



Lakshmaiah Sreerama poses with students who collaborated with him in his research and were 2005 Denise M. McGuire Student Research Award winners. From left: Jordan Vincent, Mohammad Salad, Shourjo Ghose, Steve Kron, Sreerama, Alyssa Nguyen, Emily Wessel and Megan Cleland.

Delving into cancer, chemo mysteries

Human health issues drive much of the collaborative research in the College of Science and Engineering. An abbreviated list from the 2006 Faculty Research Interest Directory includes cancer chemotherapy, ultrasound, immunology, anti-diabetic compounds, radiation oncology, endocrinology, tobacco cessation and natural products.

Among the health research efforts that produce numerous faculty-faculty and faculty-student collaborative projects are the cancer chemotherapy studies of Lakshmaiah Sreerama, professor of biochemistry and member of the Department of Chemistry since 2000.

Sreerama said his interest in chemotherapy was inspired by two mysteries: Why do some cancers not respond to current therapies? And why, after a successful course of chemotherapy and two to three years in remission, does the cancer return in some patients and not in others?

Because of novel findings by Sreerama and his research collaborators in 2001, at least one of the mysteries has been solved. Accordingly, some cancer treatment centers, including the University of Minnesota, the University of Florida at Gainesville and the University of Texas in Houston, have modified their use of cyclophosphamide, one of the usually toxic drugs in the “cocktail” that comprises chemotherapy for breast cancer patients.

“Cyclophosphamide breaks down differently for some individuals,” Sreerama said, explaining that their research revealed that aldehyde dehydrogenases, which are present in the cancer cells of some patients but not all, react with the drug to form a compound that is nontoxic to the cancer cells. In medical terms, the cancer in these patients is resistant to the drug.

Using biopsy to screen tumors for the presence of aldehyde dehydrogenases helps medical doctors determine whether to include cyclophosphamide in the cocktail or to include another chemical instead.

Sreerama said aldehyde dehydrogenases, although a culprit in cancer cells, are a plus when present in normal tissue.

“The aldehyde dehydrogenases present in normal tissue are a protectant for critical bone marrow cells that provide immunity and also against atherosclerosis and kidney toxicity that originate from the bi-products of cyclophosphamide breakdown,” he said.

Sreerama said mass spectrometry and genomic analyses are currently being used in one of his laboratory projects to identify the molecular basis for resistance to additional experimental chemotherapy drugs flavopiridol, UCN-01 and Otteliones.

A second project seeks to determine the relevance of genetic polymorphisms in aldehyde dehydrogenases to chemotherapy, carcinogenesis and chemoprevention.

Sreerama’s third chemotherapy project involves the synthesis and development of vanadium, ruthenium and titanium metal complexes as anticancer drugs.

In each of these projects, Sreerama and his collaborators use a multidisciplinary approach that involves molecular pharmacology, pharmacogenetics, immunology, chemistry, biology and clinical medical studies.

“In my lab at SCSU, we utilize cell-free systems (purified enzymes), cultured human cell models (normal and tumor), animal tumor models and human tissues in our experiments,” he said.

Some of the research projects are accomplished collaboratively, and some local faculty collaborators include Mohammad Mahroof-Tahir and Daniel Gregory from Chemistry; and Heiko Schoenfuss, Timothy Schuh, Christopher Kvaal and Oladele Gazal from Biological Sciences.

For more information about Sreerama and his research, please go online to <http://web.stcloudstate.edu/lrsreerama/>.