Monocyte migration profiles define disease severity in acute COVID-19 and unique features of long COVID

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Immune dysfunction is a key factor in acute COVID-19 pathophysiology, with monocyte abnormalities sustained during convalescence for at least 9 months following hospital discharge and corresponding to specific long COVID symptoms https://bit.ly/3xEIY0H

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Abstract

Background COVID-19 is associated with a dysregulated immune response but it is unclear how immune dysfunction contributes to the chronic morbidity persisting in many COVID-19 patients during convalescence (long COVID).

Methods We assessed phenotypical and functional changes of monocytes in COVID-19 patients during hospitalisation and up to 9 months of convalescence following COVID-19, respiratory syncytial virus or influenza A. Patients with progressive fibrosing interstitial lung disease were included as a positive control for severe, ongoing lung injury.

Results Monocyte alterations in acute COVID-19 patients included aberrant expression of leukocyte migration molecules, continuing into convalescence (n=142) and corresponding with specific symptoms of long COVID. Long COVID patients with unresolved lung injury, indicated by sustained shortness of breath and abnormal chest radiology, were defined by high monocyte expression of C-X-C motif chemokine receptor 6 (CXCR6) ($p<0.0001$) and adhesion molecule P-selectin glycoprotein ligand 1 ($p<0.01$), alongside preferential migration of monocytes towards the CXCR6 ligand C-X-C motif

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chemokine ligand 16 (CXCL16) ($p<0.05$), which is abundantly expressed in the lung. Monocyte CXCR6 and lung CXCL16 were heightened in patients with progressive fibrosing interstitial lung disease ($p<0.001$), confirming a role for the CXCR6–CXCL16 axis in ongoing lung injury. Conversely, monocytes from long COVID patients with ongoing fatigue exhibited a sustained reduction of the prostaglandin-generating enzyme cyclooxygenase 2 ($p<0.01$) and CXCR2 expression ($p<0.05$). These monocyte changes were not present in respiratory syncytial virus or influenza A convalescence.

Conclusions Our data define unique monocyte signatures that define subgroups of long COVID patients, indicating a key role for monocyte migration in COVID-19 pathophysiology. Targeting these pathways may provide novel therapeutic opportunities in COVID-19 patients with persistent morbidity.