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Establishment of ex vivo tumor tissue slice culture from HNSCC xenografts for biomarker discovery

The heterogeneity of locally advanced head and neck squamous cell carcinoma (HNSCC) impacts the response to radio(chemo)therapy, highlighting the need for personalized biomarker-based treatment strategies. Tumor slice culture (TSC) represents an ex vivo model bridging the gap between in vivo and conventional in vitro models, providing an opportunity to reduce animal numbers in experiments while retaining relevance for translational research questions. Here, we establish TSC from four HNSCC cell lines with varying radiosensitivities to implement a robust, reproducible ex vivo assay for biomarker discovery reflecting the heterogeneous response of patients to radiotherapy.

Athymic nude mice were xenotransplanted with five HNSCC tumor models of varying radiosensitivity (SAS –resistant, Cal33, FaDu –intermediate, UT-SCC-14 –sensitive). Tumors were excised and thin vital tissue slices were cut using a Vibratome. Different cutting parameters were tested. The tissue slices were irradiated with 0 –6 Gy X-ray, and immunofluorescence stainings were performed according to standardized protocols. The value of the assay for radiobiological experiments was demonstrated by the analysis of γH2AX foci (https://github.com/jo-mueller/FociCounter), indicative of radiation-induced DNA damage.

Appropriate criteria for tumor induction and harvesting were determined. Cutting parameters considering the model-dependent differences in tumor structure were successfully established. The heterogeneity of the different tumor models should be considered when good-quality slices are to be obtained.The PrestoBlue viability assay showed metabolic activity in the slices over 5-7 days. The preliminary analysis of immunofluorescence images showed a dose-dependent increase of γH2AX foci. Further validation of the assay in the preclinical radiobiology setting and its application for clinical translation will be discussed. The relationship between radiation sensitivity to DNA damage processing and tumor microenvironment heterogeneity will be explored in the future. Furthermore, this assay may be applied to patient samples from resections or biopsies, representing a promising approach to support future personalized radiotherapy concepts.

Research type

Translational research

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