MALDI MSI analysis enables a spatially resolved characterization of the proteome and metabolome in radiotherapy treated HNSCC

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Motivation

Head and neck squamous cell carcinoma (HNSCC) is known as a heterogeneous disease, mainly separated into two subgroups – human papilloma virus (HPV)-driven tumors and HPV-negative tumors that are caused by alcohol abuse and heavy smoking. There is a distinct inter-tumor and intra-tumor heterogeneity of both tumor entities, that affect therapy resistance of tumor cell populations as well as targeted therapies with drugs. As a consequence, there is a great need for an in-depth analysis of the molecular variances between HPV positive (HPV+) and HPV negative (HPV-) tumors. For this purpose, we characterized a prospective cohort of HNSCC patients (n = 65) treated with surgery and/or radiochemotherapy with known HPV status for proteome and metabolome changes by matrix-assisted laser desorption ionization time of flight mass spectrometry imaging (MALDI TOF MSI). The resulting profiles of altered mass species were analyzed for their association with the HPV status and differences in heterogeneity between HPV positive and negative tumors.

For further integration of different omics levels, a proof-of-principle study has been performed on three HNSCC cases by combining MALDI-MSI analysis (metabolic changes) and next generation sequencing (genomic and transcriptomic changes) on the same tissue section. The successful combination of the different omics approaches allowed a comprehensive characterization of heterogeneity in HNSCC and thereby contributes to an improved identification of prognostic biomarkers and druggable targets.

Research question

Can specific molecular patterns be linked to the HPV status of HNSCC?

Multilevel analysis of HNSCC

28 metabolite signature predicts HPV status

- Which pathways are relevant for HPV+ and HPV- tumors?
- Which impact has the HPV status on the clinical outcome?
- Can therapy success be predicted by metabolic or proteomic signatures?
- How beneficial are HPV signature-based heterogeneity analyses?
- What degree of consistence do the different molecular levels show?