Advancing Respiratory Virus Diagnostics: Integrating the Nasal IFN-I Score for Improved Viral Detection

Cloé Grosbois[1,2], Marine Mommert-Tripon[1,2], Delphine Parraud[3], Alexandre Gaymard[3,4], Valérie Cheynet[1,2], Bruno Lina[3,4], Guy Oriol[1,2], Frédéric Laurent[3], Caroline Dupré[4], Quentin Semanas[3], Antonin Bal[3], Laurence Generenaz[1,2], Sylvie Pons[1,2], Karen Brengel-Pesce[1,2], Audrey Guichard[1,2], William Mouton[1,4], Florence Morfin[3,4], Aurore Fleurie[1,2] and, Sophie Trouillet-Assant[1,4]

[1]Joint Research Unit Civils Hospices of Lyon-bioMérieux, Hospices Civils de Lyon, Lyon Sud Hospital, Pierre-Bénite, 69310, France, [2]Open Innovation & Partnerships (OIP), bioMérieux S.A., Marcy l'Etoile, 69280, France, [3]Infective Agents Institute, Hospices Civils de Lyon, Croix-Rousse Hospital, Lyon, 69004, France, [4]International Center of Research in Infectiology, Virpath team, Lyon University, INSERM U1111, CNRS UMR 5308, ENS, UCBL, Lyon, 69000, France.

Background

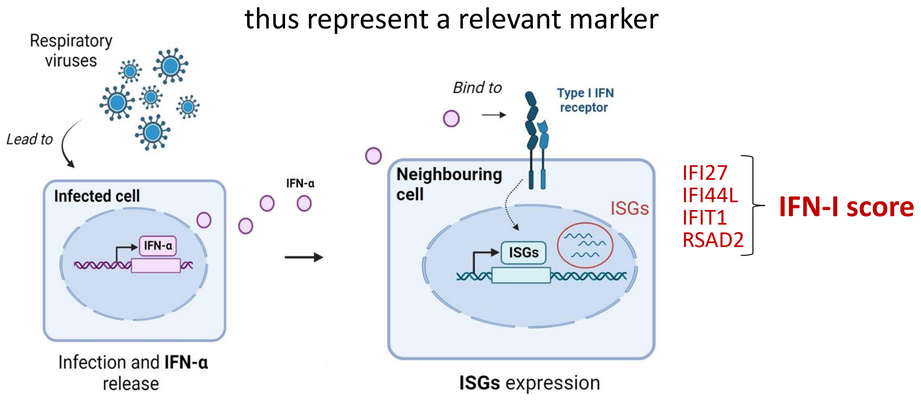
Respiratory viral infections (RVIs) are a **major public health problem**

Diagnosis of RVIs rely on **first-line PCR-based tests** targeting:

IAV, IBV RSV SARS-CoV-2

However, **less commonly tested** viruses like **hMPV, ADV, HRV or PIV** can cause **acute respiratory tract infections → need rapid** and **reliable diagnostic tools** to **improve RVIs diagnosis** and **optimize test** use

Type I Interferon (IFN-I) is mainly **expressed** in **response to viral infections** and could thus represent a relevant marker



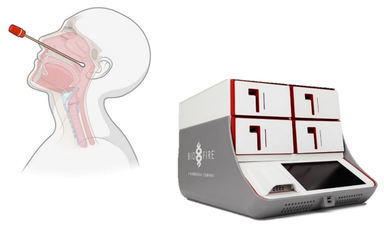
IFN-I score calculated through **quantification Interferon Stimulated Genes** (ISGs) **expression**, proposed as an **alternative** to the **IFN-I release assessment**

Objective: To assess whether the nasal IFN-I score could be a meaningful marker for RVIs and enhance their diagnosis when combined with first-line tests

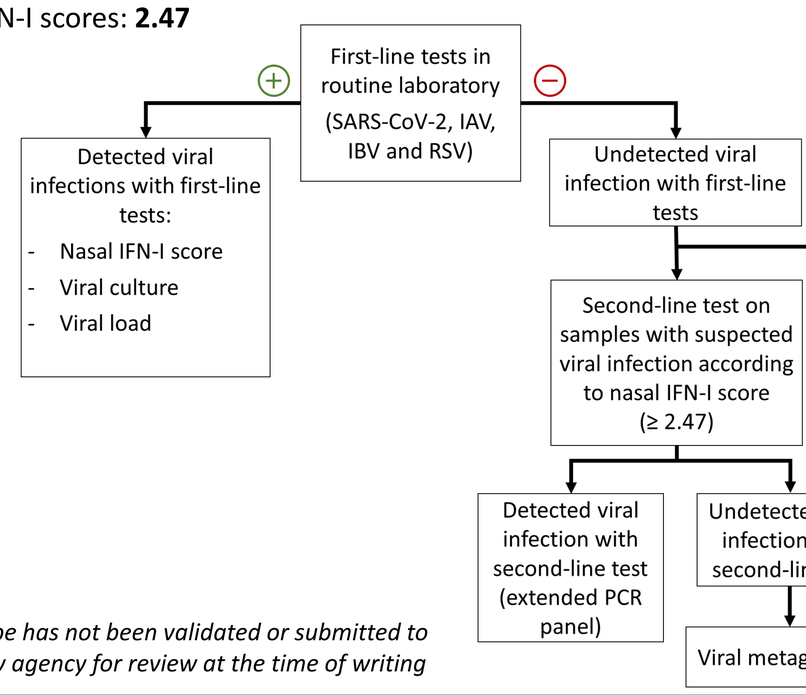
Cohorts and methods

Prospective study named **RESPIFERON** (NTC06017310)

- **788 nasopharyngeal swabs (NPS)** from **patients with RVI suspicion**
- **11/2022 → 04/2024**
- Using a FilmArray® IFN-I prototype*: **IFN-I score** was calculated through **mRNA expression of 4 ISGs**
- Nasal IFN-I score **positive threshold** determined using Healthy Controls (HCs) IFN-I scores: **2.47**



BioFire® FilmArray®

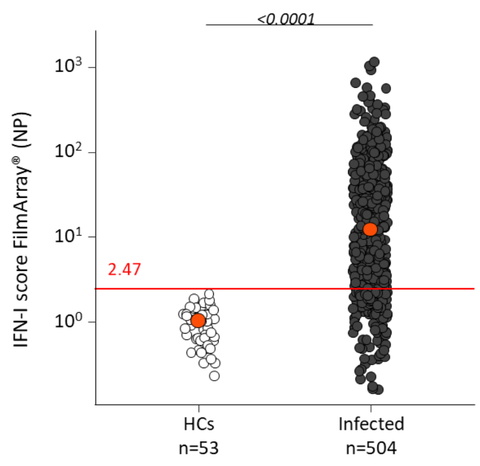


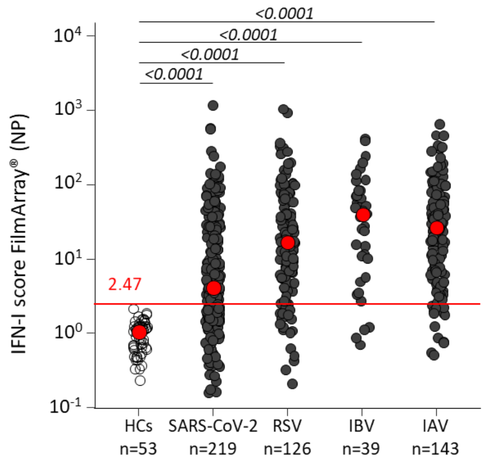
**This prototype has not been validated or submitted to any regulatory agency for review at the time of writing*

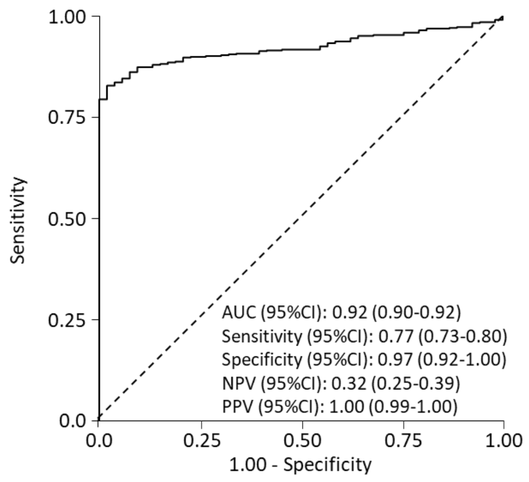
Results

1. Performances of the nasal IFN-I score to detect RVIs caused by SARS-CoV-2, IAV, IBV and RSV

Among the 788 NPS, 504 were positive with first-line tests:







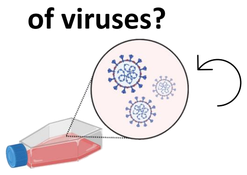
Significantly **higher** nasal **IFN-I score** in NPS of **patients with infection caused by SARS-CoV-2, IAV, IBV and RSV** compared HCs

Strong capacity of the nasal **IFN-I score** to **discriminate HCs from patients with infection** independently of the virus involved

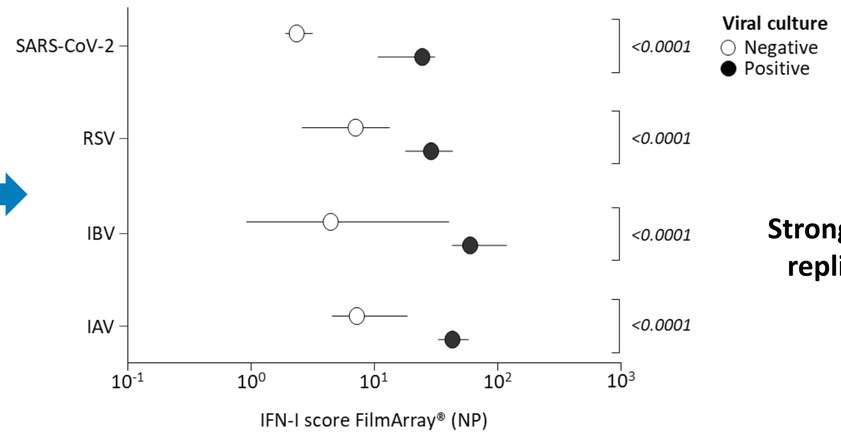
Nevertheless, **23% of positive NPS** in **first-line tests** with nasal **IFN-I score < 2.47**

Considering that virus-specific **PCR tests** could also **amplify nucleic acid traces** from **inactive virion**

Could the nasal **IFN-I score reflect** the **replicative capacity of viruses?**



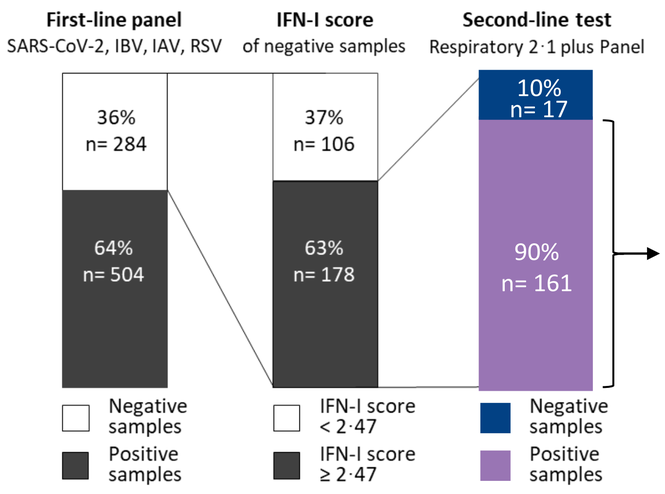
Viral culture performed on positive NPS with first-line tests:

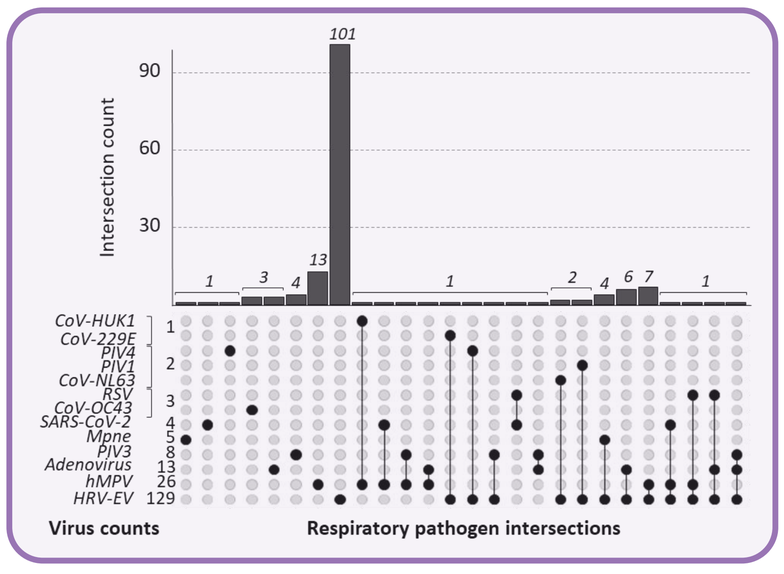


Significantly **higher** nasal **IFN-I score** in NPS with **positive viral culture**

Strong performance of the nasal **IFN-I score** in **discriminating replicative viral infections** among **positive** NPS in **first-line tests** with an **AUC (95%CI)** of **0.85 (0.82-0.89)**

2. Improvement of viral detection of samples classified as negative by the first-line tests by the nasal IFN-I score





284 negative NPS in **first-line tests**, according to the **nasal IFN-I score (≥2.47)** we **suspected the presence of RVIs** in **178 NPS** → following the second line-test (extended PCR panel that detected 23 pathogens) we **confirmed** the **presence of virus in 90% of samples initially classified as negative**

Viral metagenomics analysis on negative NPS:

Number of NPS	Pathogens identified in viral metagenomic
1	Human rhinovirus
3	Picornaviridae
1	Human parvovirus B19
1	Cytomegalovirus

Metagenomic analysis on **15 NPS** with **a nasal IFN-I score ≥2.47** but **without virus** detected after **first- and second-line tests → 6/15 NPS with a pathogenic virus**

Contact
Sophie Trouillet-Assant, PhD
sophie.trouillet-assant@chu-lyon.fr

Reference
eBioMedicine
Part of THE LANCET
Discovery Science

SCAN ME

Conclusion

The study highlights the potential of integrating the nasal IFN-I score into clinical workflows to improve RVI diagnosis and enhance preparedness for emerging viruses.