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Abstracts

MB-48. PEROXIREDOXIN 1 IS A POTENTIAL THERAPEUTIC TARGET IN GROUP-3 MEDULLOBLASTOMAS

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The poor prognosis of Group-3 medulloblastomas is associated with its resistance to conventional therapeutic strategy of radiation and chemotherapy. Thus, there is an urgent need to elucidate targets that render these tumors sensitive to conventional approaches. We identified Peroxiredoxin1 (PRDX1) as a candidate therapeutic target to radio-sensitize Group-3 medulloblastomas. We hypothesized that targeting PRDX1 in Group-3 medulloblastoma cells would induce oxidative stress and sensitize them to ionizing radiation. Accordingly, Group-3 medulloblastoma (D425-Med) cells treated with Adenanthin, a small molecule inhibitor of PRDX1, were hypersensitive to radiation when compared to controls. Similar results were observed when PRDX1 expression was down regulated using RNAi. Mechanistically, targeting PRDX1 resulted in an increase in reactive oxygen species, oxidative DNA damage as indicated by surrogate markers γ-H2A.X and 53BP1, and an induction of the apoptotic pathway when compared to controls. Athymic nude mice with flank tumors of D425-Med cells that received Adenanthin (10mg/kg body weight) presented decreased tumor growth and survived longer than the control group that received placebo. Ongoing experiments using orthotopic murine models of Group-3 medulloblastoma in which PRDX1 is targeted using RNAi or Adenanthin will help us further validate our hypothesis that PRDX1 is a potential therapeutic target in these tumors. Our preliminary data strongly suggests that PRDX1 is a potential therapeutic target that sensitizes Group-3 medulloblastomas to ionizing radiation. The results from these experiments will be presented in this meeting.