Characterization of intratumoral myeloid cell-mediated inhibition of anti-tumor immunity

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Background and central scientific questions or problem:

Multiple tumor cell intrinsic and T cell-centric mechanisms of immune evasion and resistance to immune checkpoint blockade (ICB) have been described. ICB resistant tumors and tumors with insufficient anti-tumor effector cell activity are often infiltrated by large numbers of mononuclear and polymorphonuclear myeloid cells, which contribute to the failure of ICB. In preliminary work, we have identified two main mechanisms, by which tumor-associated neutrophils (TAN) limit the intratumoral activity of T cells and NK cells. First, we found that TAN, once activated within the tumor microenvironment (TME), produce neutrophil extracellular traps (NETs), induce partial epithelial-mesenchymal transition in tumor cells, and physically shield tumor cells from cytolytic NK and T cells. Secondly, we identified intratumoral areas of direct TAN-T cell interaction in which TAN downregulated effector function of T cells once these were in close proximity to the neutrophils. Until now, the exact functional and phenotypic characteristics of these intratumoral tumor-promoting TAN remained elusive. It is the aim of this proposal to identify the main cell biological and key tumor-promoting programs in these TAN populations as a prerequisite for their therapeutic targeting.

Technical and conceptual approach to address the research question

The above-mentioned aim will be facilitated by recent technical developments in single cell RNASeq analysis of human neutrophils. We have established BD-Rhapsody-based scRNASeq of intratumoral human neutrophils and will use this technology, along with publicly available data sets, to characterize the major TAN signatures in patients with head and neck cancer. Multiplex antibody panels and tailored spatial transcriptomics panels of TAN, T and NK markers will be designed to decode the intratumoral spatial arrangement of TAN subsets and identify potential functional molecules in those subsets that induce intratumoral T cell suppression and EMT-mediated immune evasion. In vitro models in the lab are available to validate identified candidates via gene editing and with specific blocking experiments. This approach will allow us to identify potential mechanisms and targets to interfere with intratumoral TAN-mediated inhibition of T and NK cells.

Scientific expertise within the group: innate immunity in tumor host-interaction, tumor-associated myeloid cells, clinical and pre-clinical models of immunotherapy, multi-omics tissue analysis and digital pathology, neutrophil biology, 3-D models of tumor-immune interaction.

Website:
https://hno.uk-essen.de/forschung/ag-brandau/

Introductory video on myeloid cells in cancer:
https://youtu.be/NjlKTSJgaXE

Selected publications:

https://www.nature.com/articles/s41423-025-01283-w

https://www.science.org/doi/10.1126/sciimmunol.aaw9159?url_ver=Z39.88-2003&rfr_id=ori:rid:crossref.org&rfr_dat=cr_pub%20%200pubmed

https://www.biorxiv.org/content/10.64898/2026.01.20.700440v1