Study identifies common gene variants associated with gallbladder cancer
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"Using the latest technologies to look at the causes - notably the genetic underpinnings - of this understudied disease just makes a lot of sense," says study co-leader Nilanjan Chatterjee, PhD, Bloomberg Distinguished Professor in the Department of Biostatistics at the Bloomberg School and a professor of oncology at the Johns Hopkins Kimmel Cancer Center.

The gallbladder is a tiny organ in the abdomen which stores bile, the digestive fluid produced by the liver. When gallbladder cancer is discovered early, the chances for survival are good, but most gallbladder cancers are discovered late as it is difficult to diagnose since it often causes no specific symptoms.

To search for which genes might be important in gallbladder cancer, investigators at the Tata Memorial Centre gathered blood samples from 1,042 patients who were treated at the Centre's Hospital in Mumbai between Sept. 2010 and June 2015. The researchers also collected blood samples during this time from 1,709 healthy volunteers with no known cancers who were visiting patients at the hospital.

To make the groups comparable, they were matched by their ages, sex and geographic regions in India from which the patients came from.

The scientists then ran these blood samples through a whole genome analysis of common single nucleotide polymorphisms (SNPs), places where the genome between different individuals vary by changes in single nucleotides, the smallest units that make up the genome.

Through a series of biostatistical and bioinformatics analyses, they found highly significant association for multiple DNA variants near two genes—ABCB4 and ABCB1—known to be involved in moving lipids through the liver, gallbladder and bile ducts. A previous study had associated ABCB4 with the...
formation of gallstones, a known risk factor for
gallbladder cancer. But the new results show for
the first time that common inherited variants in this
region may predispose individuals to gallbladder
cancer itself, independent of gallstone status,
Chatterjee says.

The researchers later replicated these results using
blood samples gathered from 447 more patients
with gallbladder cancer and 470 healthy volunteers
from Tata Memorial Hospital and Sanjay Gandhi
Postgraduate Institute of Medical Science in Uttar
Pradesh, India.

They also ran another analysis to estimate how
much variation in gallbladder cancer risk can be
explained by the discovery of additional common
variants. They say they hope to conduct similar
studies of larger groups of people in the future.

"Gallbladder cancer, like many other cancers and
complex diseases, is likely to be associated with
many genetic markers, each of which may have
small effects, but in combination they can explain
substantial variation in risk," Chatterjee says.

The researchers estimate as much as 25 percent of
gallbladder cancer risk could be explained by
common genetic variants. Although the specific
genetic variants the current study has identified
explain a small fraction of this risk, the fact that they
are in close proximity to genes known to be
important for transporting a certain class of lipids
from liver to gallbladder could provide an important
clue to the cause of the disease.

The team is currently planning to investigate the
ABCB4/ABCB1 region in more depth by fully
sequencing this region in some of the current study
participants to understand whether there are
additional risk variants there. They also plan to
conduct larger studies to look for additional genes
associated with gallbladder cancer. By better
understanding the function of the genetic risk
variants, as well as by investigating environmental
and lifestyle causes, Chatterjee says, researchers
might eventually be able to develop new treatments
or interventions to prevent this disease from
occurring in patients at high risk.