

# *Agricultural Experiment Station (AES)*



**University of  
the District of  
Columbia**

## **Nutrient Modulation of P53-ATF3 Signaling in Breast Cancer**

**Deepak Kumar, Ph.D.**

Vitamin E includes a family of micronutrients consisting of four tocopherols and four tocotrienols ( $\alpha$ ,  $\beta$ ,  $\gamma$  and  $\delta$ ) both of which are present in various components of the human diet. Tocotrienols are minor constituents of vitamin E but possess several more powerful anti-cancer, cholesterol lowering, natriuretic (prevent hypertension and cardiovascular diseases caused by salt intake) and neuroprotective properties that are often lacking in tocopherols. Despite possessing these preventive/therapeutic advantages, tocotrienols have not been extensively studied compared to tocopherols.  $\gamma$ -Tocotrienol ( $\gamma$ -T3) induces apoptosis in a variety of cancer cell lines including estrogen receptor (ER) + and ER- breast cancer cells but do not affect the proliferation of normal mammary cells. Dr. Kumar and co-workers have identified ATF3, a transcription factor, as a novel target of  $\gamma$ -T3 in breast cancer cells. They have demonstrated that  $\gamma$ -T3 induces apoptosis in caspase-3 deficient MCF-7 cells via caspase-7 dependent pathway. ATF3 interacts with p53 tumor suppressor protein and prevents its degradation by stabilizing p53 in the cells. P53 induces cell death in response to DNA damage by carcinogens thereby preventing cancer. This study holds promise in identifying  $\gamma$ -T3 as a chemo-preventative in breast cancer and/or its role in inhibiting the progression of breast cancer.

Dr. Kumar and his collaborator at Georgetown University are also working on elucidating the mechanisms of action of the common endocrine disruptor, Bisphenol-A present in the environment. The proposal is funded by AES to Dr. Kumar and his collaborator, Dr. Rebecca Riggins at the Lombardi Comprehensive Cancer Center at Georgetown University. Endocrine disrupting chemicals when absorbed into the body interfere with endocrine system by either mimicking or blocking hormones. Bisphenol A [BPA; 2, 2-bis (4-hydroxyphenyl) propane]

**Community Outreach  
and Extension Services**

September 2009

### **Special point of interest:**

*“Tocotrienols are minor constituents of vitamin E but possess several more powerful anti-cancer, cholesterol lowering, natriuretic (prevent hypertension and cardiovascular diseases caused by salt intake) and neuroprotective properties that are often lacking in tocopherols.”*



## Breast Cancer Research (continued from page 1)

is an endocrine disruptor found as aquatic pollutant that originates mainly from plastic industry. Several studies have linked BPA exposure to fish toxicity, ecosystem misbalance, diabetes, insulin (INS) resistance, mammary tumorigenesis in rodents, and poor survival outcome and response to chemotherapy in human breast cancer. The molecular mechanisms involved in BPA toxicity are not well understood. Microarray technology is a powerful way to simultaneously detect the expression of mammalian genome and identify the genes regulating BPA toxicity. Using the microarray data, this proposal is aimed to study the changes in gene expression and help understand the mechanism of action of BPA using MCF-10A mammary epithelial cells as a model.

Both projects train UDC undergraduate students and propagate cutting edge research at UDC. The data generated will be published and used in applying further collaborative extramural funding from external agencies.

---

### About Deepak Kumar, Ph.D.

Dr. Deepak Kumar is an Associate Professor and the Assistant Chair of the Department of Biological and Environmental Sciences at the University of the District of Columbia. He also holds an adjunct assistant professor appointment in the Department of Oncology at the Lombardi Comprehensive Cancer Center. Dr. Kumar is utilizing nutrigenomic approaches to characterize the molecular mechanisms involved in cell death induced by a vitamin E compound, gamma-tocotrienol in breast cancer cells.

**University of the District of Columbia**  
**Agricultural Experiment Station**  
4200 Connecticut Avenue, N.W.  
Intelsat Building, Suite 6L-21  
Washington, DC 20008  
(202) 274-7132 telephone  
(202) 274-7119 fax

*In cooperation with the U.S. Department of Agriculture and District of Columbia Government, Cooperative Extension Service and Agricultural Experiment Station programs and employment opportunities are available to all people regardless of race, color, national origin, gender, religion, age, disability, political belief, sexual orientation, marital status or family status.*