Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Journal of Clinical Virology 128 (2020) 104450

Contents lists available at ScienceDirect

Journal of Clinical Virology

journal homepage: www.elsevier.com/locate/jcv

Type I interferons can be detected in respiratory swabs from SARS-Cov-2 infected patients

Letter to the Editor,

There is an urgent need to understand the pathogenesis of severe acute respiratory syndrome - Coronavirus -2 (SARS-CoV-2) infection. Recent reports suggest that SARS-CoV-2 fails to induce significant amounts of interferon (IFN) in tumour tissue explant cultures [1] and in *in vitro* cell and animal models [2], the latter specifying that IFN expression may however be obtained at high multiplicity of infection. Since IFNs are known to play a key role in the response to viral infections, the aforementioned low ability of SARS-CoV-2 to induce all IFN types is significant from a pathogenetic point of view and such failure may be one of the keys to explaining the pathogenesis of COVID-19. Indeed, it has been proposed that the lack of induction of significant amounts of all types of IFN may influence the kinetics of SARS-CoV-2 load in nasopharyngeal secretions [1], possibly explaining the high transmissibility of the infection, and that a reduced innate antiviral defence is associated with elevated inflammatory cytokine production [2]. The above data has led to the conclusion that the use of exogenous IFN to stimulate antiviral immunity might be successful for treating SARS-CoV-2 infection [3]. All the above results await interpretation from the perspective of infection pathophysiology, considering the recent finding on IFN-induced expression of ACE2 receptor [4].

It is our firm opinion, however, that further observation is required before drawing general conclusions about the lack of induction and production of IFNs in SARS-CoV-2 infection.

Indeed, in the framework of a project addressing the pathogenesis of the SARS-CoV-2 infection, we were able to detect type I IFN genes (IFN alpha and omega), but not type II IFN genes (IFN-gamma), in pelleted cells from oropharyngeal and/or nasopharyngeal swabs of COVID-19 patients hospitalized at Sapienza University Hospital "Policlinico Umberto I" in Rome, Italy.

Specifically (see Table 1 and the relative methods), type I IFN genes were detected in 47 out of 50 patients who were COVID-19-diagnosed by RT-PCR (RealStar® SARS-CoV-2 Altona Diagnostic – Germany) after RNA extraction (QIAamp® Viral RNA - Qiagen) of samples taken from oropharyngeal and/or nasopharyngeal swabs. The producing cells have not been characterized, but we believe that the data have added value since they were obtained in ex vivo experiments directly from COVID-19 patients and not from experiments performed on explanted tumour cells [1] or on cellular lines/animal model [2].

Although we do not currently know whether or what type or subtypes of IFN are produced in respiratory secretions and whether the IFNs subtypes we have detected display a beneficial or detrimental effect on the natural history of COVID-19 [5], we strongly believe that, in light of the data or comments recently reported by Chun [1], Blanco-Melo D [2], and O'Brien [3] and the number of active clinical treatment trials with IFNs now underway [6], it is urgent and critically important to deliver data indicating that an IFN response (at least type I IFN) does exist in the respiratory tract of SARS-CoV-2-infected patients.

Table 1
Level of type I and II Interferon (IFN) measured in respiratory swabs of COVID-19 patients (n = 50).

Genes	Ct < 40*	%	$2^{-\Delta\Delta Ct}$ **
IFN-alpha	47/50	94.0	4.13 (1.22–31.29)
IFN-omega	47/50	94.0	7.92 (1.30–219.18)
IFN-gamma	0/50	NA	NA

* Data are expressed as number (percentage) of COVID-19 patients (n = 50) with Ct values lower than 40.

** IFN expression data were calculated using $2^{-\Delta\Delta Ct}$ method. Each IFN raw Ct value was tagged as undetermined when fell between levels of 40 and 45. Raw Ct values were normalized using the endogenous control (β-glucuronidase) according to the equation: ΔCtIFN = CtIFN - CtGUS. Differences between patients and healthy donors (n = 10) were calculated based on the ΔΔCt measure, where ΔΔCtIFN = ΔCtSARS-CoV-2 – mean (ΔCtHealthyDonors). Expression of IFNs and housekeeping genes mRNAs were evaluated using RT/Real Time PCR [7]. Data are expressed as median (range).

Declaration of Competing Interest

None.

Acknowledgements

There is no funding for this work. We would like to thank the COVID-19 ViroInfection Study Group of Sapienza University.

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https://doi.org/10.1016/j.jcv.2020.104450
Received 6 May 2020

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