From the University of Mississippi Medical Center Division of Public Affairs

ANTI-CANCER DRUG DISCOVERY PARTNERSHIP FORMED BETWEEN UMMC CANCER INSTITUTE AND NATURAL PRODUCTS CENTER AT OLE MISS

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JACKSON, Miss. – A new partnership to search for cancer-fighting drugs combines compound-identification and screening expertise at the University of Mississippi's National Center for Natural Products Research with the drug development and clinical-trials capabilities at the University of Mississippi Medical Center Cancer Institute.

An agreement announced today between the Oxford-based NCNPR and the Cancer Institute in Jackson creates the Drug Discovery Core, which will be directed by Dr. David Pasco, assistant director of the Natural Products Center and research professor in pharmacognosy.

The drug discovery process begins at the NCNPR, where researchers collect plants and other natural products, create extracts and screens them for activity against given targets. Under the new agreement the most promising anti-cancer compounds will be further isolated and sent to Jackson for development and testing.

"Cancer institutes usually have some type of drug discovery program," Pasco said. "Since Dr. Miele's arrival, Dr. Larry Walker (director of the NCNPR) and I have been talking with him about this venture."

Dr. Lucio Miele took the Cancer Institute directorship in summer 2009. He's worked to expand the institute's research mission by hiring scientists, purchasing high-tech equipment and forging partnerships with other institutions. Founding the Drug Discovery Core is a milestone in that effort.

"Development of new anti-cancer agents is one of the most important aspects – if not the most important aspect – of cancer research," Miele said. "The Natural Products Center has tremendous experience and this agreement increases the synergy between our two campuses.

"Natural products are a rich source of drug discovery and have yielded some of the most potent drugs we still use -- the best example being Taxol," Miele said, referencing a drug that UM researchers had a hand in developing as the NCNPR was first forming.

Cancer research has advanced to the point where scientists have identified most genes and gene mutations responsible for causing cancer. Those are the targets of drug developers.

"There are several hundred genes identified," Pasco said. "But they all belong to about 12 different signal-transduction pathways."

Blocking those pathways with specially designed drugs can essentially keep genes from switching on or off.

In Oxford, Pasco and his team finished screening about 30 plant extracts this spring. Those extracts are used in traditional Chinese and Indian medicine, some with proven anti-cancer properties.

The screenings assessed the activity of each extract along the dozen or so pathways. About 25 extracts showed activity on the majority of the signaling pathways.

Lest the process seem overly simple, think of each pathway as a struck piano key. The note alone may not be significant, but played in sequence with others, it can create an ominous concerto – a tumor.

Shutting down the concerto requires blocking several pathways at once. Hence, identifying natural products capable of blocking multiple pathways could be a major step in our quest for better cancer drugs.

"Specific collections of these pathways are involved in the expression of cancer," Pasco said. "And there's a lot of crosstalk among those pathways. That's what makes cancer so difficult to treat."

Investigators will search the screening results for unique patterns of activity among the various signaling pathways.

"Once we find an interesting extract, we can tear it down further to get at the active compound," Pasco said.

Sometimes it's multiple compounds that work together in one extract to make it promising. Getting to the core of that scenario is one of the NPNPR specialties, Miele said.

Ultimately, by combining several compounds, scientists in the Drug Discovery Core hope to create pharmaceuticals that act on a number of key pathways.

"Because cancer is so complicated, you need to use a range of compounds to prevent the tumors from becoming resistant to the compounds you're using," Pasco said.

Those combinations of compounds – candidate drugs – will be sent to UMMC labs in Jackson for testing on various cancer cell lines, Miele said. That phase of drug development is called *in vitro* testing, meaning in-glass.

Once proven *in vitro*, researchers would test the drugs on tumors in animal models – likely mice or rats. The next phase would take candidate drugs to carefully regulated clinical trials administered by the Cancer Institute.

The NCNPR was created to ally academia, government and the pharmaceutical and agrochemical industries. Its goal is to integrate research, development and commercialization of potentially useful natural products. It is the nation's only university-affiliated research center devoted to improving human health and agricultural productivity through the discovery, development and commercialization of pharmaceuticals and agrochemicals derived from natural products.

The Cancer Institute, founded in 2004, combines cutting-edge care for patients, basic science and clinical research, and education and training of the next generation of cancer care providers. Patients at the Cancer Institute receive care from a team of specialists from multiple disciplines – including radiologists, geneticists, radiation oncologists, surgeons, medical oncologists, behavioral specialists – tailored specifically to their needs.

The institute's research focuses on three programs: Cancer genetics, which seeks to prevent onset and control growth of cancer by understanding gene sequences and controls involved in gene expression; molecular oncology and cell signaling, which investigates the makeup and communication paths of cancerous cells; and drug discovery and experimental therapeutics, which seeks to develop drugs, biologics and devices to more effectively treat cancer and improve patient recovery.

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