# Method to sensitize cancer radiotherapy and chemotherapy

## Unmet Need

While radiotherapy and/or chemotherapy are used for >90% of cancer patients in clinical settings, the therapeutic outcomes are far from ideal for many types of tumors due to the development of drug resistance and tumor recurrence following radiotherapy and chemotherapy. Currently, 90% of failures in the chemotherapy are during the metastasis of cancers related to drug resistance, and >20% recurrence happens after chemoradiotherapy for locally advanced diseases such as non-small cell lung cancer. There is a need for new strategies that can sensitize tumors to current treatments to decrease local recurrences and increase the systemic efficacy of chemotherapeutic agents.

## Technology

Duke inventors have developed a method to increase the efficacy of current anti-cancer therapies. This is intended to be used to sensitize tumors to radiotherapy and/or chemotherapy, so as to decrease local recurrence and/or increase chemotherapeutic efficacy. Specifically, radiation and chemotherapy can upregulate the level and activity of hypoxia-inducible factor 1 (HIF-1) through nitric oxide (NO) mediated S-nitrosylation, leading to increased tumor angiogenesis and drug resistance. Thus, using agents that inhibit the expression, activation, or nitrosylation of HIF-1 in tumor cells can enhance treatment efficacy. These agents include nitric oxide synthase (NOS) inhibitors, NO scavengers, and HIF-1 nitrosylation inhibitors. This has been demonstrated through in vitro and in vivo models of breast, melanoma, adenocarcinoma and colon cancer. The results collectively show that radiation increases the number of tumor-associated

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### Patent Information

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### Department

Radiation Oncology

### Publication(s)

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### External Link(s)

• From the lab of Dr. Chuan-Yuan Li
• Exploring the role of HIF-1 in early angiogenesis and response to radiotherapy (Radiotherapy and Oncology, 2007)
• Molecular mechanisms involved in tumor repopulation after radiotherapy (Translational cancer research, 2013)

macrophages, producing NO through inducible NOS and resulting in HIF-1 stabilization in the irradiated tumor. A general NOS inhibitor, $N^{\omega}$-nitro-L-arginine methyl ester (L-NAME), was administered in mice models with two different aggressive tumors, murine mammary adenocarcinoma and murine melanoma. Both showed that the inhibition of NO production by L-NAME significantly enhanced the therapeutic efficacy of radiotherapy and reduced tumor vasculature.

## Other Applications

This technology could also be used to treat inflammatory responses through inhibition of HIF-1 nitrosylation and stabilization, inspiring the development of new drugs to treat inflammatory diseases.

## Advantages

- Significantly enhances, at least two-fold, the efficacy of radiotherapy and/or chemotherapy for cancer treatments
- Novel target of regulation mechanism of HIF-1 through NO-mediated S-nitrosylation
- Demonstrated to be effective and safe in various types of mouse tumor models
- Could be a treatment strategy for inflammatory diseases