Cytokine and Chemokine Profiling of the Cerebrospinal Fluid of Melanoma Patients with Brain Metastases Predicts Clinical Outcomes

**Introduction:** A method of profiling melanoma patients with brain metastases was developed by measuring cytokine and chemokine values in cerebral spinal fluid (CSF) from 22 melanoma patients with brain metastases. Traditionally, the cerebrospinal fluid (CSF) is thought to merely provide a homeostatic environment for the normal function of the brain. However, recent data have emerged to challenge this view. Not only does the CSF bath the brain to provide homeostatic support but also provide a conduit for signaling during both neurodevelopment and the maintenance of primary and metastatic brain tumors. Therefore, given the potential importance of cytokines and chemokines in modulating the function of metastatic melanoma of the brain, we postulated that these immunomodulatory proteins could be detected in the CSF and may shed light on the biology of melanoma brain metastasis. Using assays for cytokines and chemokines that are known to be associated with melanomas, we were able to detect differences in the levels of these immunomodulatory proteins in the CSF between patients with melanoma brain metastasis and non-disease controls. Further, statistical analysis of the expression profiles of these proteins within each CSF sample enabled us to segregate these melanoma patients into 5 major clusters (Figure 1a), which correlated with different clinical outcomes. Importantly, the identity of these clusters required the inclusion of multiple cytokines and chemokines in the analysis while individual cytokines and chemokines were insufficient for such grouping of patients. Figure 2 shows the comparison of CXCL10, IL1β, IL4, IL5, IL10, and IL13 reveals differences between non-disease and melanoma CSF samples. In the melanoma cohort, there is a statistically significant decrease in IL1β, IL4, IL5, IL10, and IL13, while CXCL10 chemokine is elevated. Finally, Figure 3 shows that Cluster 1 and 5 exhibit similarities in specific cytokine and chemokine levels and patient outcomes. These patients have the shortest overall survival and time from diagnosis to brain metastasis; they exhibit elevated CCL2, CCL3 and CXCL10 while IL1β, IL12, TNFα, and IFN-γ were low. Our data suggest that the relationship between the immune system and melanoma is an important factor in determining the outcome and that CSF cytokines and chemokines may serve as prognostic and/or predictive biomarkers to monitor patients with melanoma brain metastasis.

**Figure 1**

[Image of heat map showing cytokine and chemokine expression levels in different clusters of melanoma patients' cerebrospinal fluid, with clusters 1 and 5 highlighted for comparison.]
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Figure 2

![Graphs showing cytokine and chemokine levels in normal and melanoma cerebrospinal fluid.]

Figure 3

![Heatmap showing cytokine and chemokine expression levels in different clusters.]

References:


