TEXAS TECH UNIVERSITY
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News Release

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NIH Awards Grant to TTUHSC Researcher

Project To Investigate New Therapy Targets for Rare Cancer

Pulmonary lymphangioleiomyomatosis (LAM) is a rare form of cancer that affects up to eight of every one million women of reproductive age worldwide. This disease is characterized by the uncontrolled growth (proliferation) of tumor cells that are biologically similar to smooth muscle cells in the lungs, kidneys and lymphatics; these cells will spread and invade various locations throughout the body. Currently there are approximately 1,500 confirmed cases in the U.S.

The most common symptom associated with LAM is shortness of breath, especially upon exertion. In most cases, the disease progresses slowly and over time can lead to lung collapses and ultimately respiratory failure.

To better understand the role of extracellular vesicles (EV) in the spread and progression of LAM, the National Institutes of Health (NIH) recently awarded a four-year, $2.8 million grant to Magdalena Karbowniczek, M.D., Ph.D., a professor of immunotherapeutics and biotechnology at the Texas Tech University Health Sciences Center (TTUHSC) Jerry H. Hodge School of Pharmacy. Based upon the study's progress and the availability of funds, the NIH could extend the grant to five years and approximately $3.5 million.

EVs are tiny nanometer size particles released by healthy cells to "communicate" with other cells. Karbowniczek said they also are thought to facilitate cancer metastasis; however, their role in LAM has not yet been explored.

"We hope to establish EVs — and the mechanisms that control their release from [some] cells and uptake by other cells — as targets for new LAM therapy," Karbowniczek said. "There are currently medications that target EVs that are tested in clinical trials for other cancers; therefore, if we discover that EVs are promoting LAM progression and spread, they can be repurposed for LAM."

There are two main types of LAM: sporadic LAM, which develops spontaneously, and LAM associated with tuberous sclerosis complex, an inheritable genetic condition manifesting with multiple tumors in different organs. The therapeutic options for LAM patients are very limited, as the only drug currently available for LAM is everolimus, an analog of rapamycin that in some patients can slow the progress of disease. However, everolimus does not stop lung destruction, and the disease relapses once treatment ends.

"We hope that through studies funded by this grant we will be able to identify new therapeutic targets, and that knowledge gained through this work will be instrumental for the development of new therapies for LAM patients," Karbowniczek added.

The project is a collaboration with the University of Cincinnati (UC); Jane Yu, Ph.D., a professor of internal medicine at the UC College of Medicine also is a co-principal investigator (PI) on this grant. Karbowniczek and Yu have collaborated for almost 20 years after initially investigating LAM together as postdoctoral

trainees under Lisa Henske, M.D., a world-renowned LAM expert at Fox Chase Cancer Center in Philadelphia.

TTUHSC co-investigators for the grant include Irene La-Beck, Pharm.D., and Maciej Markiewski, M.D., Ph.D. UC co-investigator Frank X. McCormack, M.D., who leads international randomized trials for LAM, also will provide expertise necessary for these studies.

“This multi-PI grant unifies [our] expertise in LAM again and formalizes a long-lasting collaboration for the benefit of LAM patients,” Karbowniczek said.

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