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Expression profiling of non-coding RNA in coronaviruses provides clues for virus RNA interference with the human immune system response

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Due to viral infection, the human immune system activates a complex response whose magnitude also depends on the interplay between the virus and the host's immune response regulation. The most dangerous effects induced by the SARS-CoV-2 infection are an exacerbated inflammatory response and an extensive lung pathology. Related to the damages caused by the inflammatory response, an important aspect that deserves to be investigated is the host cell response at a very early stage of the virus infection. An extensive analysis of transcriptome profiles of infected cells is the most effective analysis approach to investigate to what extent and which gene signalling pathways are directly involved at this stage. To elucidate these aspects can immediately bring to the identification of biomarkers of infection and targets for new and more effective therapeutic approaches.

It is noteworthy that non-coding RNAs (ncRNAs) are essential regulators of human gene expression. Recent studies have demonstrated that viruses belonging to the family of SARS-CoV-2 can regulate the expression of small (sRNA) and long non-coding RNAs (lncRNA) (Morales *et al.*, 2017; Liu and Ding, 2017). We have investigated the potential of the SARS-CoV-2 genome transcription to produce fragments of RNAs that can interfere with the host regulatory non-coding RNAs (small non-coding RNAs) by using a large scale bioinformatics analysis on data available in public repositories.

Comparing the SARS-CoV-2 genome sequence (NC_045512.2) with RNA-Seq data of human lung cancer cells infected with MERS-CoV [GEO ID GSE139516], mouse lung cells affected by SARS-CoV [GEO ID GSM907704] and bronchial lavages and Peripheral Blood Mononuclear Cells (PBMC) from COVID-19 patients (Xiong *et al.*, 2020) we discovered that small fragments of ncRNAs from SARS-CoV-2 might interfere with the activity of endogenous miRNAs that target genes involved in the inflammatory response, in particular with the allergic asthmatic reaction (IL4-IL13 signalling pathway).

The analysis was carried out with a bioinformatic pipeline developed using Python, BASH and R, and the software BLAST, STAR and mirdeep2 for the comparative analyses.

These preliminary results open the way for more effective treatment of COVID-19 patients and defence from future coronavirus pandemics. For further information: http://bioinformatics.ba.itb.cnr.it/CoV-ncRNASig

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