

## Bankhead-Coley Cancer Research Program

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Bridge (1-year project)*

**Project Title:** Nanoparticle-Mediated Targeting of Natriuretic Peptide Pathway for Lung Cancers

**Project Summary:** Lung cancer is the leading cause of cancer death for both men and women. More people die of lung cancer than of colon, breast, and prostate cancers combined. Herein, we propose to develop a targeted integrative gene expression and regulation (TIGER) technology for treatment of lung cancer using a novel anti-tumor agent, natriuretic peptide KP73-102, through a chitosan-based nanoparticle gene delivery system. The research team previously reported that chitosan-based nanoparticles successfully deliver polynucleotide drugs to protect mice from respiratory syncytial virus (RSV) infection (Zhang et al., *Nature Medicine*, 2005). The team has found that KP73-102, a novel peptide of pro-atrial natriuretic peptide, is capable of attenuating NFkB activation and inducing apoptosis in lung adenocarcinoma cells. These studies have led to the hypothesis that chitosan nanoparticles capable of de novo production of KP73-102 in the lung may provide a novel means of prophylaxis and/or treatment for metastatic lung cancer. The proposed TIGER system will be mediated by adenoassociated virus Rep protein or Sleeping Beauty transposon. KP73-102 by TIGER technology will minimize its toxicity. The team will first test the TIGER system on cells in vitro and then will further investigate the potential of KP73-102 for treatment of lung cancer in a murine model. We believe that KP73-102 nanoparticle therapy may offer a safe and effective treatment of patients with lung cancer and other adenocarcinomas in the future.