New aspirin-based prodrug may prevent damage caused by chemotherapy

January 10 2014, by James Hataway

(Medical Xpress)—Researchers at the University of Georgia have developed a new prodrug that promises to reduce many of the negative side effects caused by cisplatin, a commonly prescribed chemotherapy treatment.

Cisplatin may be used to treat a variety of cancers, but it is most commonly prescribed for cancer of the bladder, ovaries, cervix, testicles and lung. It is an effective drug, but it often causes severe and irreversible damage to a patient's kidneys, hearing and sense of balance.

UGA researchers combined cisplatin with aspirin in a new single prodrug formulation they call Platin-A, which prevents these negative side effects by reducing inflammation. They reported their findings recently in *Angewandte Chemie*, a journal published by the German Chemical Society.

"We know that inflammation plays a major role in the development of these side effects," said Rakesh Pathak, lead author of the paper and postdoctoral research associate in the UGA chemistry department. "By attaching aspirin to cisplatin, we can help control this response and reduce damage to the body."

Reducing these negative side effects will not only provide the patient with a better quality of life during and after treatment, but it may also make oncologists less hesitant to prescribe cisplatin.

Prodrugs like Platin-A enter the body in a mostly inactive state, but they are converted to their active state after going through normal metabolic processes. Prodrugs allow scientists to have more control over the simultaneous release of both drugs and how long it remains active.

"You could administer aspirin separately from chemotherapy, but it would not be as effective as this prodrug formulation," said Shanta Dhar, assistant professor of chemistry in the UGA Franklin College of Arts and Sciences and principal investigator for the project.

"It's a bit like making a cocktail," she said. "You could drink each of the ingredients one by one, but it works much better if you put it all in the same glass first."

Both Dhar and Pathak caution that their experimental results are preliminary and they must do more work before this is tested in living organisms. However, they say the new formulation shows great promise.

While this project focused specifically on prostate cancer and one chemotherapy drug as a model, they believe that the same approach could work for many other forms of cancer and their preferred treatment.

"We are now developing a platform where we can plug in any chemotherapy with any anti-inflammatory and find out which combinations work best," Dhar said.

The researchers also plan to incorporate this technology into their ongoing work with nanotherapeutics. Dhar's NanoTherapeutics Research lab has created numerous nanoparticles, each one 1,000 times finer than the width of a human hair, which they use to attack pathogens and deliver drugs.

"If we use nanoparticles to deliver our prodrug, we can control where it goes and how it breaks down with even more precision," said Dhar, who is also a member of UGA's Cancer Center, Nanoscale Science and Engineering Center, and Center for Drug Discovery. "This is our next step."

More information: onlinelibrary.wiley.com/doi/10 … e.201308899/abstract

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