Specific immune signatures of T cells as biomarkers of the post-COVID Syndrome and predictors of long-term health dysfunctions and possible therapeutic interventions.

The COVID-19 global pandemic had caused more than 626 million cases and 6.56 million deaths till October 2022, devastating social life, health and economics. The anti-COVID vaccines significantly decreased the number of severe cases and deaths, however mild infections are still quite often (also due to new virus variants). In Poland, with limited number of vaccinations, the predictions of SARS-CoV-2 infections, even if milder, are still high. Importantly, many COVID convalescents who recovered from infection, still experience severe symptoms that last even longer than 3 months. Recently, WHO defined criteria for post-COVID Syndrome and presented a list of symptoms, which include respiratory and circulatory problems, chronic fatigue, neurological symptoms, such as taste and smell problems, cognitive dysfunctions ("brain fog"), depression, metabolic disorders as well as blood clotting and thrombotic complications. All those symptoms can severely affect health and life and can influence future medical care. The cause of the post-COVID Syndrome is still not clear, however broad-spectrum of clinical manifestations associated with the involvement of multiple organs indicates a systemic illness. Understanding mechanisms, identification of prognostic and diagnostic markers, also to predict the possible severe health problems to implement adequate treatment, is absolutely critical and urgent for the future perspective of the post-COVID era.

Many studies, including ours showed that the post-COVID-related disturbances can appear not only after severe but also mild SARS-CoV-2 infection. Especially, the immune T cells dynamic changes, neurological symptoms and chronic fatigue, do not correlate with the severity of disease. We have found that immune deregulation such as T cells dysfunction and polarization towards exhaustion/senescence state, immune cells cytotoxicity, dysfunction of Treg cells, deregulated autoimmunity and others, have been observed in COVID convalescents. This can severely affect activation of the immune system, including response to future SARS-CoV-2 infections or vaccines Altogether it indicates that the immune system might be one of major drivers of the post-COVID long-term health problems, even if we still do not know all of the immune changes and their consequences.

Our already published data, together with preliminary results, led us to hypothesize that the specific immune signatures might be related to different symptoms of the post-COVID Syndrome, appearing after either mild or severe SARS-CoV-2 infection. This might be a potential biomarker of the post-COVID Syndrome, but also can serve as predictor of long-term post-COVID health dysfunctions, which seem to be related or dependent on the immune system dysfunction.

Realization of this translational project allows to address this urgent need and expand knowledge about the role of immune T cells deregulation and correlation with long-term health dysfunctions in post-COVID patients. Translational aspect will identify and verify potent biomarkers of post-COVID health dysfunctions. Finally, obtained data might lead to development of possible implementation into diagnostics/health care.

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