Genes of carcinogenic liver fluke revealed

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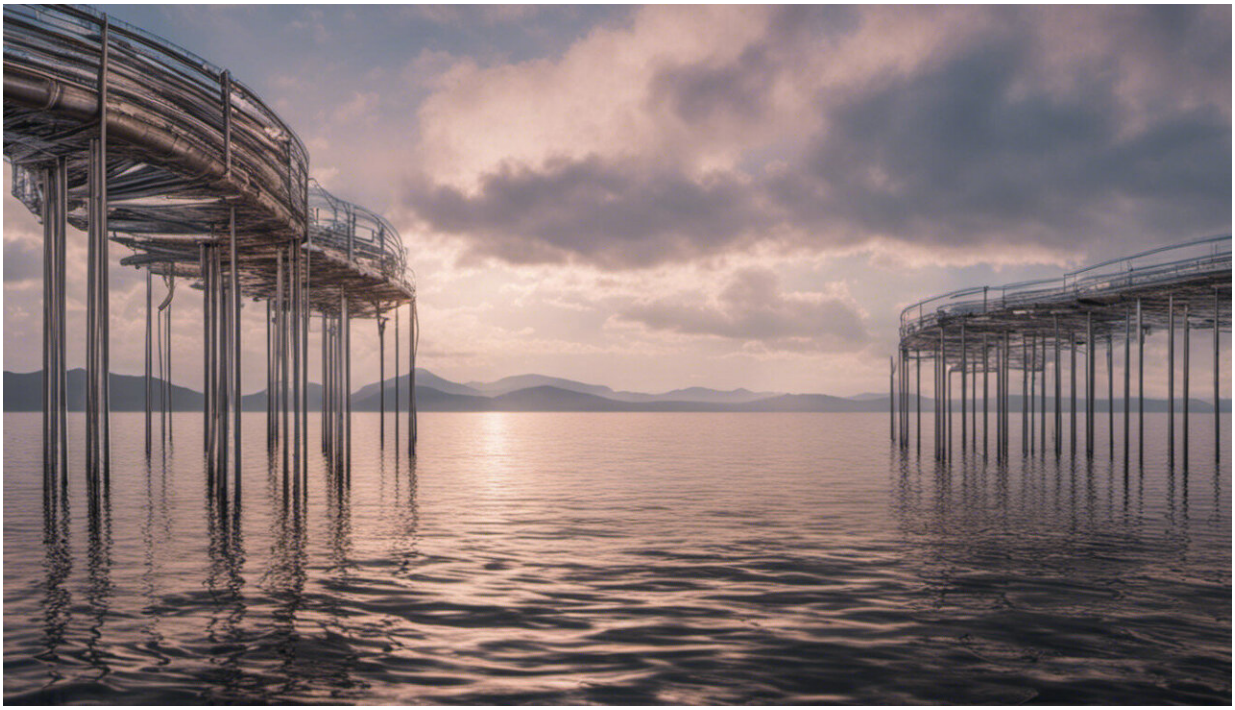

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The tiny liver fluke, Opisthorchis viverrini causes damage out of all proportion to its size. Consumed as cysts within raw fish by people in Thailand, Laos and Cambodia, it causes the tropical disease, Opisthorciasis, putting its victims at risk of cancer. Despite affecting millions of people in Asia, no vaccine exists and there is only one drug available for use. Now, A*STAR researchers have sequenced its genome, shedding light on how it copes with its strange life cycle, and

suggesting new approaches to treatment.

O. viverrini, also known as OV, has a long life cycle that begins with eggs infecting freshwater snails, explains Niranjan Nagarajan of A*STAR's Genome Institute of Singapore. "Infected snails release OV larvae into the water and they encyst themselves in freshwater fish," says Nagarajan. "Eating uncooked infected fish can lead to infections in people." Its presence can also cause fibrosis, inflammation and the deadly cancer, cholangiocarcinoma.

Using genetic material from 25 flukes, Nagarajan worked with a large international team to produce a 'draft' genome for the organism that reveals genes that serve OV well in its peculiar niche.

The fluke makes its home in the supposedly 'inhospitable' human bile duct, says Nagarajan, which is not an easy place to live. "It contains bile acids and other toxins, and the level of oxygen is variable and often low," he explains.

The researchers found genes for 'a repertoire of antioxidants' that were needed to cope with bile acids and other toxins found in bile. And OV has genes that enable it to dine on bile lipids, with enzymes that break down the fat droplets known as micelles.

"Strikingly we also identified a massively expanded family of 25 lipid-binding proteins," the authors said.

The fluke hemoglobin has an unusually high affinity for oxygen, and this helps OV to survive at these low oxygen levels, adds Nagarajan.

On a more sinister note, they found that OV can digest the epithelial cells that line the bile duct itself, known as cholangiocytes.

Several mechanisms probably come into play to cause cholangiocarcinoma, says Nagarajan, and OV will have a role in this.

"OV-induced inflammation, damage to the biliary tract due to the fluke's attachment or feeding and its secretion of proteins that can induce cell proliferation, could all increase risk of cancer," says Nagarajan.

He hopes that knowledge gained from the genome will lead to new strategies to combat the fluke, for example by reducing its ability to survive in bile.

More information: Young, N. D., Nagarajan, N., Lin, S. J., Korhonen, P. K., Jex, A. R. et al. "The Opisthorchis viverrini genome provides insights into life in the bile duct." *Nature Communications* 5, 4378 (2014). dx.doi.org/10.1038/ncomms5378

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