with radiation and TMZ. We also confirmed the radiosensitizing effect of Cpd188 of GBLC28 cell which was originated from a patient with high level of STAT3 expression and unmethylated MGMT.

Conclusion: Targeting STAT3 using Cpd188 could be a viable therapeutic approach to improve the outcome of current standard therapy for glioblastoma patients having high p-STAT3 expression regardless of MGMT methylation status. Work supported by the grant (#R2013R1A1A2074531) from the Ministry of Science, ICT & Future Planning to In Ah Kim.

PO-0981
Activation of immune cells and enhanced efficacy of radiotherapy by anti-TIP1 antibodies in cancer D. Hallahan1, V. Kapoor2, D. Thota1, H. Yan1 1Washington University School of Medicine, Radiation Oncology, St. Louis, USA 2Washington University, Radiation Oncology, St. Louis, USA

Purpose or Objective: Purpose: Stress responses in cancer cells are exaggerated over that of normal tissues include signal transduction pathways such as GRP78, PKC, PLC, Rho and others. Many of these regulators of cell viability translocate of the cell membrane during the stress response. Mechanisms of protein transport include motor and scaffold proteins such as Tax Interacting protein-1 (TIP-1), which translocates to the surface of the cell membrane of cancer cells following exposure to ionizing radiation. TIP1 is a scaffold protein that moves proteins to and from the cell membrane. It is over expressed in poor prognosis cancers.

Material and Methods: Methods: We studied radiation induction of TIP1 by western immunoblot and flow cytometry. We used siRNA to knock down TIP1 in human GBM and NSCLC cell lines. We utilized Anti-TIP1 antibodies administered IV to mouse models of human cancer xenografts such as Tax Interacting protein-1 (TIP-1), which translocates to the surface of the cell membrane of cancer cells following exposure to ionizing radiation. TIP1 is a scaffold protein that moves proteins to and from the cell membrane. It is over expressed in poor prognosis cancers.

Results: Results: Membrane protein western blots showed a significant increase in the expression of TIP-1 protein at 4 and 24 hrs following irradiation with 3 Gy as compared to 0 Gy untreated control tumors. Significant levels of the TIP-1 membrane protein were also present in the irradiated tumors, but not in untreated controls, as demonstrated by immunohistochemistry. Near-infrared imaging studies showed significant targeting and binding of anti-TIP-1 Ab to irradiated tumors compared to untreated tumors and IgG controls at 72 hrs. Knockdown of TIP1 and blocking Abs that bind to the PDZ domain of this protein were administered IV to mice bearing irradiated human cancers.

PO-0982
Therapeutic potential of the YB-1/Notch3 interaction in prostate cancer N. McDermott1, A. Meunier1, C. Haynes2, A. Flores3, A. O’Callaghan1, L. Marignol1 1Division of Radiation Therapy, School of Medicine, Radiation Therapy, Dublin, Ireland Republic of Ireland 2Mount Sinai School of Medicine, International Health, New York, USA

Purpose or Objective: YB-1, a protein increasingly associated with tumour progression and treatment resistance in prostate cancer, is the only known ligand of the Notch-3 receptor. The Notch pathway is an evolutionarily conserved signaling system whose inhibition is under scrutiny as a novel therapeutic approach. We have previously identified elevated Notch-3 mRNA expression in high grade prostate cancer. This study investigated the anti-tumour properties of the YB-1 inhibitor Fisetin, a dietary flavonoid, in an isogenic model of radioresistant prostate cancer cells in vitro.

Material and Methods: An isogenic model of radioresistance was generated in 22Rv1 prostate cancer cells through exposure to 30 x 2-Gy dose fractions. YB-1 and Notch-3 expression were determined by western blotting in parent, aged-matched and radioresistant cells following irradiation (5Gy) and/or 60uM Fisetin treatment (24hrs). Patterns of expression were related to modification in cell cycle distribution through analysis of PI staining by flow cytometry and clonogenic survival. The anti-tumour effects of fisetin were compared to those of two notch inhibitors DAPT and Batimastat.

Results: Following a cumulative total dose of 60Gy, the resulting subline RR22Rv1 was associated with a significant increase in clonogenic survival (1.3 fold increase in survival after 2Gy and 2.2 fold increase after 10Gy) when compared to both parent 22Rv1 and aged-matched controls. YB-1 was detected in the cytoplasm of all three lines. Expression levels were elevated following irradiation (4Gy) in RR22Rv1. Radiation (5Gy) inhibited activation and nuclear translocation of Notch-3. Fisetin treatment led to a loss of Notch-3 cytoplasmic expression in RR22Rv1 cells. DAPT and Batimastat did not affect clonogenic survival of 22Rv1 and RR22Rv1 cells. Fisetin induced G2 cell cycle arrest and significantly reduced clonogenic survival in untreated and 5-Gy irradiated parent and RR22Rv1 cells.

Conclusion: This study identifies potential role of the YB-1-Notch-3 interaction in the radioresistance of prostate cancer cells, and highlights fisetin as a novel therapeutic agent for the management of prostate cancer.

PO-0983
Nanoparticle mediated tumor vascular disruption: A novel strategy in radiation therapy S. Kunjachan1, A. Detappe2, R. Kumar3, S. Sridhar3, G.M. Makrigiorgos3, R. Berbeco2 1Harvard Medical School - Brigham and Women's Hospital-Dana-Farber Cancer Institute, Department of Radiation Oncology- BWH/DFCI/HMS, Boston, USA 2Harvard Medical School - Brigham and Women's Hospital-Dana-Farber Cancer Institute, Radiation Oncology- BWH/DFCI/HMS, Boston, USA 3Harvard Medical School - Brigham and Women's Hospital-Dana-Farber Cancer Institute, Radiation Oncology- BWH/DFCI/HMS, Boston, USA

Purpose or Objective: More than 50% all cancer patients receive radiation therapy. Despite recent innovations, clinical delivery of curative radiation doses is strictly restricted by the proximal healthy tissues. Chemical/biological agents to augment the radiosensitization of cancer cells are limited by severe off-target toxicity concerns. We propose a dual-targeting strategy using tumor vascular-targeted gold nanoparticles (which amplify radiosensitization) combined with the conformal image-guided radiation therapy to induce tumor vascular disruption. This is a unique concept with a clear translational path.