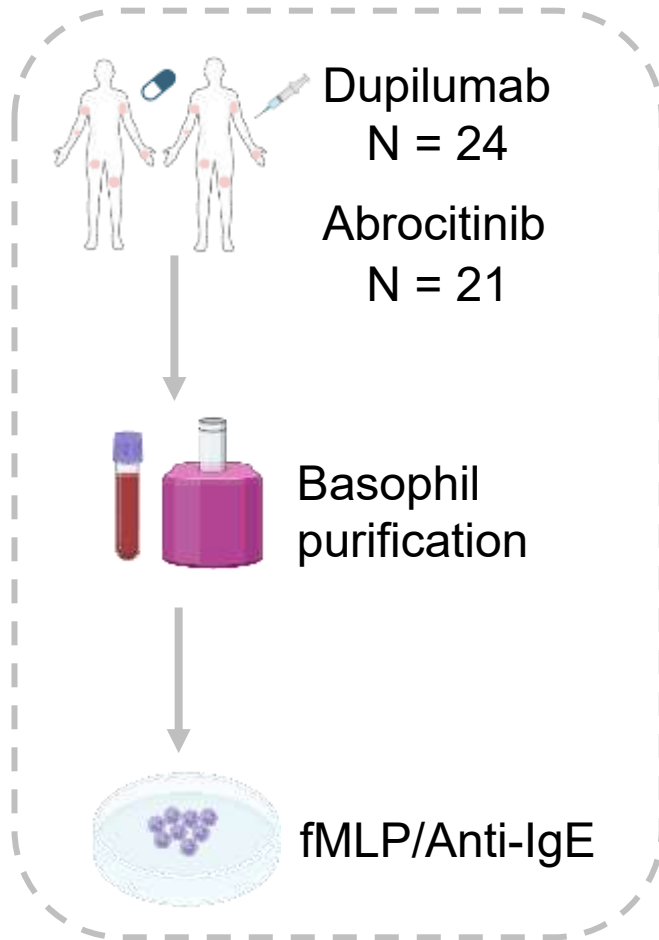
CD63 in Abrocitinib Group






Responder: Patients reached EASI-75 after a 12-week treatment

Unpublished

Differential effects of targeted therapies on MRGPRX2



Summary

	Biomarker				MRGPRX2	
	FcεRIα	MRGPRX2	CD63	CD203c	fMLP	anti-IgE
AD vs HC	↑	↑	↑	—	↑	↑
Therapy						
Dupilumab 	—	↓	—	↑	↑ ✗	↑
Abrocitinib 	—	—	—	↓	↑ ✗	↑ ✗

Acknowledgements



Sun Yat-Sen University



Southern Medical School



Contact:

Fang Wang

Department of Dermatology, Dermatology Hospital,
Southern Medical University 2 Lujing Road,
Guangzhou, Guangdong 510091, China
Email: wangf78@smu.edu.cn

Xiaobao Huang

Department of Dermatology, The First Affiliated Hospital,
Sun Yat-sen University
58 Zhongshan Er Road, Guangzhou, Guangdong, China
Email: huangxb8@mail2.sysu.edu.cn