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BIOMARKERS FOR GLIOMA BRAIN TUMOUR FOUND IN PERIPHERAL BLOOD

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Multipurpose: Besides indicating whether the tumour is low- or high-grade, the macrophages can also indicate the chances of survival of patients with glioma, says Aurobind Vidyarthi

Researchers have found potential gene biomarkers that can be used for prognosis and early diagnosis of the most aggressive form of primary brain tumour called glioblastoma. The biomarkers can help in knowing if the tumour is at an initial stage (low-grade) or advanced stage (high-grade).

The multi-institutional research work carried out by a team led by Javed N. Agrewala from Institute of Microbial Technology (CSIR-IMTECH), Chandigarh, now at IIT Ropar, looked at immune cells called macrophages in the tumour microenvironment to understand their role in suppressing or boosting the immune system to keep the tumour under check. The role of certain macrophages in suppressing the immune system leading to progression of cancers such as breast, prostate, bladder and cervical cancers is already known.

Based on patient tissue samples the researchers identified two macrophages — M1 and M2 — that were associated with the tumour. These were identified using hallmark gene markers (CCL3 gene for M1 macrophage and CD163 for M2 macrophage). The M1 macrophage is protective for glioma while the M2 macrophage is not. The M2 macrophage control the immune response and intimately interacts with the tumour and supports tumour progression.

“We observed that as the glioma progresses from low-grade to high-grade, the amount of M1 macrophages reduced and the amount of M2 macrophages increased,” says Prof. Agrewala. “Thus the ratio of M2 macrophage marker CD163 versus M1 macrophage marker CCL3 can ascertain the glioma progression.”

In the low-grade glioma, the ratio of M2/M1 macrophages (or CD163/CCL3) is less while it is high in the case of high-grade glioma tumour.

“Besides indicating whether the tumour is low- or high-grade, the macrophages can also indicate the chances of survival of patients with glioma,” says Aurobind Vidyarthi from CSIR-IMTECH, the first author of a paper published in *Cancer Immunology, Immunotherapy.* He is currently a post-doc at Yale University, New Haven, U.S. “In low-grade glioma patients we see both M1 and M2 macrophages. But if there are more M2 macrophages (as indicated by the gene marker expression) than M1 macrophages, the survival is less. Likewise if there are more M1 macrophages then the patient has better chances of survival.”

Most studies have looked at only the local immune response in the tumour region. But these researchers went a step ahead and looked for macrophage phenotypes and different T cells in peripheral blood samples collected from glioma patients.

“Interestingly, compared with healthy individuals, there was elevated level of M2 macrophages in peripheral blood too. This indicates that the influence of glioma is so prominent that M2 macrophages can be found in the blood,” says Dr. Vidyarthi. Besides M2 macrophages, the researchers also found in the blood PD-1 expressing CD4 T cells. During chronic infection and tumour, the T cells become exhausted. “So instead of promoting, the exhausted CD4 T cells end

up suppressing the immune system at the systemic level. Consequently, both CD4 T cells and M2 macrophages suppress the immune system at the systemic level," says Prof. Agrewala. "Thus the gene biomarkers in blood samples can be used for early diagnosis and prognosis of the gliomas. We need to carry out studies on more samples before being certain."

Researchers from Postgraduate Institute of Medical Education and Research, Chandigarh were also a part of the study.

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