The Role of the Human Papillomavirus in Head and Neck Cancers: Cancer Stem Cell Diversity and Response to Radiation.

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Introduction

Cancer stem cells (CSCs) play a fundamental role in tumour progression, metastases and recurrence. These are the most treatment resistant of tumour cells, accelerating their replication and tumour repopulation in response to tumour depletion[1]. The human papillomavirus (HPV) has emerged as a discrete aetiology in head and neck cancers (HNC). They demonstrate consistently better responses to radiotherapy initiating several clinical trials to de-escalate treatment[2]. This study investigates the *in vitro* differences in CSC responses in head and neck cancers to radiation in terms of their HPV aetiology.

Method

Six HNC cell lines were investigated. UM-SCC-47, UPCI-SCC-090 and UPCI-SCC-154 are HPV+ and UM-SCC-1, UM-SCC-17a and UM-SCC-22a are HPV-. Cells were irradiated in T25 flasks with 4 Gy using a Varian 6 MV linac and a RS2000 irradiator at 160 kVp and 25 mA. Flasks were filled with medium, encased in a paraffin wax block and mounted on 7 cm of RW3 to provide full scatter conditions. Sham-irradiated flasks were used as controls. CSC proportions of cell populations were measured at 24, 48 and 72 hours, and again at 10 days post irradiation. CSCs were identified by putative cellular markers CD44 and aldehyde dehydrogenase (ALDH), using flow cytometry.

Results

Triplicate analysis of non-irradiated UM-SCC-47 cell cultures showed a mean CD44+/ALDH+ population to be 2.87%$\pm$0.219, 5-fold that of the UM-SCC-1 population which was 0.57%$\pm$0.077. UM-SCC-47 and UM-SCC-1 showed increased ALDH+/CD44+ proportions of population following 4 Gy irradiation. The proportional increase for UM-SCC-47 was 3 to 4 times the control within 72 hrs post irradiation. After 10 days these cultures no longer presented significant differences in CSC population against the control. UM-SCC-1 showed the most significant CSC increase 24 hrs post irradiation and a persisting elevation in CSCs 10 days after irradiation.

Conclusion

CSCs display significant heterogeneity between cell lines warranting investigation of the effect aetiology has on intrinsic population numbers and treatment responsiveness.

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