Scientists Use Nanoparticle to Discover Disease-causing Proteins

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The linear ion trap mass spectrometer in Andy Tao&acutes lab allows the Purdue biochemist to quickly analyze biological samples such as snake venoms. It has the capability to analyze several hundred proteins in one hour. Here, Tao peers through the small window of the nanosprary ion source. (Purdue Agricultural Communication photo/Tom Campbell)

A complex molecule and snake venom may provide researchers with a more reliable method of diagnosing human diseases and developing new drugs.

Purdue University researchers bound a complex nanomolecule, called a dendrimer, with a glowing identification tag that was delivered to specific proteins in living venom cells from a rattlesnake. The scientists

want to find a better way to ascertain the presence, concentration and function of proteins involved in disease processes. They also hope the new method will facilitate better, more efficient diagnosis in living cells and patients.

Most diagnostic methods must be done on minute dead blood or tissue cell samples in a laboratory dish, said Andy Tao, a Purdue biochemist and senior author of the study. Because molecular interactions and protein functions are disturbed when samples are collected, researchers can't obtain an accurate picture of biochemical mechanisms related to illnesses such as cancer and heart disease.

Tao and his research team used dendrimers because they can pass through cell walls efficiently with little disturbance to the cells and then label specific proteins with isotopic tags while cells are still alive. This allows the scientists to determine the activities of proteins that play roles in specific diseases. Proteins carry genetic messages throughout the cell causing biochemical changes that can determine whether a cell behaves normally or abnormally. Proteins also are important in directing immune responses.

The Purdue scientists report on their new strategy to discover proteins and protein levels, called soluble polymer-based isotopic labeling (SoPIL), in the current issue of the journal *Chemical Communications*. The study also is featured in the journal's news publication *Chemical Biology*.

"The problem with the current method of using proteomics - protein profiling - is that we use very small sample amounts so sensitive that we can't effectively use existing technologies to study them," Tao said. "In addition, to study a specific protein and its function, we want to preserve its natural environment and see where two molecules meet and what the interaction is when they bind.

"Taking small samples of blood, cells or tissue to study extracted proteins in laboratory dishes damages the sample and the natural environment is destroyed."

The dendrimers would carry one of the stable isotopic or fluorescent labels to identify the presence or absence of a protein that can be further developed for use as a disease indicator, or biomarker.

Snake venom cells were used because they have a very high concentration of proteins similar to some found in human blood, Tao said. The proteins apparently are part of the biochemical process that affects blood clotting or hemorrhage. Understanding how the proteins behave could help determine predisposition to heart disease and cancer and also be useful in diagnosis and drug development.

In future research, Tao plans to investigate how dendrimers are able to enter the cell so easily, what happens to them once they are in the cell and whether there are any long-term effects.

Source: Purdue University