Inhibition of SphK1 reduces radiation-induced migration and enhances sensitivity to cetuximab treatment by affecting the EGFR / SphK1 crosstalk.

Abstract:
SphK1 is known to play a role in tumor progression, resistance to radiochemotherapy, and migration patterns. As the overall survival rates of squamous cell carcinoma of the head and neck (HNSCC) remain poor due to limitations in surgery and irradiation and chemotherapy resistance, SphK1 is an important enzyme to investigate. The purpose of this study was to elucidate the impact of SphK1 on irradiation efficacy of HNSCC in-vitro with emphasis on EGFR signaling. By immunohistochemical staining we found a positive correlation between EGFR and SphK1 expression in patient specimens. In colony formation assays irradiation sensitive cell lines showed a poor response to cetuximab, an EGFR inhibitor, and SKI-II, a SphK1 inhibitor, and vice versa. In irradiation sensitive cells an enhanced reduction of cell migration and survival was found upon simultaneous targeting of EGFR and SphK1. In the present study, we elucidated a linkage between the two signaling pathways with regard to the efficacy of cetuximab treatment and the impact on the migration behavior of tumor cells. We investigated the biological impact of inhibiting these pathways and examined the biochemical implications after different treatments. An
understanding of the processes involved could help to improve the treatment of patients with HNSCC.