Designing Panels for Assessment of Type I Interferon Signature in Autoinflammatory Diseases: Investigating Biomarkers and Diagnostic Approaches

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Human type I interferonopathies

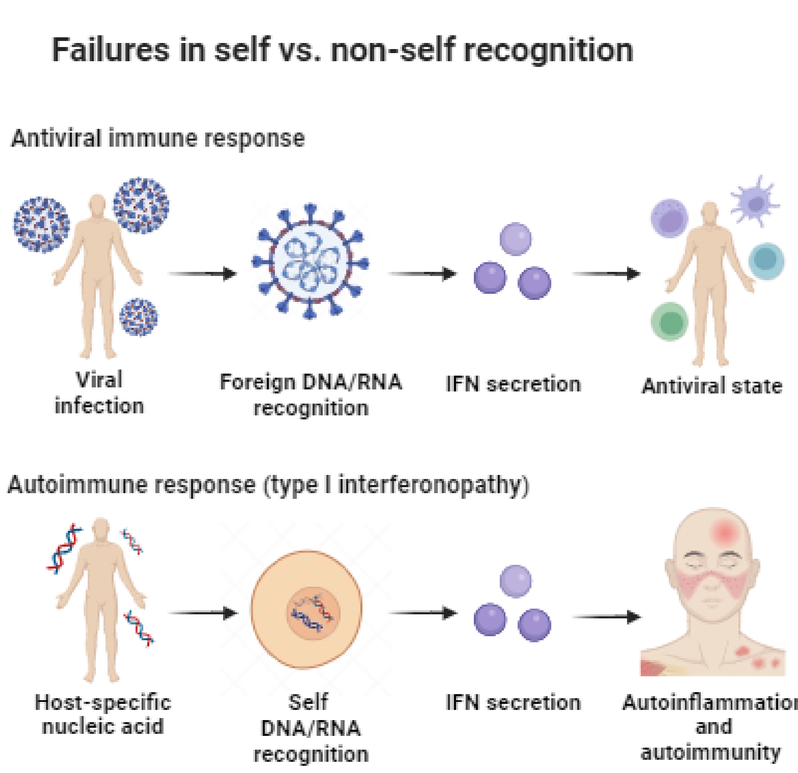
Monogenic disorders in which type I interferon **(IFN)** response upregulation may be directly relevant to disease pathogenesis.

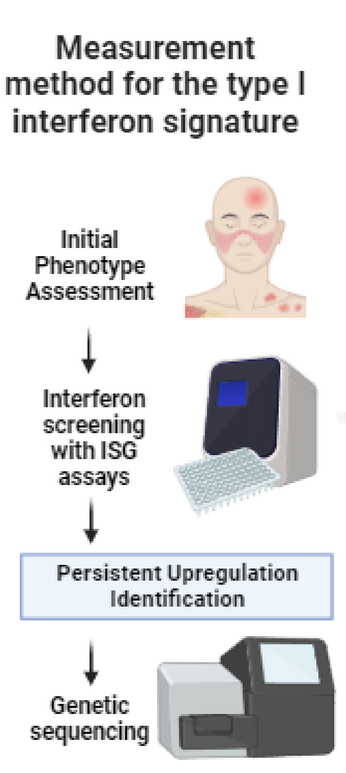
There is **no routine clinical test** in use for detecting dysregulation type I interferon signaling

To identify the phenotype of the interferon response we are using an **"interferon panel"** composed of **Interferon-Stimulated Genes (ISGs)** to examine the effects and consequences of type I interferon signaling.

The newly designed panel should:

1. Tailored to blood and Fibroblast samples
2. Contained ISGs and cytokines that show the upregulation of the IFN significantly
3. More precise and cost-efficient than the previously used assays





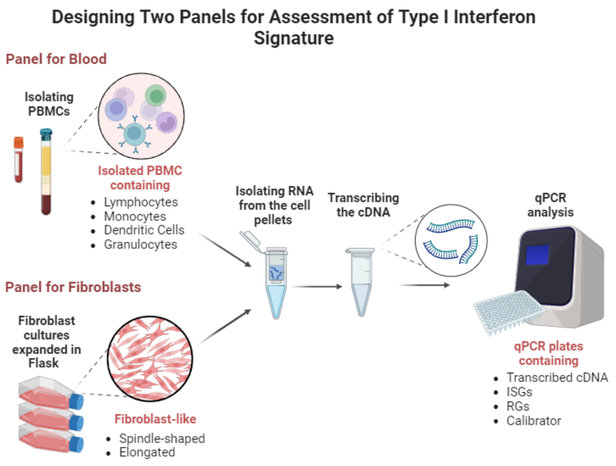
"Methods"

Sample collection and workflow

First, we identified a suitable nonhuman intra-assay calibrator to standardize CT values across multiple samples and assays.

Second, we assembled a comprehensive control cohort consisting of a diverse range of individuals, totaling at least 63 for blood samples and 37 for fibroblast samples, representing a spectrum of genders and age groups.

At last, we designed a qPCR assay containing suitable reference genes and ISGs.



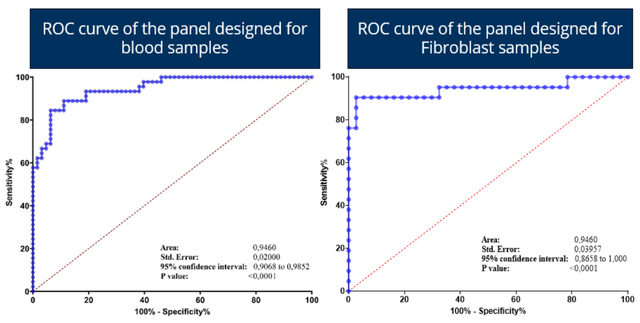
Results

Statistical analysis

The results of our statistical analysis showed that our panels designed for blood and fibroblast samples show a significant difference between the control and patients.

In the figure below you can see the **receiver operating characteristic curve (ROC)** that illustrates the diagnostic ability of our test.

The ROC shows us that our panels have demonstrated exceptional **specificity** and **sensitivity**, enabling us to significantly reduce the occurrence of **false positives** and **false negatives**, thereby ensuring precise and accurate patient identification.



Discussion

what we achieved and what comes next...

We have accomplished the development and validation of a robust calibrator, ensuring its stability for utilization as an intraassay reference to normalize CT values across various qPCR assays.

We have meticulously designed **two distinct panels** to cater to different sample types: one tailored for blood samples, comprising two reference genes and seven ISGs, and another tailored for fibroblast samples, encompassing five ISGs and one cytokine.

We have managed to design a unified panel that **encompasses all sexes and age groups**, it simplifies diagnostic procedures by streamlining the testing process, making it more cost-effective and efficient.

A unified panel promotes equitable healthcare access, as it caters to diverse patient populations without the need for age or sex-based distinctions.

This approach also facilitates broader research initiatives, as data from different demographics can be readily compared and analyzed.

Figures:

Fig. 1: failure in self vs. nonself recognition/measurement method for type 1 interferon signature

Fig. 2: methods used for designing two panels for assessment of type 1 interferon signature

Fig. 3: ROC curve providing the efficiency of the diagnostic test

References:

1 Lee-Kirsch, M. A. (2017). The Type i Interferonopathies. Annual Review of Medicine, 68, 297–315. https://doi.org/10.1146/annurev-med-050715-104506

2 Kralik, P., & Ricchi, M. (2017). A basic guide to real time PCR in microbial diagnostics: Definitions, parameters, and everything. In Frontiers in Microbiology (Vol. 8, Issue FEB). Frontiers Research Foundation. https://doi.org/10.3389/fmicb.2017.00108

3 Kovarik, P., Castiglia, V., Ivin, M., & Ebner, F. (2016). Type I interferons in bacterial infections: A balancing act. In Frontiers in Immunology (Vol. 7, Issue DEC). Frontiers Media S.A. https://doi.org/10.3389/fimmu.2016.00652

4 Fox, L. E., Locke, M. C., & Lenschow, D. J. (2020). Context Is Key: Delineating the Unique Functions of IFNα and IFNβ in Disease. In Frontiers in Immunology (Vol. 11). Frontiers Media S.A. https://doi.org/10.3389/fimmu.2020.606874

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