MedicalXpress

Milk thistle extract, silibinin, reduces self-renewal of colorectal cancer stem cells

April 7 2014

Colorectal cancer stem cells thrive in conditions of inflammation. A University of Colorado Cancer Center study presented today at the American Association for Cancer Research (AACR) Annual Meeting 2014 shows that the chemical silibinin, purified from milk thistle extract, affects cell signaling associated with inflammation and thus also the formation and survival of colorectal cancer stem cells.

"We have been deeply involved in this line of research that extends from silibinin to its chemopreventive properties in colorectal cancer, and the current study takes another important step: we see both a likely chemopreventive mechanism and the result of this mechanism in animal models," says Sushil Kumar, PhD, postdoctoral fellow in the lab of Rajesh Agarwal, PhD, co-program leader of Cancer Prevention and Control at the CU Cancer Center and professor at the Skaggs School of Pharmacy and Pharmaceutical Sciences.

The group compared mice chemically treated to develop inflammation-dependent colorectal cancer given silibinin to a control group not given the drug. The results were clear: mice given silibinin showed less incidence of macroadenomas indicative of colorectal cancer, whereas nearly all mice in the control group developed the disease. In addition, in the silibinin group, Kumar and co-authors saw minimal colon inflammation, and minimal incidences of rectal bleeding and rectal prolapse as frequently observed in control mice.

"Results indicate that silibinin feeding indeed provided the mice with

protective effect," Kumar says.

In addition to demonstrating chemopreventive benefit of silibinin, the current study adds to our understanding of how silibinin offers this benefit. The answer is found in colorectal cancer stem cells (CSCs), which both replicate themselves and also give birth to the cells of colorectal cancers themselves. In the presence of inflammation, CSCs both reproduce themselves (self-renewal) and produce colorectal cancer cells at a greater rate, and cells produced in these conditions are also signaled to survive at greater rates.

A key component of this expansion and survival signaling are chemicals called interleukins (IL-4 and-6), which are essential in increasing the number of CSCs and also regulate CSCs survival and function. Silibinin blocks this interleukin 4/6 signaling and so decreases levels of CSC self renewal -promoting mRNAs.

"We have been following this CSC signaling back to its source and we see now that silibinin affects the signaling of colorectal cancer stem cells very near their genesis," Kumar says.

It is notoriously difficult to gain approval for clinical trials of chemopreventive agents due to the necessity of treating many, healthy people to affect the very few who would otherwise have developed disease. But Kumar and colleagues hope to further refine the science of silibinin's chemopreventive properties while eventually exploring this chemical as a strategy for cancer prevention in a human population.

Provided by University of Colorado Denver

silibinin-self-renewal-colorectal-cancer.html