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NUS scientists engineer bacteria to treat severe liver-related brain dysfunction

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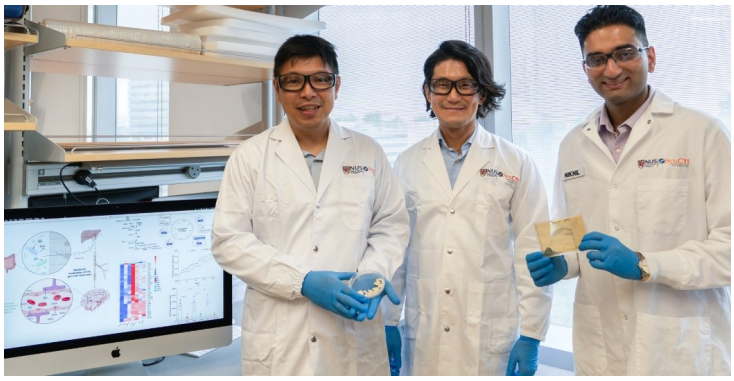

When the liver fails, toxins – such as ammonia – that should be filtered from the blood build up and reach the brain. The result is hepatic encephalopathy (HE), a devastating neurological complication of liver disease that can cause anxiety, confusion, memory loss and, in severe cases, coma. HE is a common endpoint of liver cirrhosis, driving frequent hospitalisations and placing a heavy burden on patients and healthcare systems worldwide.

Current treatments offer only partial relief. The two mainstay therapies — lactulose and the antibiotic rifaximin — work primarily by reducing ammonia production in the gut, but neither corrects the full spectrum of metabolic disruptions that drive the disease.

A research team from the National University of Singapore (NUS), led by Professor Matthew Chang from the NUS Synthetic Biology for Clinical and Technological Innovation (SynCTI) has recently achieved a major breakthrough on this front.

The researchers, who are also from the NUS Yong Loo Lin School of Medicine, have engineered strains of a naturally occurring beneficial gut bacterium to function as programmable therapeutics capable of restoring metabolic balance across the gut, liver and brain. The researchers redesigned *Lactobacillus plantarum* WCFS1 — a well-characterised commensal bacterium — into two complementary therapeutic strains. The first strain absorbs excess ammonia from the gut and converts it into branched-chain amino acids (BCAAs), essential nutrients that are depleted in HE patients. The second strain breaks down L-glutamine in the gut before it can be converted into yet more ammonia, cutting off a key source of the toxin.

Laboratory studies using a cocktail of both strains for HE showed that the combination reduced circulating ammonia by up to 10-fold and lowered brain ammonia to levels comparable to those in healthy conditions.

A patent application has been filed to support translation of the technology towards clinical use. The team’s next steps include evaluating the long-term performance of the engineered strains and expanding the platform to target other diseases linked to metabolic imbalance.