

Abstracts

**TMIC-18. TUMOR-ASSOCIATED MICROGLIA/MACROPHAGES ARE ASSOCIATED WITH POOR PROGNOSIS IN HIGH-GRADE GLIOMAS AND CONTRIBUTE TO THE GLIOBLASTOMA STEM CELL-LIKE NICHES**

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**BACKGROUND:** In glioblastomas tumor-associated microglia/macrophages (TAMs) constitute up to 30% of the tumor. TAMs can interact with glioblastoma stem-like cells (GSC) and favor progression by acquiring a pro-tumorigenic M2 phenotype. The aims of this study were to investigate the prognostic impact of TAMs in gliomas and the physical interaction between TAMs and GSC in situ in glioblastomas. **METHODS:** Using automated quantitative double immunofluorescence 242 patient samples were stained with

anti-IBA-1 and anti-CD204 to detect TAMs and M2 TAMs, respectively. Area fractions (AF) of IBA-1 and CD204 in total tissue and of CD204 within the IBA-1+ area were obtained by software classifiers (i.e. IBA-1(total), CD204(total), and CD204(IBA-1)). The interplay between TAMs and GSC was examined on 10 glioblastomas with double immunohistochemistry using IBA-1 and stem cell markers. **RESULTS:** Our results showed that IBA-1(total), CD204(total) and CD204(IBA-1) increased with grade ( $p < 0.0001$ ). In univariate analyses, high CD204(total) (HR 3.96 95%CI 1.57-10.03,  $p = 0.004$ ) and CD204(IBA-1) (HR 2.86, 95%CI 1.17-6.97,  $p = 0.021$ ) were associated with shorter survival in grade III tumors. Similar was found for CD204(total) (HR 1.38 95%CI 1.02-1.85,  $p = 0.035$ ) in grade IV tumors. In multivariate analyses, high CD204(total) was associated with poorer survival (HR 3.18, 95%CI 1.03-9.81,  $p = 0.045$ ) in grade III tumors. In grade IV tumors CD204(total) (HR 1.70, 95%CI 1.24-2.33,  $p = 0.001$ ) had independent prognostic value, and similar tendency was observed for CD204(IBA-1) (HR 1.19, 95%CI 0.87-1.63,  $p = 0.27$ ). IBA-1(total) was insignificant regarding prognosis in all grades. In glioblastomas TAMs and GCS, especially CD133+ and podoplanin+ cells, accumulated around vessels and necroses. Further, the density of GSC tended to be higher around TAMs in these areas indicating an interaction between the two populations. **CONCLUSIONS:** Our results suggest that TAMs are important in the tumor microenvironment and contribute to glioma stemness and aggressiveness possibly explained by their M2 polarization which has prognostic impact in high-grade gliomas.