Abstract for the 9th German Mass Cytometry User Forum

Characterizing the Drivers of Gastroesophageal Adenocarcinoma Development using the B6.IL-1beta$^{(EBV)tcw}$ mouse model

Martin Borgmann[1,2,3], Ira Godbole[1,3], Celine Ritzkowski[1], Julia Strangmann[1], Konrad Kurowski[4], Bertram Bengsch[1,2,5,6], Michael Quante[1,2,6]

[1] Department of Internal Medicine II, University Hospital Freiburg, University of Freiburg, 79106 Freiburg, Germany
[2] Spemann Graduate School of Biology and Medicine (SGBM), University of Freiburg, Freiburg, Germany
[3] Faculty of Biology, University of Freiburg, Freiburg, Germany
[4] Universitätsklinikum Freiburg (UKF), Institut für Klinische Pathologie, Breisacher Str. 115a, 79106 Freiburg
[5] Signaling Research Centers BIOSS and CIBSS, Germany
[6] German Cancer Consortium (DKTK), Partner Site Freiburg, Germany

Gastroesophageal adenocarcinoma (GEAC) is a malignancy of the distal esophagus at the squamocolumnar junction. Most GEAC patients have a history of Barret's esophagus (BE), a metaplastic adaptation to chronic reflux. BE is initially caused by inflammation and, in rare cases, can progress over a dysplastic intermediate state to GEAC. Besides genetic alterations, changes in the microenvironment are key drivers in enabling disease progression. To study these, we use B6.IL-1beta$^{(EBV)tcw}$ mice, which is a well-characterized model of GEAC, with dysplastic lesions developing at the squamocolumnar junction of the gastric cardia. This model offers unique opportunities to study dynamic interactions between the immune system, stroma, and epithelial transitions over time. Our goal is to identify factors that drive progression from BE to GEAC to enhance patient care by tailoring preventive measures. A total of 198 formalin-fixed, paraffin-embedded (FFPE) gastric cardia tissues from B6.IL-1beta$^{(EBV)tcw}$ mice aged 4 to 12 months, covering all disease stages and various experimental conditions (aggravating and ameliorating), were combined into tissue microarrays. Imaging mass cytometry enabled detailed, spatially resolved proteomic profiling of cell types and activation states. For image pre-processing we followed the Bodenmiller-Steinbock pipeline, and advanced single-cell and spatial analyses were performed using R and Python. In standard PL2 mice, the metaplastic marker TFF2 declined with age and was further reduced by NSAID treatment. Stathmin 1, a microtubule destabilizer linked to cancer progression, also decreased. Markers of immune infiltration (CD45), regulatory T cells (Foxp3), and mesenchymal cells (Vimentin) increased with age. E-cadherin expression declined, indicating epithelial disruption. Fibronectin was elevated in high-fat diet mice, coinciding with earlier biomarker shifts. INOS remained consistently higher across ages, while pYAP expression decreased over time. These data highlight age- and diet-related changes in immune and stromal components within the gastric cardia microenvironment, alongside reductions in metaplastic (TFF2) and cancer-associated markers (Stathmin1), particularly under NSAID treatment. Together, these findings reflect progressive remodeling that underpins GEAC development in the PL2 model.