PTP1B has proven time and again to be tough to block without unintended consequences, but Peti hopes a less direct approach than others have taken will make a difference. Rather than targeting the main catalytic parts of the enzyme directly, he's looking at the behavior of a more peripheral but nevertheless influential structure called the "c-terminal segment." It's an underexplored region that could be targeted very specifically, likely with a combination of surgical strikes on more than one area. A key requirement of any drug is that it only affects insulin signaling and not other interactions by similar enzymes.

Sure enough, along with colleague Nicholas Tonks at the Cold Spring Harbor Laboratory, Peti has begun to characterize a drug that works in this area. They plan to use NMR to improve the understanding of the drug's workings further and use that knowledge to improve its abilities.

Peti's third approach under the ADA award is more traditional in that it depends "simply" on characterizing the structure of a complex of proteins, together known as GM:PP1. That complex controls the balance between storing glucose in the form of a larger "glycogen" molecule and breaking glycogen down into glucose. GM:PP1 accomplishes the latter by turning on an enzyme called glycogen phosphorylase.

Peti's idea is to figure out how a drug could inhibit GM:PP1's recognition of glycogen phosphorylase so that it doesn't break down glycogen into glucose so readily. Peti already knows where he wants to look on the proteins to try the idea and has developed a means of screening drugs that might interact with those areas.

Success with any of the three approaches is hardly guaranteed, but if there is a chance he can save anyone else from the kind of difficulty his grandmother endured, Peti is eager to try. ❖

NIH awards URI pharmacy professor $1.3M grant to fight cancer with nanoparticles

KINGSTON — The National Institutes of Health have awarded a University of Rhode Island pharmacy professor a $1.3 million grant to further study a new class of inorganic nanoparticles that target primary cancer, and help control the disease's spread (metastases) and recurrence.

WEI LU, assistant professor of biomedical and pharmaceutical sciences in the College of Pharmacy, has discovered in his preliminary research that hollow copper sulfide nanoparticles are effective in delivering chemotherapy and heat through a laser that can burn the tumor.

The Kingston resident will be using the four-year NIH grant to further his laboratory study with a focus on breast cancer, the second most frequently diagnosed malignancy in women worldwide.

"We are developing a novel cancer therapeutic technology that has several innovative features: biodegradability, multimodality and simplicity," said Lu, who is teaming with Pharmacy Professor Bingfang Yan, a specialist in genetic and environmental factors that combine to regulate the expression of genes involved in drug response and the cellular switches related to tumor formation.

"One nanoparticle can carry hundreds or even thousands of drug molecules to a target like a tumor cell," Lu said.

He wants to enhance photothermal ablation therapy, a process that uses lasers in cancer treatment.

"As is the case with surgical removal of a tumor, getting all of the cancer is critical, " Lu said. "The new nanoparticles provide a three-way punch to the tumor: a more widespread ability in a tumor to distribute heat and burn the tumor, a more efficient and comprehensive way to deliver chemotherapy, and better use of heat to activate the chemotherapeutic agents and immunotherapeutic agents. The new nanotechnology offers promise in tumor eradication.

"Such nanoparticles are introduced intravenously and are absorbed into a tumor." Lu said. "This study is using near-infrared laser light instead of ultraviolet light or visible light because it penetrates tumor tissue better and has much lower side effects. In addition, these particles are readily degradable in the body, minimizing potential organ toxicity."

URI PHOTO BY JOE GIBLIN

Wei Lu, assistant professor of biomedical and pharmaceutical sciences in URI's College of Pharmacy, in his lab conducting research on novel nanoparticles to battle metastatic breast cancer.

Lu, who came to the University in 2010, said he could not have competed for the NIH award if it weren't for the support of the Idea Network of Biomedical Research Excellence, a $45 million initiative funded by NIH and headed by URI to increase research capacity among biomedical faculty in Rhode Island. ❖