Genetic Mutation Differences Patterns of SARS-CoV-2 in Immunocompromised Patients vs. Controls

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BACKGROUND

The mutational dynamics of SARS-CoV-2 in immunocompromised patients remain relatively understudied. This study examined a cohort of immunocompromised patients hospitalized with SARS-CoV-2 infection to assess the distinct evolutionary trajectories of SARS-CoV-2 in these individuals compared to their immunocompetent counterparts.

→ We compared the genetic diversity of SARS-CoV-2 between these groups over time.

METHODS

- **88 imunnocompromised hospitalized patients and 54 non-immunocompromised subject** from Pitié-Salpêtrière Hospital (Paris, France) diagnosed with SARS-CoV-2 infection by RT-qPCR were enrolled.
- Samples were collected at the **time of infection (D0)** and during their **follow-up.**
- **Whole Genome Sequencing** was performed according to the ARTIC protocol on the Oxford Nanopore platform
- Consensus sequences were generated using a pipeline including minimap2 and Clair3.

Table 1 : Baseline patients' characteristics

	All (n=142)	Immunocompromised (n=88)	Controls (n=54)
Sex, n(%)			
Male	74 (52.1)	47 (53.4)	27 (50.0)
Female	68 (47.9)	41 (46.6)	27 (50.0)
Age			
mean	69,3	69,5	69,1
Immunosuppression status, n(%)			
HIV infection	2 (1.4)	2 (2.3)	
Cancer	31 (21.8)	31 (35.2)	
Hematological diseases	27 (19.0)	27 (30.7)	
Immunosuppressive diseases and immunosuppressive treatments including Rituximab	7 (4.9)	7 (8.0)	
Solid organ transplant	21 (14.8)	21 (23.9)	
Control	54 (38.0)		54 (100.0)
Mean viral load at D0, Ct value	19.8	20.0	19.5
Median follow-up time (days)		6	4

Greater genetic diversity in immunocompromised patients over time

RESULTS

- 5 isolated mutations overexpressed associated with immunocompromised patients (gene N and ORF1ab) (Figure 1)
  - N :R14C; G137-
  - ORF1ab : L897S; N5592K; P:5558T
- Greater number of mutations for each gene in immunocompromised patients (Figure 2)

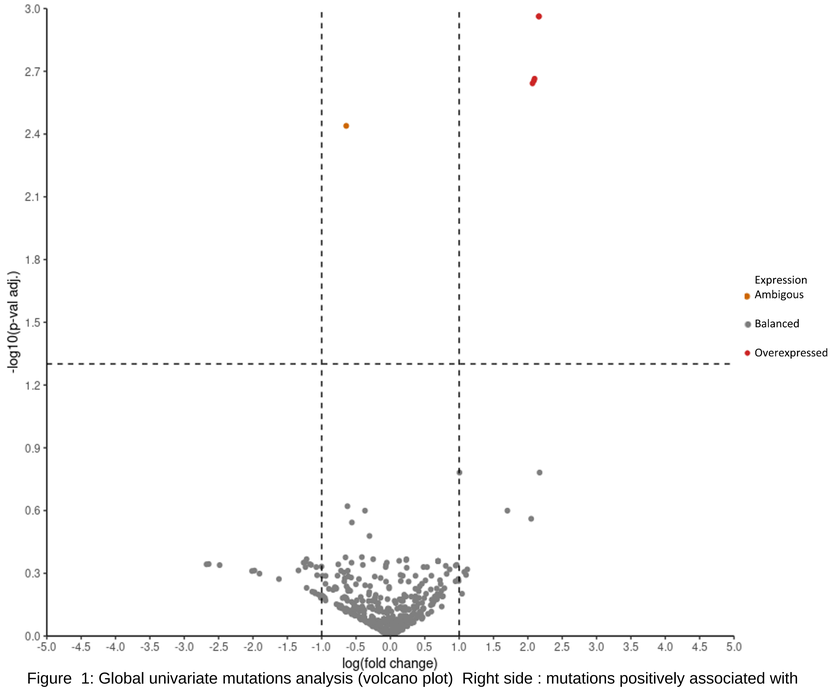


Figure 1: Global univariate mutations analysis (volcano plot) Right side : mutations positively associated with immunocompromised status. Left side : Mutations positively associated with non-immunocompromised subjects.

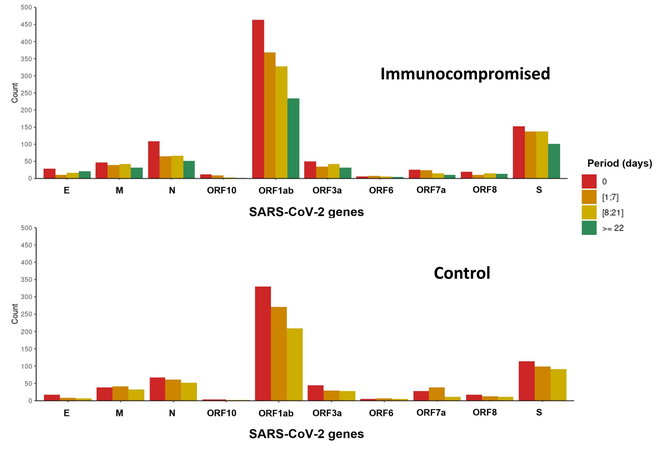


Figure 2: Detected mutation across group, time and SARS-CoV-2 gene

CONCLUSIONS

- Study suggested a greater genetic diversity in immunocompromised patients.
- Isolated mutations in N and ORF1ab gene could affect protein structure.
- In silico approach : N:G137- appears to stabilize the nucleocapsid over time compared to the non-mutated nucleocapsid.

ADDITIONAL KEY INFORMATION

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