

Bankhead-Coley Cancer Research Program

Lokeshwar, Balakrishna

*Urology Department
University of Miami*

*2006 Program
Bridge (1-year project)*

Project Title: Antitumor and c Hemopreventive Activity of the Ecuadorian Plant Extract BIRM

Project Summary: Systematic investigations of promising plant products have led to the development of potent anticancer drugs with unique modes of action and high efficacy (e.g., Taxol, Taxotere, Vinblastine, etc.). Prostate cancer strikes the elderly, many of whom have co-morbid conditions such as diabetes and heart disease, which make them less tolerant to aggressive treatments including chemo, radiation, and even hormonal therapies. It is estimated that in Europe and the United States, more than 50 percent of men with CaP experiment with one or more complementary therapies. These treatments include high dose vitamins and minerals, herbal preparations and supplements of soy, saw palmetto, etc. However, determining the efficacy of complementary treatments without preclinical evaluation is extremely difficult. The goal of the present proposal is to investigate the preclinical efficacy of a formulation from an indigenous plant found in the Andes whose use is taking hold in the United States. Through a patient contact, this research team acquired a plant product by the name of BIRM (Biological Immune Response Modifier, Life Root-Ecuadorian oral solution; BIRM Inc., Quito, Ecuador). BIRM is a root extract of the Andean variant of the Dulcamara (*Solanum dulcamara* L). In Ecuador and Columbia BIRM is dispensed by local clinicians and pharmacies for AIDS and cancer. BIRM has been extensively consumed for over two decades. Its use is rising in the United States. Preliminary studies performed in our laboratory showed that BIRM is effective in killing prostate cancer cells. At low concentration, BIRM slowed the growth of prostate tumor cells by arresting them in their non-growth phase. At higher concentration (>1 percent) it killed them by a cellular suicide (apoptosis) mechanism. BIRM also accelerated the degradation of androgen receptor in prostate cancer cells that are dependent on androgen for proliferation. Transplanted human prostate tumors either disappeared or grew significantly slower in mice or rats when they were given BIRM in drinking water or by direct deposit in their stomach. None of the treated animals showed visible toxicity to BIRM after 4 weeks of continuous treatment, indicating it is non-toxic to normal tissues. These results led the research team to propose a hypothesis that BIRM is a potent chemopreventive agent that will prevent the development and progression of prostate cancer. Prolonged use at non-toxic dose is essential for chemoprevention of recurrent prostate cancer, as the rate is slow (>2-10 years). Since prostate cancer develops and progresses in several distinct stages, it is necessary to evaluate the efficacy of a therapeutic at every stage of the disease. The transgenic mouse model (TRAMP) of prostate cancer, is close to an ideal model. Prostate cancer in TRAMP mouse develops from early adulthood and progresses to androgen-independent stage within a defined period, much like the disease in man. This team proposes to test this natural product on prevention and cure of prostate cancer in TRAMP mice by administering the drug at different doses in drinking water. The uptake of the active product will be measured in mouse blood using a surrogate marker of BIRM consumption (uronate levels). The efficacy of the treatment with BIRM will be measured by the delay in tumor progression and histology at different periods during treatment. The second aim will be to identify the mechanism by which

Bankhead-Coley Cancer Research Program

BIRM is able to stop tumor cells from proliferation, accelerating their death and degradation of androgen receptor, the main culprit in androgen unresponsive growth of the cancer. Effect of BIRM on the levels and extent of modification in the key molecules involved in cell proliferation and cell death will be investigated. Together, these studies should help in determining whether BIRM is a novel therapeutic that is safe to consume and effective in preventing prostate cancer from advancing. On the other hand, although unlikely, the studies should also reveal whether BIRM is unsuitable for consumption. A majority of its publicized activity is due to the placebo effect, and it is even dangerous when consumed in large quantities.