

## Study finds link between liver cancer and gut bacteria in obese mice

27 June 2013, by Bob Yirka

(Medical Xpress)—A team of cancer specialists from several Japanese research facilities has found that an acid produced by a type of gut bacteria appears to be involved in causing an increase in the rates of liver cancer in obese mice. In their paper published in the journal *Nature*, the team reports that increased levels of deoxycholic acid (DCA) found in obese mice leads to higher rates of liver cancer.

Scientists and other health care workers have known for some time that obese people tend to have higher rates of <u>liver cancer</u>. Until now, however, the link between obesity and such cancers has been a mystery. Suspecting gut microbiome differences between lean and obese people might offer some clues, the researchers performed several tests on mice.

The first test involved causing some mice to become obese by feeding them excess fat, while feeding another group normally. Doing so did not appear to increase the chances of any of the mice getting liver cancer. Suspecting that it was possible that obesity along with another carcinogen might cause a different outcome, the researchers fed both groups chemicals known to increase liver cancer rates. The chemicals caused all of the obese mice to get liver cancer, but only 5 percent of the lean mice. The researchers noted also that the obese mice that got cancer also had higher levels of senescent-associated secretory phenotype (SASP). Senescence is the process by which cell division slows as people grow older. In most cases, higher levels result in fewer tumors developing. In other instances, SASP has been shown to increase the likelihood of developing certain cancers such as those that develop in the liver.

Because increased SASP levels have been linked to changes in the gut microbiome, the researchers fed another group of mice a mixture of <u>antibacterial</u> <u>agents</u> that killed most of the <u>microbes</u> in their

guts, then repeated their first exercise. They found that in the absence of <u>gut bacteria</u>, liver cancer rates for the obese mice plummeted. The next challenge was to figure out why gut bacteria was causing the change.

After an exhaustive process of elimination, the researchers found obese mice had elevated levels of deoxycholic acid (DCA)—a by-product of the metabolism of bile by some gut bacteria—in their bloodstreams. Further tests found that artificially raising or lowering DCA levels caused associated raising or lowering of liver cancer rates.

The net result of the all the testing by the team showed that obese mice tended to have more of the DCA producing microbes in their guts than lean mice, which in turn led to more liver cancers—a finding that will need to be tested to see if it applies to humans as well. If so, drugs that lower such rates may be developed to help prevent liver cancer in people.

More information: *Nature* (2013) doi:10.1038/nature12347

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