In the Spotlight

Sheila Roberson, Director of Alumni and Public Relations, 706-542-5303, roberson@rx.uga.edu
University of Georgia College of Pharmacy, Athens, GA 30602

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Writer: Molly Berg, mberg14@uga.edu
Contacts: Shelley Hooks, 706-542-2189, shooks@rx.uga.edu
　Mandi Murph, 706-583-0216, mmurph@rx.uga.edu

UGA researchers discover mechanism that could lead to better ovarian cancer treatment

Athens, Ga. – Resistance to chemotherapy is a major problem for those suffering from ovarian cancer—a problem that prevents a cure from a disease dubbed the "silent killer." University of Georgia researchers are giving patients new hope with recent findings that help pinpoint the mechanisms causing chemoresistance.

Over the last five years, UGA College of Pharmacy associate professors Mandi Murph and Shelley Hooks have discovered that a type of protein known as RGS10 impacts the effectiveness of ovarian cancer chemotherapy. Murph also discovered that mTOR signaling, a protein encoded by the mTOR gene, drives the effects of RGS10.

Resistance to chemotherapy that was previously very effective is a major roadblock that prevents better outcomes in this disease. Finding mTOR as the mechanism of RGS10's effects could help explain the unique features of chemoresistant cancer cells.

"Chemoresistance to ovarian cancer is what kills women," Hooks said. "It's the deadliest gynecologic cancer. Most women with ovarian cancer will have their tumors come back."

"Within two years, 85 percent of women will have their cancer come back in a more aggressive form," Murph said. "It is during that time that they won't respond to the chemotherapy."

Their article, "Cellular deficiency in the RGS10 protein facilitates chemoresistant ovarian cancer," reviews over five years worth of research on RGS10 and was published in Future Medicinal Chemistry.

Their findings on RGS10 have jump-started an interest in the protein as well as created several major research articles on the topic.

"RGS10 is basically an off switch. It does very little," Murph said. "However, it's important because when it gets turned off, a person will become resistant to chemotherapy.

"mTOR essentially determines the survival of [cells], which in turn indicates whether chemotherapy will be

successful. It's exciting to have found this piece of the puzzle."

In their past articles, Hooks and Murph tested cells to see how they would react to common chemotherapy medicines. They were able to manipulate the sensitivity of ovarian cancer cells to common chemotherapy treatments like paclitaxel, cisplatin and vincristine by changing RGS10 expression.

"Depending on the expression levels of RGS10, the chemotherapy for ovarian cancer is more or less effective," Hooks explained. They also found that RGS10 is epigenetically silenced, meaning that the protein is turned off due to external or environmental factors and not genetics.

"If there were a way to reverse silencing of the RGS10 protein, then we could potentially restore sensitivity to drugs," she explained. "It would mean a better chance of survival for women with ovarian cancer."

While RGS10 is responsible for chemoresistance, it could also be the key to improving treatment of chemotherapy.

"Chemoresistance prevents us from curing the disease," Murph said. "If we can cure chemoresistance, we can cure ovarian cancer."

Currently, platinum chemotherapy drugs, like paclitaxel and carboplatin are used as a one-size-fits-all treatment for ovarian cancer patients. However, chemoresistance to platinum drugs remains a serious challenge to curing ovarian cancer.

Murph recommends more research on mTOR inhibitors to see how they can be modified to respond to chemotherapy.

"Five years ago, this field of RGS10 cancer research didn't exist," she said. "But Dr. Hooks and I have been able to create this area of research and lead it. Before no one knew or cared about RGS10 effects in cancer cells. Now we have more research that could contribute to improving chemotherapy."

To read more about Hooks' and Murph's RGS10 protein research, visit http://www.ncbi.nlm.nih.gov/pubmed/26293348. To learn more about Murph's mTOR signaling research, visit http://www.ncbi.nlm.nih.gov/pubmed/26319900.

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Note to editors: Images of Mandi Murph and Shelley Hooks are available at http://multimedia.uga.edu/media/images/MandiMurph-30550-006.jpg and http://multimedia.uga.edu/media/images/hooks_shelley27847-007.jpg.

This release is available online at http://news.uga.edu/releases/article/mechanism-better-ovarian-cancer-treatment-1015/.