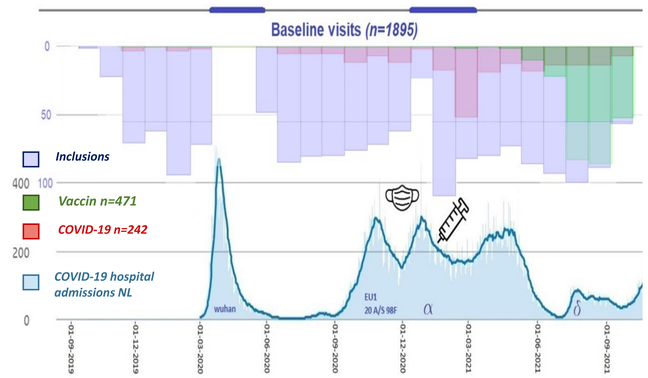
# COVID-19 VACCINATION IMPACTS FUNCTIONAL IMMUNE RESPONSES AND PLASMA PROTEOME IN PLWH

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## BACKGROUND

The impact of COVID-19 infection or COVID-19 vaccination on the immune system of people living with HIV (PLWH) is unclear. We therefore studied the effects of COVID-19 infection or vaccination on functional immune responses and systemic inflammation in PLWH.




## METHODS

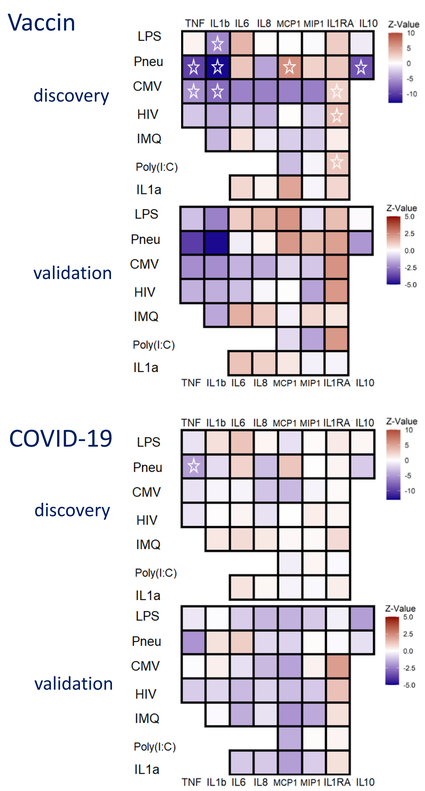
Between 2019 and 2021, 1895 virally suppressed, asymptomatic PLWH were included in the Netherlands in the 2000HIV[1] study: 1514 participants enrolled after the start of the COVID-19 pandemic were separated into a discovery and validation cohort.

- **PBMCs were incubated with different stimuli for 24 hours**: cytokine levels were measured in supernatants.
- **~3000 targeted plasma proteins were measured with Olink® Explore panel**
- Past COVID-19 infection was proven when a positive PCR was reported or when serology on samples from inclusion proved positive
- Compared were unvaccinated PLWH with and without past COVID-19 infection, and PLWH with or without anti-COVID-19 vaccination excluding those with past COVID-19 infection

COVID-19 **vaccination** in PLWH leads to **increased systemic inflammation** but **less ex-vivo cytokine production** capacity after PBMC stimulation

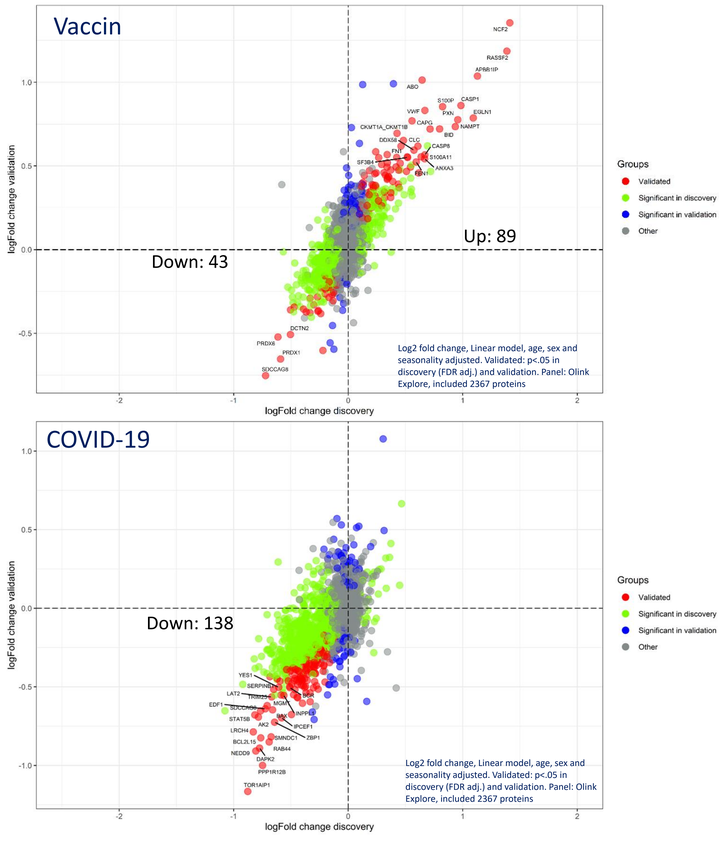
## RESULTS

### A: functional capacity




Heatmap showing Z values from logistic regreggsion
★ p< .05 in discovery (FDR adj) and validation
Pneu: S.pneumoniae

### B: plasma proteome




## RESULTS

Median days since vaccination and COVID-19 +PCR were 33(IQR 16-66) and 137 (IQR 56-206) respectively. Alcohol, smoking, drug use, BMI, age, latest CD4 count were comparable between groups.

- **Vaccinated PLWH had lower TNF-α and IL-1β production** capacity upon restimulation with a range of microbial stimuli, while production of IL-1Ra was increased. In COVID-19 infected PLWH a reduced production of TNF-α to S. pneumonia was significantly different (fig A)
- Targeted proteomics showed 89 upregulated and 43 downregulated proteins in the vaccinated participants. Participants with past COVID-19 infection display lower levels of 138 plasma (fig B)

**Top* enriched pathways**
**KEGG/Reactome *in vaccinated group**

| | Vaccin | COVID-19 |
|---|---|---|
| Innate immune system | UP | Down |
| Integrin signalling / plug formation | UP | - |
| Neutrophil degranulation | UP | - |

## CONCLUSIONS

COVID-19 **vaccination** in PLWH leads to an **increased systemic inflammation** as assessed by targeted plasma proteomics, but **reduced ex vivo cytokine production capacity** of PBMCs upon microbial stimulation. This pattern is different from that of COVID-19 infection that leads to a decreased inflammatory profile and only minimal effects on cytokine production capacity.

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[1] Vos et al Front Immunol 2022 Dec 20; 13:982746 www.2000HIV.com