The miroenvironment of high-grade gliomas can strongly support tumor expansion. It is well established that tumor-associated myeloid cells (TAM) largely contribute to the glioma-mass. Furthermore, it is suspected that TAM have profound intratumoral heterogeneity. However, the composition of gliomas with individual TAM-subsets and the respective pathological traits of these TAM-subpopulations remain largely unknown. Other cell-types of the brain tumor parenchyma, like vascular pericytes are potentially required during neo-angiogenesis, which is essential for the growth of solid tumors, but how pericytes are generated e.g. during neoplastic vascularization and why they cannot maintain a functional blood-brain-barrier (BBB) is not fully explored.

Concerted action of cells composing the neurovascular unit is essential for brain homeostasis[1]. Pericytes are a vital part of the neurovascular unit and regulate the architecture, permeability and tone of brain microvessels[2]. Consequently, pericytes control vascular plasticity[3,4] and pericyte-dysfunction contributes to a range of neuropathological diseases[5]. However, despite these many important roles for pericytes in health and disease the source for new pericyte in the adult brain is unknown[2]. It was established that pericytes share many important biological features with mesenchymal stem cells (MSC) and it was proposed that MSC may generate pericytes e.g. under distinct disease conditions. In a 2-photon in vivo imaging study we observed that traced pericytes in gliomas acquire an aberrant morphology, which can relate to reduced blood-brain barrier function in gliomas. We found that newly generated pericytes in GBM have an abnormal cell-morphology and speculate that this can reflect their defective physiological properties in GBM. Hence, investigating the molecular pathways that promote pericyte dysfunction can indicate a way to foster vessel normalization and the delivery of chemotherapeutics

We and others have shown throughout the last decade that the brain tumour parenchyma, and in particular TAM, largely contribute to GBM pathology[6-10]. A range of independent studies confirmed that TAM-directed adjuvant treatments mediate therapeutic effects, but there is currently no consensus on the specific molecular targets for treatment[6,8,11,12]. Furthermore, there is no coherent information available how GBM blunt immune-responses and thereby e.g. pose a threat for immunotherapy. One recent advance in research on myeloid contribution to GBM was to acknowledge the differences in developmental origin and biological activity of peripheral macrophages and microglia[13], which are commonly summarized as TAM. Consequentially it is now the time to also address the inherent heterogeneity in the microglial component of TAM[14].

Currently, we investigate the glioblastoma microenvironment with transgenic lineage-tracing models, intravital imaging, single-cell transcriptomics, immunofluorescence analysis as well as histopathology. Thereby we have already characterized a previously unacknowledged population of tumor-associated cells with a myeloid-like expression profile (TAMEP) that transiently appeared during glioblastoma growth. Although TAMEP have similarity with microglia and macrophages they are not of myeloid origin, but derive from CNS-resident, progenitors. Abrogation of this progenitor cell-population, drastically reduced glioblastoma-vascularization and -size. TAMEP were identified in human brain tumors indicating TAMEP and their progenitors as new targets for glioblastoma therapy.

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