

A Novel Therapeutic Approach for Peripheral Neural Sheath Tumors

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Neurofibromatosis 1 (NF1) is an autosomal dominant cancer predisposition syndrome that affects 1 in 3,000 individuals indiscriminately. It is primarily characterized by the growth of peripheral nerve sheath tumors (PNST) all over the body. A common PNST manifestation of NF1 is a plexiform neurofibroma (PN), and ~15% of PNs progress to malignant peripheral nerve sheath tumors (MPNSTs). To date, there are no effective therapies for MPNSTs, as tumor location complicates surgical resection, radiation therapy is last-line due to secondary malignancies, and there is no FDA-approved drug for MPNSTs. These challenges result in a dismal five-year survival rate of ~16%. Novel treatments to solve these issues are needed. Cold Atmospheric Plasma (CAP), a technology initially developed for space propulsion, has recently been investigated as a novel cancer therapy. It generates reactive oxygen and nitrogen-generating species, increasing oxidative stress within cancer cells leading to cell death. CAP has also demonstrated selectivity towards malignant cells. However, CAP has yet to be tested in any NF1-related context. Herein, the effect of CAP on NF1-related MPNSTs was investigated. NF1-mutated cell lines were found to be significantly more sensitive to CAP exposure in vitro compared to wild-type cell lines and demonstrated cell death in a dose-dependent manner. CAP also demonstrated in vivo efficacy for MPNST xenografted tumors, slowing tumor growth. This is the first application of CAP for NF1-related PNSTs and provides a preclinical basis for translating the novel therapeutic modality for the treatment of MPNSTs and other NF1-related tumors.