Ruprecht-Karls-Universität Heidelberg
Medizinische Fakultät Mannheim
Dissertations-Kurzfassung

YKL-40 as a biomarker for long-term changes in innate immunity after COVID-19 onset

Autor: Youjing Sheng
Institut / Klinik: Institut für Transfusionsmedizin und Immunologie
Doktormutter: Prof. Dr. J. Kzhyshkowska

In the complex landscape of post-COVID-19 research, a particular area of interest is the study of individuals who have recovered from the virus, known as COVID-19 convalescents. Changes in trained innate immunity, especially within the monocyte-macrophage system, play a crucial role in the convalescent period following virus infection. As a differentiation and activation marker of macrophages, YKL-40 can be involved in innate immune reactions during virus infection. YKL-40 has been identified as a biomarker for the severity of COVID-19 in the acute infection period. In this study, we explore the potential biomarker role of YKL-40 in monocyte-differentiated macrophages from COVID-19 convalescent individuals. 39 COVID-19 convalescent plasma donors and 36 healthy plasma donors were included in the study as part of the CORE project. The donation at time point 1 (T1) occurred 44-447 days after COVID-19 diagnosis, donation at time point 2 (T2) was conducted 21-60 days after T1, followed by a third donation (T3) 25-62 days after T2. Donors' baseline characteristics, including COVID-19 symptoms, were documented through a questionnaire. For the study, CD14+ selection of monocytes has been performed, and monocytes were differentiated towards homeostatic M(NS), inflammatory M(IFN-γ), and healing M(IL4) macrophages for 2 days. Challenge with LPS has been applied after 24 h of cultivation for next 24 hours. Expression of IL-1β, IL-1ra, IL-10 and YKL-40 was analyzed by RT-PCR. Compared to healthy individuals, a statistically significantly higher expression of YKL-40 was found in M(NS) (T1), M(NS)+LPS (T1), M(IL4) (T1). YKL-40 expression was further analyzed in monocyte-derived macrophages obtained at T2 and T3. The statistically significant higher expression of YKL-40 in COVID-19 convalescent donors was found in M(NS) (T2) and M(IL4)+LPS (T3). Correlation of YKL-40 expression level with clinical parameters of acute and post/long-COVID was further analyzed. A statistically significant negative correlation was found between the expression of YKL-40 and the total amount of acute symptoms in M(NS) (T1, T2). To explore the correlation between YKL-40 expression and specific symptoms, all symptoms were classified into respiratory, systemic and neurology symptoms. Donors who reported the presence of respiratory symptoms showed statistically lower expression of YKL-40 in M(NS) (T2, T3) and in M(IFNγ) (T3). The negative correlation with YKL-40 expression was also evident with the amount of respiratory symptoms in M(NS) (T1), M(NS)+LPS (T1), M(IFNγ) (T1), M(IFNγ)+LPS (T3), and M(IL4)+LPS (T2). Donors who reported the presence of the systemic symptoms showed statistically lower expression of YKL-40 in M(NS) (T2) and M(IL4) (T3), although the YKL-40 expression had no statistical significant correlation with the amount of systemic symptoms. For neurological symptoms, no statistically significant differences in the YKL-40 expression was found between donors who reported the presence or absence of the symptoms. The statistically significant negative correlation was found with neurological symptoms in M(NS) (T1, T3), M(IFNγ) (T3), and M(IFNγ)+LPS(T1, T2, T3). As post/long COVID is consider as a public health challenge, correlation with YKL-40 with post/long COVID was analyzed. Donors who reported the post/long COVID symptoms showed a statistically significantly higher expression of YKL-40 in M(NS) (T3). Among all donors with post/long COVID symptoms, people reporting the persistent difficulty in concentration showed statistically significant lower expression of YKL-40 in M(NS)+LPS (T1). In summary, our study reveals a long-term change in YKL-40 expression in monocyte-derived macrophages in COVID-19 convalescent individuals, where the strongest correlation is detected for neurological symptoms. Given the importance of monocytes/macrophages system, YKL-40 may become a potential marker for the long-term dysregulation of the innate immune system.