Contribution ID: **7** Type: **not specified**

# Activation of the p53 pathway in combination with photon or proton irradiation for the treatment of brain tumours

p53 is a critical tumour suppressor protein and its encoding gene, TP53, is the most frequently mutated gene in human cancer. Activating the p53 pathway is regarded as a plausible strategy to increase radiosensitivity of cancer cells and reduce carcinogenesis. One of the strategies is to inhibit the interaction of p53 with its negative regulator MDM2, which represents a promising clinical strategy to treat p53 wild-type tumours. Blocking the MDM2/X–p53 protein–protein interaction has been widely recognized as an attractive therapeutic strategy for the treatment of various cancers. p53 is a multifunctional transcription factor that can be activated by cellular stresses, such as hypoxia and DNA damage. Upon activation, p53 acts as a tumour suppressor and responds to cellular damage by mediating cellular responses such as cell proliferation, cell cycle arrest, DNA repair, metabolism, angiogenesis and apoptosis.

The influence of radiation on the p53 pathway, and in particular the differences between photon and proton irradiation, are not yet fully understood. The aim of this study is to investigate the impact of the MDM2 inhibitor drug, AMG 232, in combination with photon or proton irradiation in brain cancer cell lines. Both its anti-cancer and radiosensitizing effect will be investigated by assessing its functionality on a p53 wild type (wt) and p53 mutated (mut) cell line with the aid of various assays. Grade 4 brain tumour cell lines Glioblastoma Multiform (GB) and Medulloblastoma (MB) were selected for this study.

**Primary author:** MILES, Xanthene (iThemba LABS)

**Co-authors:** Dr HUNTER, Alistair (University of Cape Town); BOLCAEN, Julie (iThemba LABS)

**Presenter:** MILES, Xanthene (iThemba LABS)