

**Joshua Meyer, Class 2005
Department of Cancer Biology**

Irradiation Upregulates EGFR and Survivin in Non Small Cell Lung Cancer Cells

Joshua Meyer, T.J. Fitzgerald, MD, Dario C. Altieri, MD
Departments of Cancer Biology and Radiation Oncology
University of Massachusetts Medical School

Epidermal Growth Factor Receptor (EGFR) has long been considered an important oncogene for the growth non-small cell lung cancer. Its effect on cell survival and proliferation has been well described. Several groups have shown that EGFR is phosphorylated following irradiation, thereby switching on its tyrosine kinase activity. We have performed a series of experiments examining the effects of irradiation on the expression of EGFR and survivin, a member of the inhibitor of apoptosis (IAP) family. We have been able to demonstrate by western blotting that the expression of EGFR is dramatically upregulated 48 hours after exposure to 2, 5, or especially 10 Gy of radiation in NCI-H460 human non-small cell lung cancer cells. However, the p53-mutated NCI-H441 human non-small cell lung cancer line did not modulate EGFR levels in response to radiation.

A functional comparison of the two cell types was then performed. FACS analysis of Annexin V and Propidium Iodide staining was used to measure apoptotic rates following radiation. NCI-H460 cells showed clear sensitivity to radiation; however, NCI-H441 cells were resistant to 2, 5, and 10 Gy of radiation.

We also investigated the effects of radiation on survivin, and found upregulation in NCI-H460 cells peaking at 12 hours following treatment with 2 or 5 Gy. Following this peak, survivin levels were observed to decrease at 24 or 48 hours.

One previously reported difference in the two cell types is their p53 status, with the NCI-H460 cells possessing a wild-type p53 and the NCI-H441 cells possessing a mutated form. This is one potential explanation for the disparate behavior of these two cell types following radiation treatment. The mechanism of radiation resistance in the NCI-H441 cells is obscure, but may rely on an alternative pathway for survival. The strong upregulation of EGFR seen in NCI-H460 cells may be an avenue for increasing the proliferative or survival signal, and the concurrent upregulation of survivin point to a mechanism of this action.