

Type I interferons and interleukin 1 expression in *Mycobacterium tuberculosis* infection

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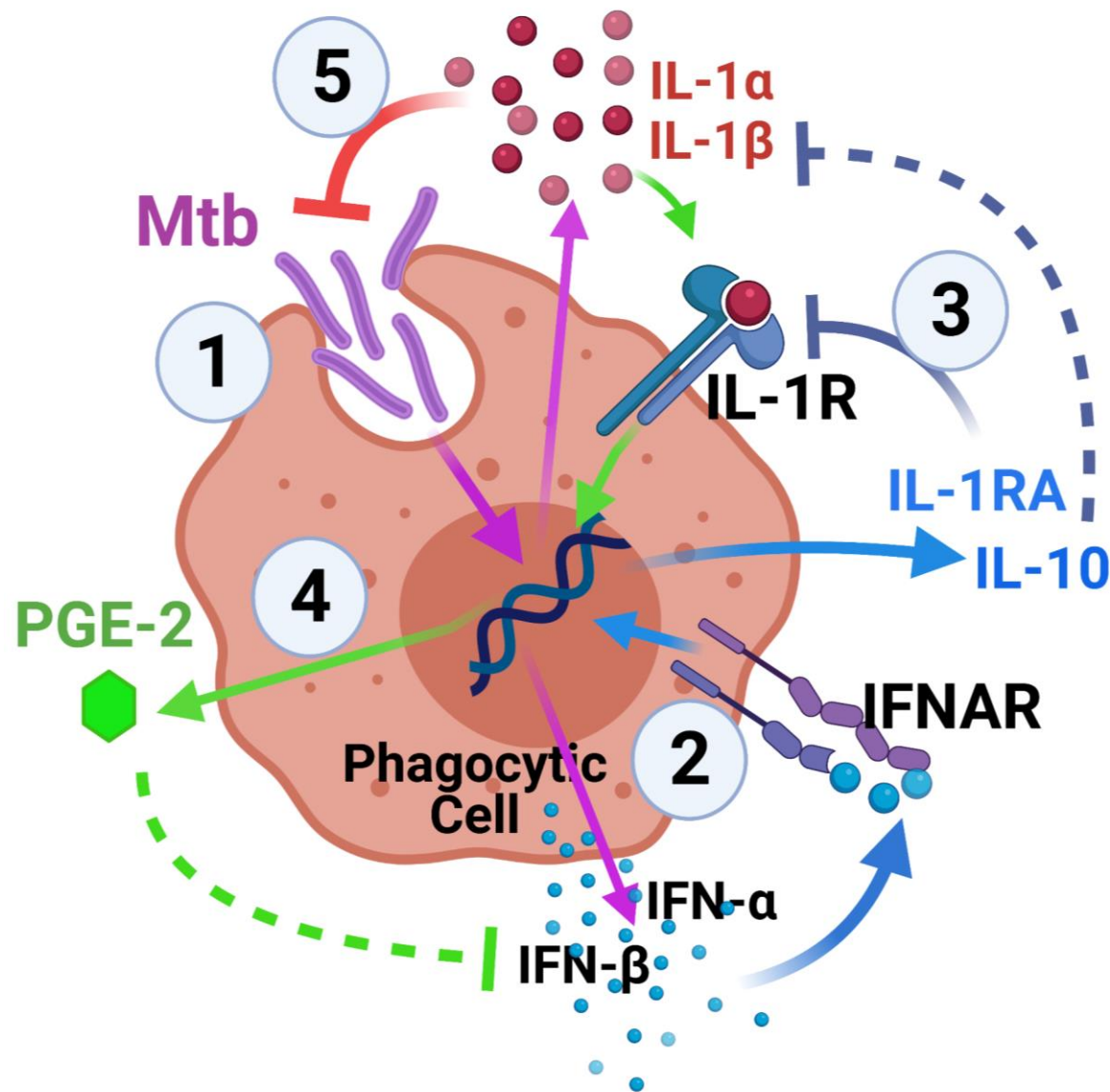
The authors have no conflict of interest to declare

Introduction

Differences in the binding affinities of IFN- α and IFN- β to the IFNAR are associated with the functional specificity of these IFNs

Research Question: Do IFN α and β have differential effects on the expression of IL-1A and IL-1B genes in individuals with distinct Mtb phenotypes?

Hypothesis: Stimulation of peripheral blood mononuclear cells (PBMCs) with IFN- α or IFN- β suppresses IL-1A mRNA expression more than the IL-1B gene in Mtb infection



- 1: Mtb induces IL-1 α/β and IFN- α/β release
- 2: IFN- α/β induces IL-10 and IL-1RA release
- 3: IL-10 and IL-1RA inhibit IL-1 signaling
- 4: IL-1 α/β signals to inhibit IFN- α/β
- 5: IL-1 α/β inhibit Mtb replication

Methodology

- Study design: Cross-sectional study
- Blood samples collected at the Health Sciences Centre, Winnipeg, Manitoba from study participants

Healthy controls (HC) (n=11)

No clinical or radiological or laboratory evidence of active disease

Tuberculin skin test TST (n=12)

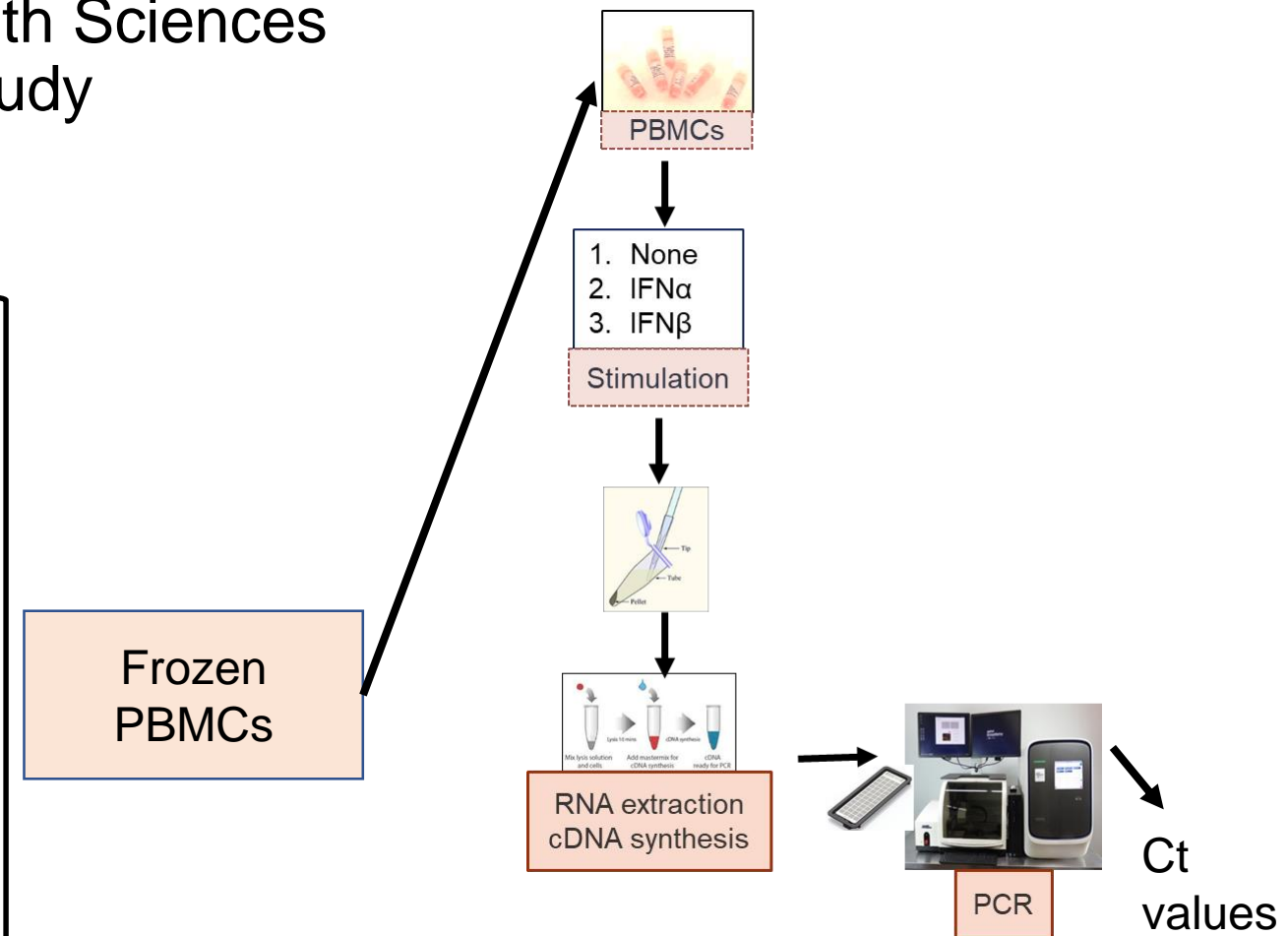
TST+IGRA-. No clinical or radiological or laboratory evidence of active disease

Latent TB infection (LTBI) (n=19)

IGRA positive; No clinical or radiological evidence of active disease

Active TB (ATB) (n=19)

Clinical or radiological or laboratory evidence of active disease



Calculations:

$$\Delta Ct = Crt_{\text{target gene}} - Crt_{\text{reference gene}}$$

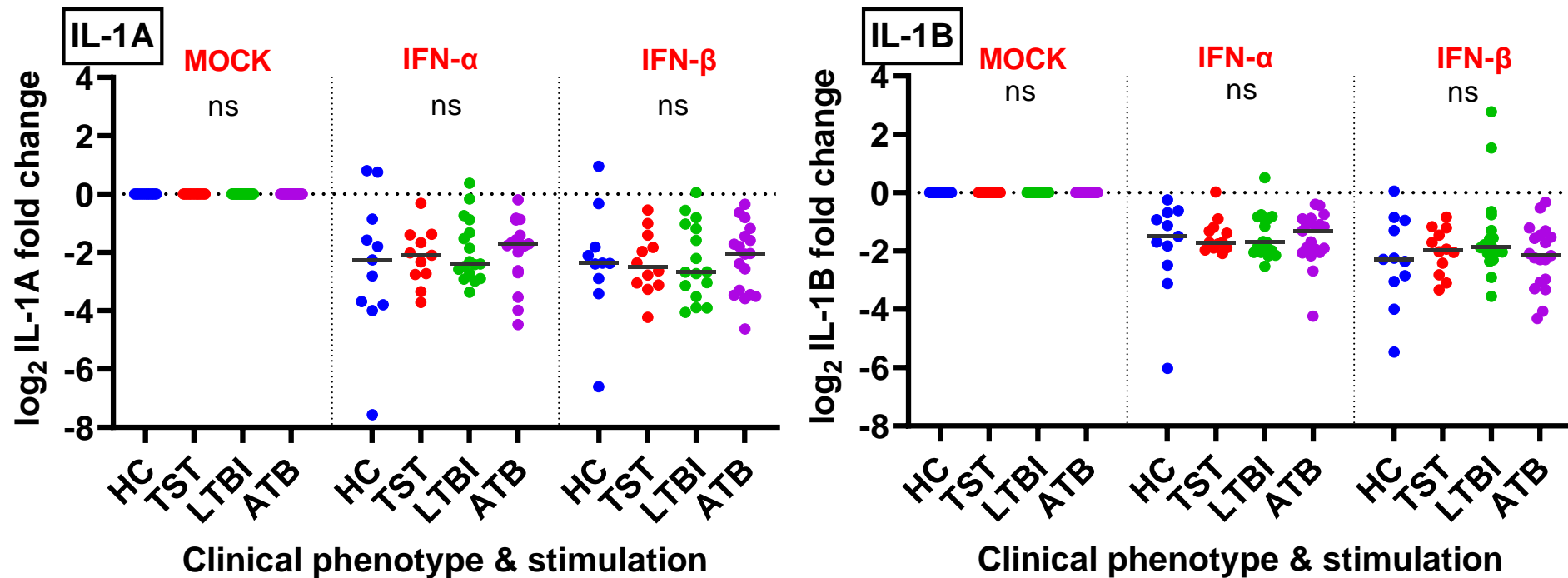
$$\Delta\Delta Ct = \Delta Crt_{\text{stimulated}} - \Delta Crt_{\text{unstimulated}}$$

$$\text{Relative expression} = 2^{-\Delta Crt}; \text{ Fold change} = 2^{-\Delta\Delta Crt}$$

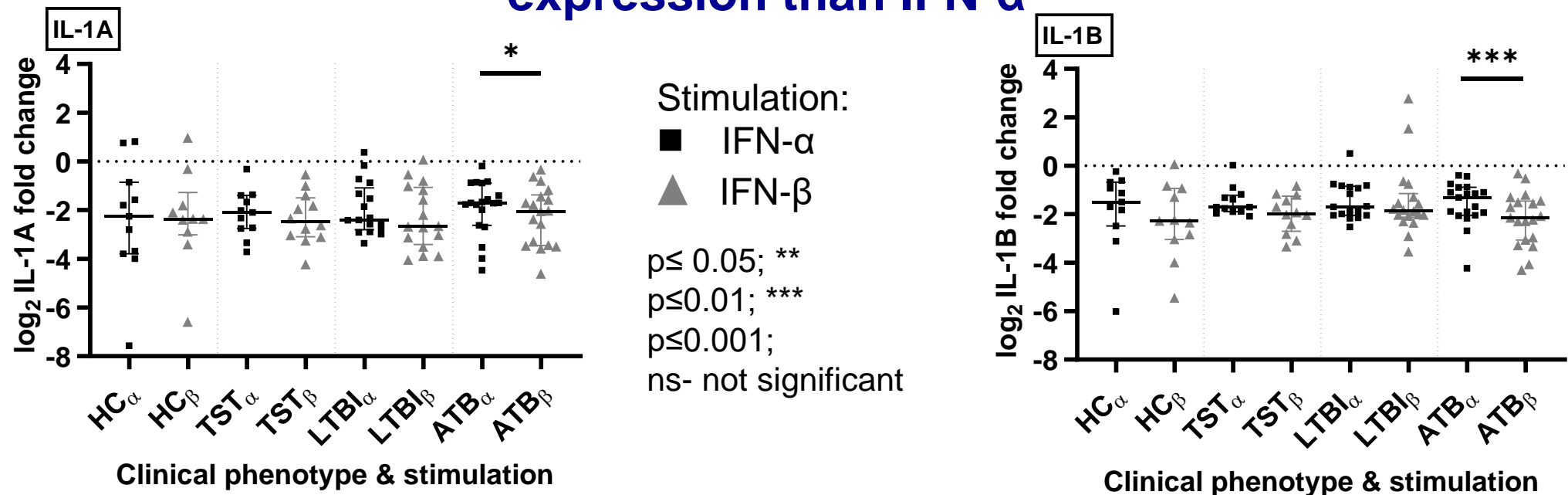
Results

Treatment of PBMCs with IFN- α/β suppresses IL-A and IL-1B expression

IL-1A/B suppression did not differ between Mtb phenotypes



IFN- β had a greater effect in suppressing IL-1A and IL-1B expression than IFN- α



Conclusion

- ❑ IFN- α - and IFN- β downregulate IL-1A and IL-1B mRNA expression in Mtb infection
 - IFN- α or IFN- β downregulates IL-1A mRNA expression more than the IL-1B gene in Mtb infection
- ❑ IFN- β downregulates IL-1A and IL-1B gene expression more than IFN- α . This was significant in active TB suggesting differential effects of IFN- α - and IFN- β in TB disease
- ❑ Given that IFN- α and IFN- β are therapeutic agents in multiple sclerosis, cancers, and chronic hepatitis, it is important to understand their effect on factors that influence TB disease control or progression
 - This could be useful for monitoring patients on IFN-based therapies