Coronavirus Diagnosis: Time for Unravelling the Secrets and Science Without Boundaries

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Aim and background

Nowadays, world is coping with a novel Coronavirus infection (Covid-19) as one of the most life-threatening and highly contagious viral diseases. Due to lack of data about immune-pathogenicity of Covid-19, recent anti-viral therapeutics have not been efficacious for all patients, yet. The widespread pandemic of Covid-19 challenge, will be more problematic when they are accompanied with long time needed for vaccine production, and overlap in diagnosis of clinical manifestations with other members of this viral family.

Hence, medical sciences progress toward more updated genetic and bioinformatics protocols in clinical trials. These protocols have facilitated more accurate prognosis and early diagnosis, eventuating to accurate immunotherapeutic purposes with less mortality and morbidity rate.

Thereafter, microRNAs (miRNAs) have been taken into account. miRNAs are small conserved non-coding single-stranded endogenous RNA (19~23 nucleotides). miRNAs exert their role through degradation or inhibition of the target mRNA translation by interaction with the 3′ untranslated region (3′UTR) of target mRNAs.

Host miRNAs can also bind to viral RNA and regulate alteration of viral pathogenesis. Viral RNA can also mediate alterations in cellular miRNA expression, leading to downstream changes in the host transcriptome.

Ultimately, a myriad of cell processes as: proliferation, post-translational gene expression, determination of the clinical prognosis of diverse subtypes, ectopic expression in diagnosis, tumour initiation or progression, viral lifecycle, evading from host immunity and targeted therapy have been regulated by host and virus-derive miRNAs. Alterations in serum levels of host miRNA and their target genes in pathologic microenvironment, introduces miRNA implementation as a logical approach for infectious diseases diagnosis and activation of antiviral agents. Accordingly, miRNA-targeted clinical outcomes of Covid-19 infection have been highly recommended for this viral catastrophic disease.

Along with substantial progresses in bioinformatics, new computing softwares are loaded for prediction of viral target genes for host miRNAs and prevent from frequent false predictions. Therefore, identification of genes targeted by the miRNAs, are first stage and their experimental validation is the end stage.

Totally, in this article (which is a part of a large-scale RNA sequencing study), authors firstly aim to review an updated molecular overview of miRNA application during Covid-19 infection. Secondly, they try to depict pros and cons of existed softwares for target gene prediction and introduce the most practical one. Later, they mixed bioinformatics and genetic data and suggest mentioned miRNAs as clinical application for Covid-19 infection.

Results

Several studies suggest that viral miR-MD2-5p and miR-MR147-3p, chiefly bind to the 3′UTR of CHAC1 and RAD9A genes. These encoded miRNAs suppress apoptosis, subvert host defence and lead to more viral spread. Additionally, viral miR-MR385-3p mainly bind to 5′UTR of TGFBR3, result in Th1 differentiation. Host hsamiR- 4661-3p was predicted to bind at the potential 3′UTR of the S gene transcript to repress expression of S gene.

Among predicting computational web-based softwares, miRTarget is designated to search both for predictive host miRNAs, sequence of targeted viral genome in the body fluids, inter-species studies and various cell lines. This software is available at: http://www.mirdb.org/ and considered as more efficient than other ones due to lessoning the sub-optimal performance and erroneous predictions. Mentioned software analyses thousands of miRNA-target interactions (MTIs) from a lot of high-throughput experimental studies. miRTarget contains 96 features to functionally predict all human miRNA targets. Interestingly, this software conducts custom prediction for new sequences of miRNAs and targeted genes that they are not previously studied. Another considerable advantages is that miRTarget is user-friendly due to limiting the search according to interested cell lines for researchers by its new web interface. All in all, these are not considered in previous softwares. One of disadvantages related to miRTarget is that we cannot search for miRNAs according to the diseases or signalling pathways. Apparently, this software, still serves as more comprehensively annotated and experimentally validated MTIs databases in the field of miRNA related research.

In this study, firstly the sequence of envelope protein gene (gene code: 43740570) and orf1a polyprotein; orf1ab polyprotein (gene code: 43740578) related to Covid-19 were extracted from NCBI website by authors. Results of data extraction showed that human hsa-miRNA-4288 with Score 98 and has-miRNA-451b with Score 97 (also a tumour suppressor gene) can sequentially target the polyprotein and membrane protein Covid-19 fragment, respectively. Two mentioned miRNAs are most likely to functionally bind to the Covid-19 virus genome. Given that these microRNAs can naturally target many genes in the body, their usage in diagnosis or therapy must be tissue-specific and highly controlled. According to high rate of Covid-19 transmission, tumour suppressive nature of miR451b and tumour stimulatory properties of miRNA4288, the need to use diagnostic, prognostic and therapeutic applications microRNAs should be justified by in vitro researches superior to clinical trials. Haematological malignant, transplanted, immunocompromised and immune-deficient persons are considered as high risk groups since they majorly should postpone their consecutive pharmacologic process. We propose to conduct cellular researches to investigate ex vivo application of this miRNA on the Covid-19 genome.

Conclusion

Although health coordinators are doing meticulously efforts for eradication of Covid-19, inaccurate/late diagnosis, insufficient level of hygiene, complying with quarantine regulations, and high recurrences all impose a burden of extortionate socio-medical expenditures on health system with increased possibility of chronic nosocomial infections until complete recuperation.

Inaccurate diagnosis and subsequently inefficient treatments, would be direct consequence of immune evasion of the virus, repressed apoptosis and abnormal activation of host immunity which are influenced by virus-encoded and host-derived miRNAs. Notably, their stability, being low-cost, reliability, repeatability, being able to differentiate between SARS-CoV-2 with other human coronaviruses, clarify early stages and improve accuracy of detection rate, provide promising insight and rationality from miRNA perspective into accreditation of diagnosis and clinical outcomes.

From bioinformatics aspect, not only highly-trained experts should be recruited for identification of relevant targeted miRNA and predicted genes, but they also could speed up miRNAs researches in biomedical sciences. To achieve these, further investigations, and integrated collaboration between laboratory scientists, medical virologists, immunologists, bioinformatics and infectious diseases specialists are needed, definitely.

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