

Mohan Natarajan, Ph.D.

Professor, Department of Otolaryngology
Head and Neck Surgery
Cancer Biology Track
Location: 313F MED
Phone: (210) 567-5663
Fax: (210) 567-0098
E-mail: Natarajan@uthscsa.edu



I am currently working on three projects:

i) Development of peptide-based vectors for selective targeting of squamous cell carcinomas:

Head and neck squamous cell carcinoma is one of the most common malignant tumors claiming almost one death each hour in the U.S. Diagnosis at a later and more advanced stage, complexity of the head and neck region hindering complete removal of the tumor, high rate of recurrence and aggressive metastasis may account for the unfavorable clinical outcome. Although chemotherapy has been proven a powerful and important choice in cancer management, the effectiveness is limited by the low availability of the drugs by the tumor(s) due to the extensive distribution in the body. We hypothesize that small molecules such as peptide-based vectors can be used as a vehicle to selectively deliver anti-cancer agents and therapeutic radionucleotides without triggering immunogenic responses. Additionally, when conjugated with radiotracers, this tumor-specific peptide based vector can be used for early diagnosis and positive prognostic approaches. The current proposed project is aimed to validate the efficacy of a 14-mer peptide called ASMp1 peptide (Patent pending).

ii) Mechanism of tumor recurrence: Tumor reappearance after treatment is a major clinical challenge in achieving disease-free survival of breast cancer patients. With an increased survival rate achieved in recent years, there will be an associated increase in tumor recurrence and aggressive metastasis. Emerging evidence demonstrated a tight association between radiotherapy and relapse of tumor at the treatment site. Radiation, while alleviate cancer burden, can itself be involved in redevelopment of the disease at the treatment site and increase the risk of recurrence at distant sites. Either in breast-conserving surgery or mastectomy, radiation therapy is used as an effective treatment for local control of breast cancer along with chemotherapy and hormonal intervention. About 90% of breast cancer patients undergo radiation therapy in concert with other treatment strategies as primary treatment and 38% receive as a follow-up to prevent recurrence. Surviving tumor cells at the treatment site after radiation therapy may elicit signaling mechanisms that may be responsible for clonal selection, tumor cell proliferation/tumor growth and metastasis. The relationship linking those altered responses after radiation exposure and re-growth of tumor remain elusive and unknown. In this study, using an innovative *in vitro* and *in vivo* model (positive margin tumor model with multi-modal [SPECT, PET and Optical] imaging) systems, we propose to investigate and establish the significance of the interplay of two decisive signaling mediators (eNOS and ER- α) and how those signaling mediators orchestrate a series of events, that could be responsible for tumor reappearance and metastasis.

iii) Radiation health effects and bystander signaling - To study the effect of low LET radiation on cell signaling that leads to a sustained phenotypic expression. This study is aimed to validate radiation health risk that would potentially minimize the uncertainties and provide insight needed to develop strategies for better health risk assessment. This would assist in establishing new exposure standards to protect the general public and vulnerable subpopulation such as work force involved in cleaning process or first responders of radiation accidents or dirty bomb explosion.