Title: Regulation of microRNAs in response to herpes simplex virus type-1 (HSV-1) infection in idiopathic pulmonary fibrosis

Dr. Eliza 30759 Tsitoura e.tsitoura@med.uoc.gr 1, Dr. Katerina 30760 Antoniou kantoniou@med.uoc.gr MD 2, Anna 30761 Psaraki annapsaraki@hotmail.com 2, Ms. Ismini 30762 Lasithiotaki papanikolaou_ismini@yahoo.gr MD 2, Prof. Dr Demetrios 30763 Spandidios spandido@hol.gr 1, Dr. George 30765 Sourvinos sourvino@med.uoc.gr 1 and Prof. Dr Nikolaos 30766 Siafakas siafak@med.uoc.gr MD 2.  

1 Laboratory of Virology, Medical School, University of Crete, Heraklion, Greece, 71003 and 2 Department of Thoracic Medicine, University Hospital, Medical School, University of Crete, Heraklion, Greece, 71003.

Body: Chronic viral infections have been proposed to cause repetitive epithelial injury in Idiopathic Pulmonary Fibrosis (IPF), either initiating or exacerbating the disease. We recently demonstrated the incidence of HSV-1 in IPF patients. Furthermore, we showed that bronchoalveolar lavage fluid (BALF) cells were permissive to HSV-1 ex vivo, resulting in the upregulation of fibrotic growth factors and angiogenetic markers. MicroRNAs are small RNA molecules involved in the regulation of most cellular processes and they have been linked with several diseases. Altered expression patterns of anti-fibrotic and pro-fibrotic microRNAs have been previously associated with IPF. Our study focuses on the BALF of IPF patients and the expression patterns of several miRNAs previously implicated in fibrogenesis. We subsequently examined the changes in the miRNA expression patterns of BALF cells induced during the course of HSV-1 infection. Our results indicate that microRNA expression analyses in the cellular fraction of BALF is practical and highly informative. Among the miRNAs which were differentially regulated between IPF and control groups, the hypoxia inducible miR-210 was significantly upregulated whereas, miR-29c and miR-185 were significantly downregulated in IPF samples. Overall, we observed a downregulation of anti-fibrotic microRNAs similarly to what has been previously described from whole tissue analyses. HSV-1 infection of BAL cells from IPF patients resulted in the downregulation of miR-29b and Let-7d and the upregulation of miR-155 in several cases suggesting that HSV-1 infection may change the microRNA profile and enhance the profibrotic patterns of IPF BALF cells.