

Introduction

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)

- Rare but severe delayed drug hypersensitivity reaction (DHR) with exanthema, eosinophilia and organ manifestations.
- 10 – 18% of patients with DRESS develop further DHRs to structurally unrelated drugs from the initial DRESS elicitor:

➔ **Multiple drug hypersensitivity (MDH) syndrome**

Research Question

Are there **immunological biomarkers** for MDH in patients with DRESS?

Methods

Cohorts

- 9 **healthy** donors (HD)
- 21 **DRESS** patients
8 single-drug sensitised (Mono) & 13 MDH
- 7 **MPE** patients
5 Mono & 2 MDH

Homeostasis
50mL blood

Isolate &
purify PBMCs

Immunophenotyping Assays

- Cell culture (**Cyto-LTT**)
- **Cytokine** profiling

Type I IFN γ **Type II** IL-5, IL-13 **Cytotoxic** Granzyme B (GzB), Granulysin (GL)

Flow cytometry (T cells)

- Activation markers (CD69, OX40, CD38)
- Exhaustion markers (PD-1)

Which drugs trigger DRESS?

Table 1: β -lactam antibiotics are common elicitors of DRESS

DRESS elicitors	N=21 DRESS
β -lactam antibiotics	12
Non- β -lactam antibiotics	7
Antiepileptics	3

Culprit drug diagnostic performance:

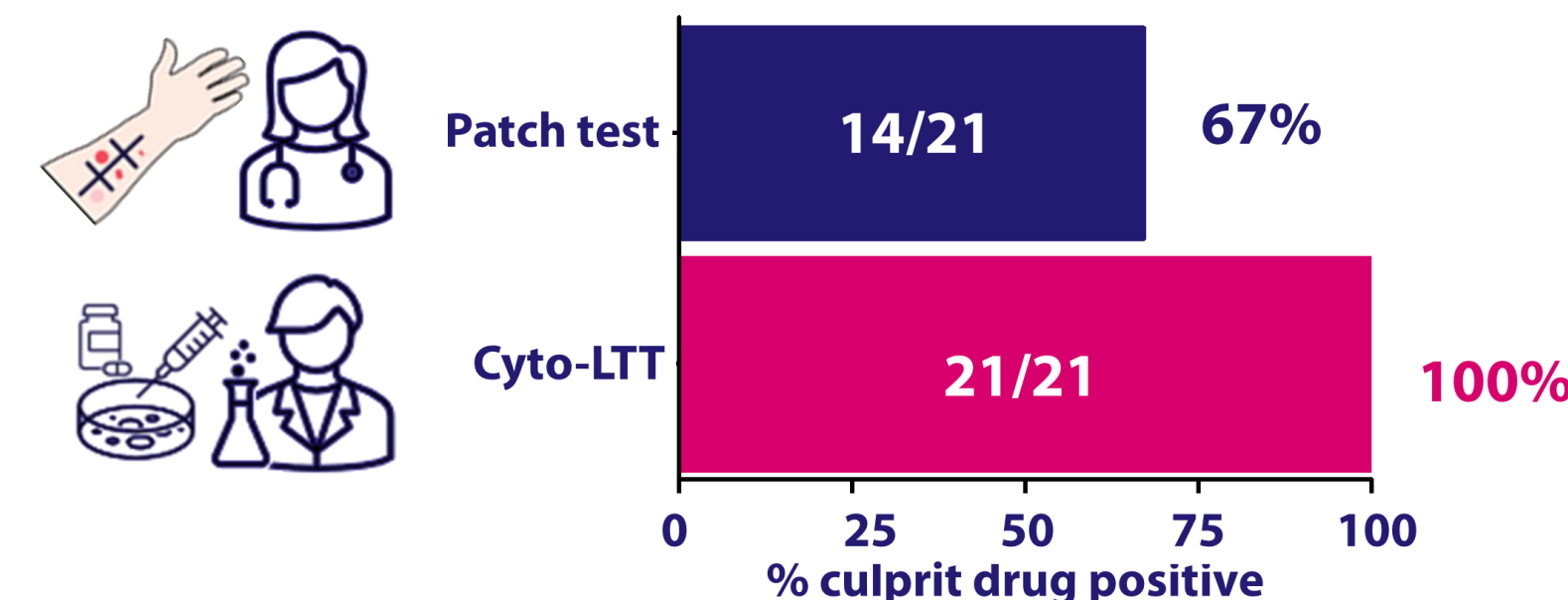


Figure 1: Cyto-LTT detects DHR drug elicitor better than skin patch tests

PBMCs reaction to culprit drugs in DRESS is characterised by IL-5 vs. MPE with increased IFN γ

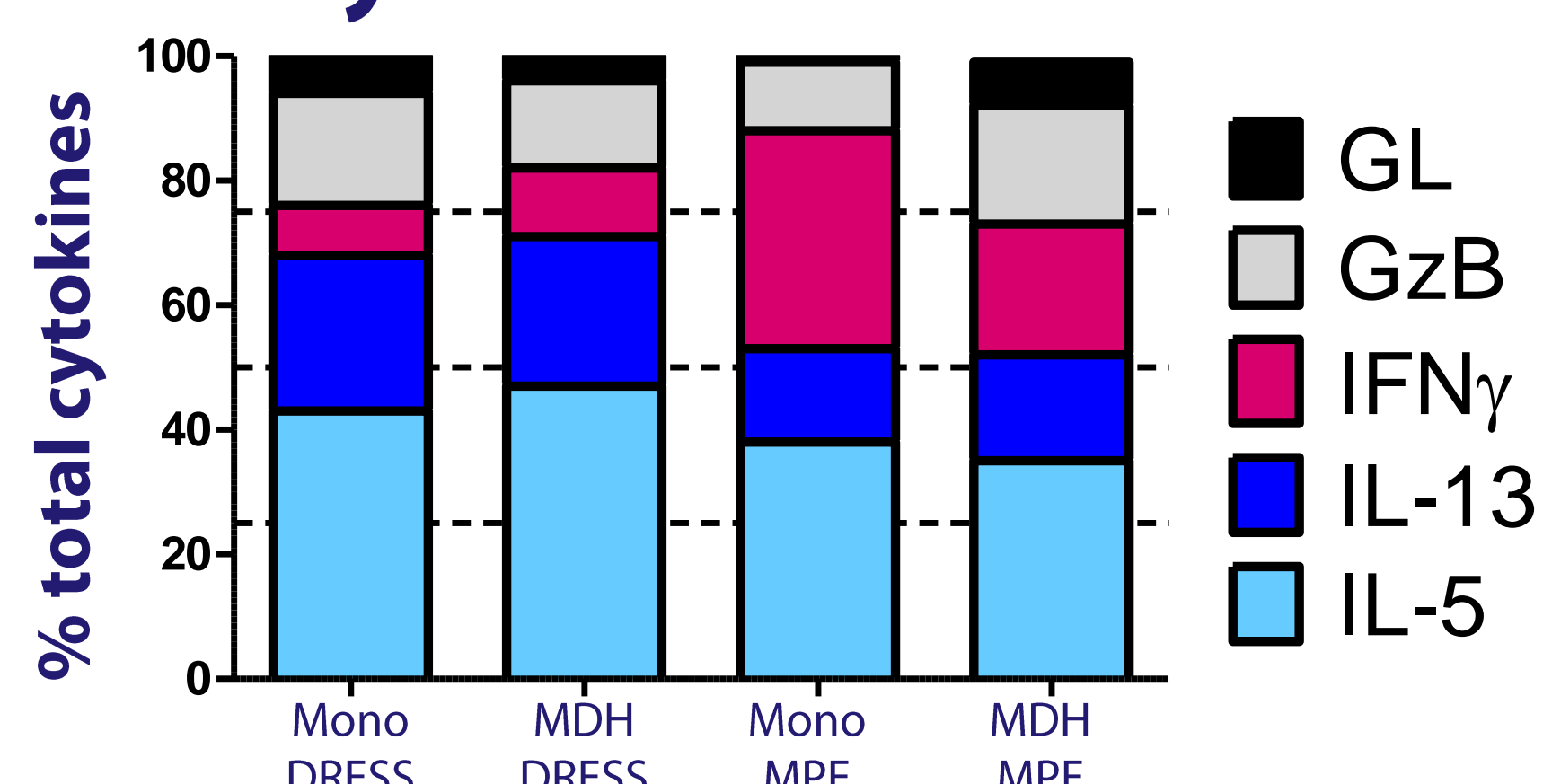


Figure 2: Cytokine dominance in cell cultures of DRESS and MPE patients' PBMCs

MDH individuals release 10X more cytokines than Mono-drug sensitized individuals

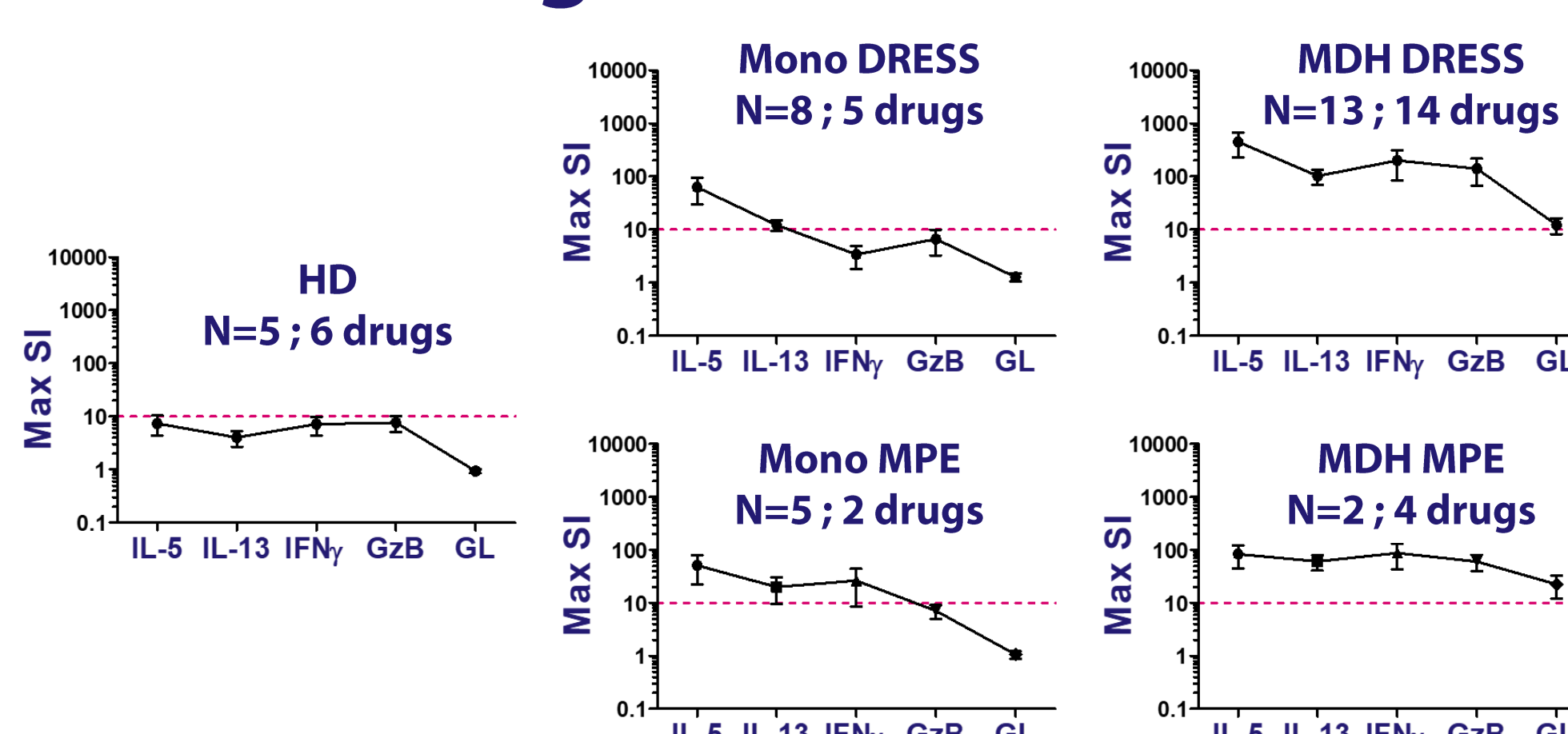


Figure 3: Cytokine release profiles in HD, DRESS & MPE individuals

T cells of DRESS patients remain chronically activated (years) after disease resolution

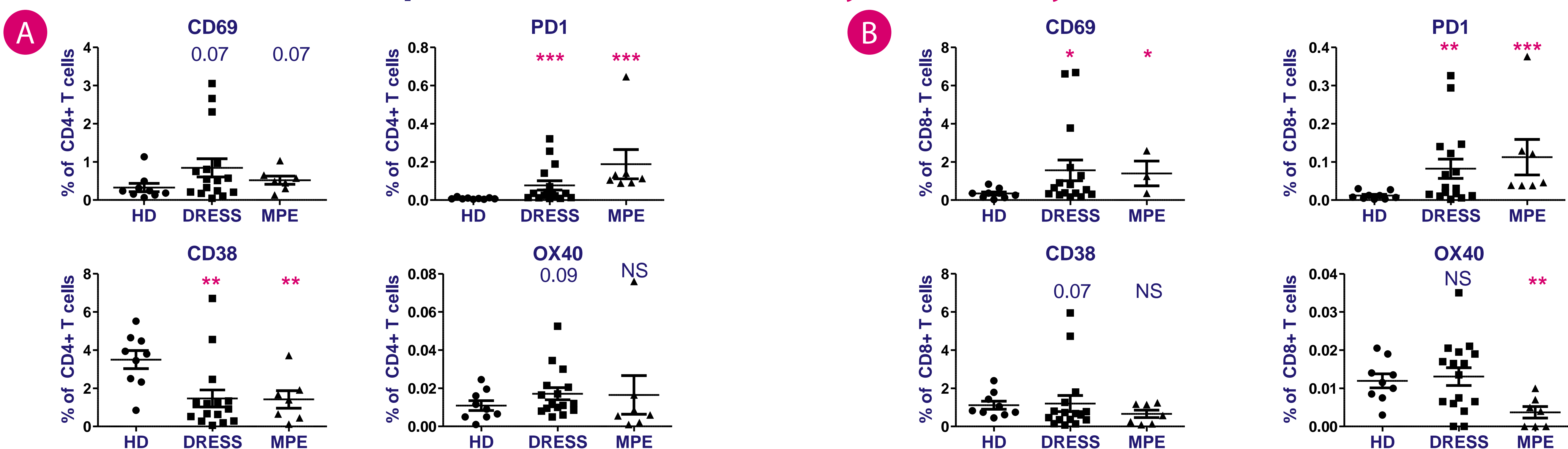


Figure 4: Flow cytometric analysis of peripheral blood T cell activation and exhaustion markers as a percentage of (A) CD4⁺ T cells or (B) CD8⁺ T cells. Statistics: Students t test in relation to HD; * p<0.05, ** p<0.05, *** p<0.005.

Conclusion & Outlook

- Mono DRESS & MDH DRESS individuals have signs of **chronic T cell activation**.
- MDH individuals have a **10X stronger cytokine response** against culprit drugs.
- **DRESS is a chronic disease** based on the immuno-profiles that remain after disease resolution.

References

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