

MEDIA RELEASE

Gut bacteria could hold the key to treat and prevent strokes in young people, which are on the rise.

Cerebral cavernous malformations (CCMs) are a relatively common cause of stroke and seizure with no effective medical treatment available to patients. One in six Australians will have a stroke in their lifetime. Game-changing new research by scientists at the Centenary Institute, in collaboration with multiple institutions in the United States, recently published in *Nature*, has found that gut bacteria could be the key to prevent potentially deadly strokes. This discovery could lead to the first effective, non-invasive treatment option for patients with CCM. Dr Xiangjian Zheng (Head of the Centenary Institute's Cardiovascular Signaling Laboratory) says, "the current work identifies genetic factors and environmental factors work together to cause disease, which gives us scientific base for a totally new direction to seek for non-invasive treatment for this devastating disease." This is a welcome revelation for patients with CCM who, presently, are given little hope due to the lack of therapies available to treat or prevent the disease. Currently, lesions can only be treated by surgery when the damage is accessible. Alternatively, patients are given palliative therapies.

Researchers have built on previous knowledge, whereby they discovered that the damage in three particular genes, CCM1, CCM2 and CCM3, are the underlying causes of this disease. The occurrence of symptomatic lesions and lesion severity are highly variable among CCM gene mutation carriers, suggesting both genetic and environmental factors influence the occurrence of this disease.

Scientists used mouse models to search for the molecular "driver" of CCM disease. They discovered those with the same genetic defect, maintained in different environments, give different outcomes of disease severity. To search for the underlying reason for this phenomena, they discovered inflammation-related activation of the molecular apparatus (TLR4 signalling) can trigger the disease in resistant mice with damaged CCM genes. The inflammatory signal, causing CCM, can come from bacterial infection. They found the composition of bacterial community or 'microbiome' in the gut has a major effect of disease outcome. This means abolishing gut bacteria could prevent CCM disease.

It's widely known that the health of our microbiome, often referred to as the 'second brain', significantly influences our overall health. This new study reveals the microbiome could also be the secret to specifically preventing strokes caused by CCM – especially in the young. Identifying gut bugs and inflammatory factors as major drivers for this brain vessel disease, opens the door to design non-invasive intervention strategies to prevent or stabilize CCM disease. This will have a major benefit to patients, many of them under 40, who currently have no treatment options available to them.

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