SARS-CoV-2 VARIANTS-DEPENDANT INFLAMMASOME ACTIVATION

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BACKGROUND

Innate immunity is the first line of defense in response to pathogens, which acts locally and also leads the stimulation of adaptive immunity through at least with IL-1β secretion.
It has been shown that SARS-CoV-2 infection triggered the NLRP-3 inflammasome activation and the IL-1β secretion.

- **The aim of this study was to analyze and compare the level of IL-1β secretion that is one of the most important innate immunity cytokines, in monocyte-like cells infected with 6 different variants of the SARS-CoV-2**.

METHODS

Six SARS-CoV-2 variants were isolated from COVID-19 hospitalized patients. Viral stocks were obtained by inoculation in Vero and Vero-TRMPSS2 cells.

Historical	Alpha	Beta	Gamma	Delta	Omicron
B.1, (D614G)	B.1.1.7	B.1.351	P.1	B.1.617.2	BA.1

THP-1 monocyte-like cells were cultured with RPMI-hepes 10% FBS-0.05 mM 2-mercaptoethanol. A total of 5 x 10^4 of THP-1 cells was plated per well in 96-wells plate and differentiated with 10nM of PMA for 24h. Differenciated-THP-1 were first primed with LPS 1µg/ml for 2h and infected with different SARS-CoV-2 variants with a MOI 0.1. IL-1β was measured by luminescence in the supernatant after 24 h of infection.

A kruskall-wallis and multiple comparison tests were realized with the GraphPad prism software.

- ✓ SARS-CoV-2 **variants** triggered **Il-1b secretion** in macrophage-like cells.
- ✓ **Omicron BA.1** sublineage was **more recognized** by the **innate immune cells** than others SARS-CoV-2 variants.

RESULTS

We analyzed and compared IL-1β secretion between SARS-CoV-2 virus 6 sublineages after infection of monocytes like THP-1.

- We observed that THP-1 cells infected with SARS-CoV-2 variants presented a significantly higher IL-1β secretion than non-infected cells.
- Some SARS-CoV-2 variants led to a stronger IL-1β secretion. We observed a significantly higher level of IL-1β cells infected with Omicron BA.1 sublineage compared to other variants.
- Omicron BA.1 infected cells presented the higher IL-1β secretion (median 385.7 pg/ml IQR [302.6–426.3]) follows by the Delta and the historical variants (median 303.6 [266.3–391.9] and 281.9 [207.2–410], respectively). Alpha, Beta and Gamma variants presented the lowest IL-1β secretion (median 228.1 [192.5– 276.4], 219.1 [185.1–354.2] and 211 [149.8–228.8]).

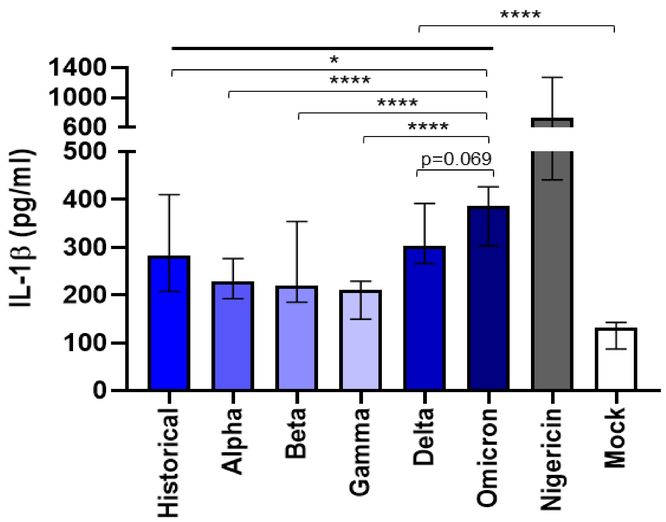

Figure1. SARS-CoV-2 variants-dependant IL-1b secretion.
The graph represented the measure of IL-1b secretion in supernatants of non (Mock) or SARS-CoV-2 infected or treat Nigericin (positive control for NLRP-3 activation) differentiated-THP-1 cells. *p<0.05 ; ****p<0.0001. Data shown result from multiple independent experiments.

CONCLUSIONS

We observed the inflammasome activation for the 6 SARS-CoV-2 sublineages with a variation in the level of IL-1β secretion.

- ✓ Indeed, our results suggested that Omicron BA.1 was more recognized by the innate immune cells than other SARS-CoV-2, which could in part, with its upper respiratory tract tropism, possibly explain its less clinical virulence.
- ✓ Taking together, these results suggest that the innate immune response and precisely, IL-1β secretion pathways were activated in a SARS-CoV-2 variants-dependent manner.

ADDITIONAL KEY INFORMATION

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