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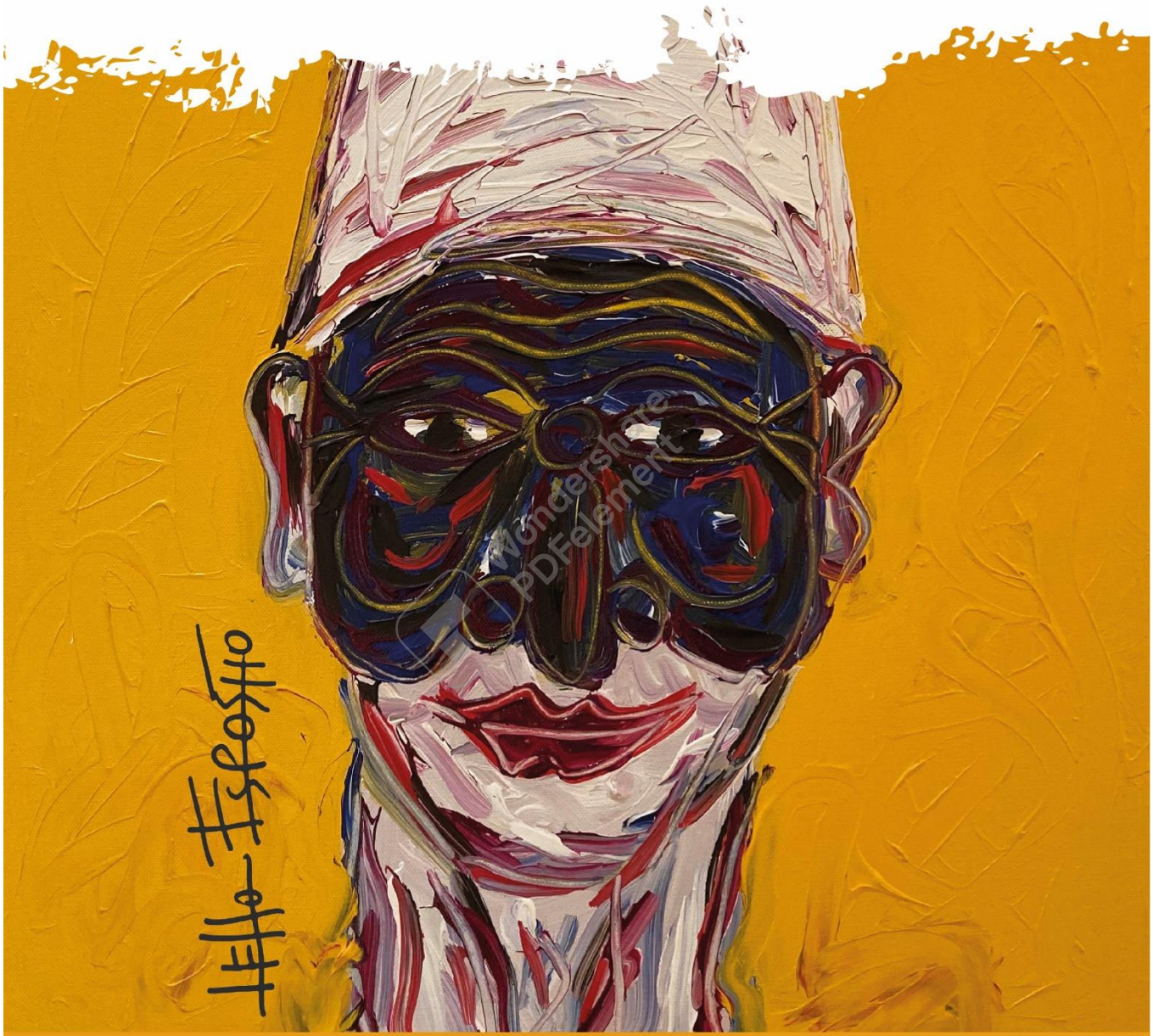

Abstract Book

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150 - Characterization of citrullination during infection with DNA and RNA viruses: a new strategy for host-targeting antivirals drugs

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Characterization of citrullination during infection with DNA and RNA viruses: a new strategy for host-targeting antivirals drugs

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INTRODUCTION. One of the strategies devised by a number of bacteria and viruses to favor its replication consists in modifying host cellular proteins at the post-translational level, thereby altering their localization, interaction, activation and/or turnover. A post-translational modification (PTM) that is increasingly recognized to play an essential role in this regard is citrullination, also called deimination, a process where the guanidinium group of an arginine is hydrolyzed to form citrulline, a non-genetically encoded amino acid. This PTM is catalyzed by the calcium-dependent protein arginine deiminase (PAD) family of enzymes, which in humans is composed of five isoforms (PADs 1-4 and 6), with different tissue-specific expression and substrate specificities. Although aberrant citrullination has been detected in several inflammatory conditions, suggesting that it may play a pathogenic role in inflammation-related diseases, a direct correlation between citrullination and viral infections has only recently emerged. In the last few years our laboratory has defined the citrullination profile, the expression of the enzymes PADs and the citrullinated substrates in the course of infection with DNA and RNA viruses, Herpesvirus and Coronavirus respectively. In addition, we evaluated a large panel of PAD inhibitors for their antiviral activity against these virus classes in a wide variety of cell lines.
MATERIAL AND METHODS. We used Human Cytomegalovirus (HCMV) and herpes simplex virus type 1 (HSV-1) as models of DNA viruses and HCoV-OC43 and SARS-CoV-2 as models of RNA viruses. We tested the antiviral activity of well characterized PAD inhibitors. We used real time quantitative PCR to quantify copies of the viral genomes, Western blot analysis to evaluate the expression of PADs and viral proteins , and plaque assay to evaluate the production of new virions. Furthermore, we assessed the pattern of citrullination upon infection by using a citrulline-specific rhodamine phenylglyoxal (RhPG)-based probe.
RESULTS. Citrullinome analysis of infected cells reveals significant changes in deimination levels of both cellular and viral proteins, with interferon (IFN)-inducible protein IFIT1 being the most heavily deiminated one. Moreover, we show that in vitro IFIT1 citrullination impairs its ability to bind to 5'-pppRNA.