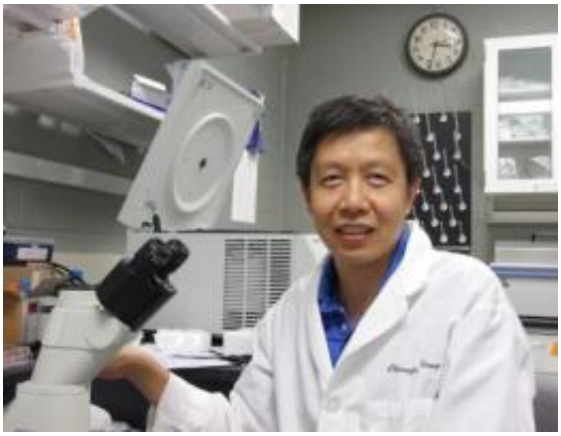
Researcher targets gene regulators on link between arsenic, cancer

July 14 2010



Chengfeng Yang, a physiology professor with Michigan State University, is studying the link between arsenic exposure and lung cancer. Credit: Courtesy photo

To determine how arsenic increases the risk of lung cancer and to identify potential treatments, a Michigan State University researcher will use $1.7 million in federal funding during the next five years to examine why certain genes disrupt cells, leading to the disease.

Chengfeng Yang, a physiology assistant professor with the College of Veterinary Medicine and MSU's Center for Integrative Toxicology, will be studying the role of very small ribonucleic acids called microRNAs. These microRNAs regulate genes, which control how a cell behaves.

The research project, which will study those processes in cultured human cells and mice, is funded by the National Institutes of Health.

"Arsenic is one of the most common environmental pollutants, and long-term arsenic exposure through drinking water is associated with increased risk of lung cancers specifically and some other cancers as well," Yang said. "The long-term goal of this study is to determine the mechanism by which this happens and to identify targets for the treatment and prevention of cancers resulting from arsenic exposure."

Since the levels of microRNAs are different when comparing normal tissue cells to cancer cells, Yang and his team are trying to determine if that difference is because of the tumor or if it is what caused the tumor in the first place.

"Does microRNA play a role in tumor development? Can carcinogens such as arsenic cause the deregulation of microRNA that leads to cancer development? That's what we need to find out," Yang said.

To accomplish that, Yang will look at two specific microRNAs - miRNA200b and miRNA200c - and the role they play in converting normal human bronchial epithelial cells to tumor cells when exposed to arsenic. Those specific microRNAs were chosen because during screening, they were the only two that were different when comparing normal cells with cells transformed by cells.

"A single microRNA has the ability to regulate more than 100 gene functions, playing an important role in cell behavior and whether cells function normally or potentially change to a cancerous cell," Yang said. "More than one-third of all human genes are believed to be regulated by microRNAs, and when microRNA levels are too high or too low, they disrupt the normal function of cells and lead to disease."

Uncovering how microRNAs react to carcinogens and lead to tumor development could help researchers discover biomarkers and identify people who may be more prone to develop tumors.

"With this information, we could potentially diagnose and treat people much sooner," Yang said.

As part of his project, Yang also will investigate the role of two genes called ZEB1 and ZEB2 in this process, because the appearance of these two genes can cause the depletion of miRNA-200b and miRNA-200c. He will further examine the role of these two genes in arsenic-induced tumors by studying mice with the ZEB1 and ZEB2 genes removed.

Provided by Michigan State University