Contribution ID: **198** Type: **poster preferred**

Radiation sensitivity markers in HNSCC

Thursday, 18 October 2012 16:52 (1 minute)

Besides surgery and chemotherapy, radiotherapy is one of the main treatment options of head and neck squamous cell carcinoma (HNSCC). Radiation resistance of some tumours causes local recurrences that go along with unfavourable prognosis. Therefore, the characterisation of the radiation response of tumour cells is a major issue for the development of personalised therapy strategies. The identification of biomarkers predicting radiation sensitivity of HNSCC would allow the development of personalised therapy approaches that spare patients unnecessary radiation exposures by adapting and optimising the applied doses during radiation therapy.

We identified cytogenetic markers (gains on chromosome bands 1q43 and 16q23-24) by CGH in a set of 117 HNSCC that correlated to a reduced loco-regional-progression-(LPR)-free survival after radiotherapy. Since the analysed tumours were exclusively treated by radiotherapy, it can be assumed that reduced LPR-free survival is caused by radioresistance of tumours that do not respond adequately to radiation therapy. Array CGH and FISH indicated 16q24.3 to be the region of interest on chromosome 16, which contains an interesting candidate gene, FancA. FancA is a member of the Fanconi Anaemia (FA)/BRCA pathway, a pathway disrupted in patients suffering from the disease FA. Interestingly, FA patients have a high risk in developing HNSCC which suggests a role of this pathway in HNSCC development. Quantitative RT-PCR confirmed increased FancA expression on RNA-level in tumours with gain on 16q24.3. In order to determine the effect of FancA on radiation sensitivity of cells, we stably transfected a cell line (OKF6/TERT1) with a FancA over-expressing vector and measured various endpoints like overall survival (by colony forming ability) and chromosomal aberrations (rate of dicentric chromosomes and translocations) after applying different doses of ɣ-radiation in comparison to non-transfected cells and vector control cells. The results suggest reduced radiation sensitivity in FancA over-expressing cells.

The findings of our study demonstrate that chromosomal gains on 1q and 16q may represent prognostic markers in HNSCC and that these alterations may explain to some extent the unfavourable prognosis of a subgroup of patients after radiotherapy, by affecting candidate genes like FancA.

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Session Classification: Poster Session 3

Track Classification: Modulation of Radiosensitivity