Gene inhibitor could help slow thrombosis in COVID-19 patients

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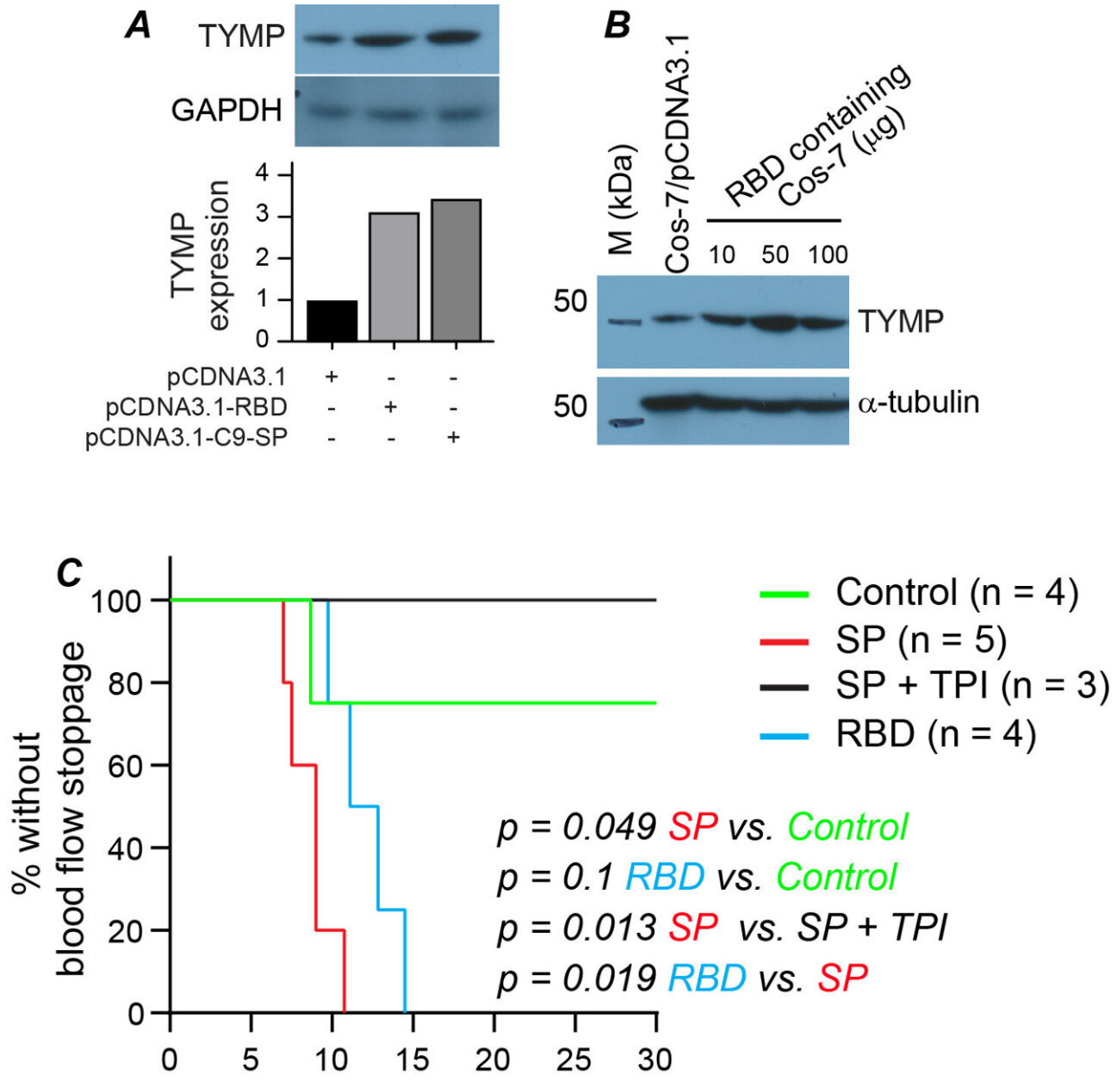

A & B. SARS-CoV-2 spike protein and its receptor-binding domain enhanced thymidine phosphorylase expression in BEAS-2B cells. C. SARS-CoV-2 spike protein and its receptor-binding domain enhanced thrombosis in the K18-hACE transgenic mice. SP-enhanced thrombosis was inhibited by Tipiracil -TPI-, a selective thymidine phosphorylase inhibitor. Credit: W. Li et al, SARS-CoV-2 Spike Protein Enhanced Thrombosis is inhibited by Tipiracil in Mice [abstract], (2022)

Findings from a new study at the Marshall University Joan C. Edwards School of Medicine show that a thymidine phosphorylase (TYMP) inhibitor could help slow thrombosis in COVID-19 patients.

Expression of TYMP, the gene that plays an important role in platelet activation, thrombosis and inflammation, is significantly increased in COVID-19 patients. The increase of TYMP occurs earlier than other inflammation markers, such as C-reactive protein, and is positively correlated to D-dimer, a marker of thrombotic event, as well as COVID-19 severity. This suggests that SARS-CoV-2 binding to host cells via its spike protein may enhance or trigger thrombosis. In addition, all COVID-19 vaccines, which use SARS-CoV-2 spike protein as an antigen to generate anti-SARS-CoV-2 antibody, also reportedly have thrombotic side effects. Control of SARS-CoV-2 associated thrombosis has significantly reduced COVID-19 mortality.

"This study is the first to demonstrate that the SARS-CoV-2 spike protein is sufficient to enhance expression of TYMP as well as activation of NF-kB, the major pro-inflammatory transcription factor in human bronchial epithelial cells," said Wei Li, Ph.D., associate professor of biomedical sciences at the Joan C. Edwards School of Medicine and lead author on the study. "Our study also indicates that TYMP could be a novel biomarker for diagnosing COVID-19 and a therapeutic target for COVID-19-associated thrombotic complication."

Li and his team presented the research last month at the International Society on Thrombosis and Haemostasis (ISTH) during its 2022 Congress, an international meeting in the field of thrombosis and hemostasis, held in London, England.

Using a human ACE2 gene, which mediates SARS-CoV-2 invading host cells, transgenic mice and a murine thrombosis model, the researchers observed for the first time that intraperitoneal injection of the SARS-CoV-2 spike protein to mice enhances thrombosis, which can be inhibited by tipiracil, a selective TYMP inhibitor and FDA-approved drug.

In addition to Li, Renat Roytenberg, Autumn DeHart, Krista Denning, Ph.D., and Hong Yue, Ph.D. served as co-authors on the study.

The researchers are seeking collaborators and plan to collect patient samples to develop TYMP as a biomarker for diagnosing COVID-19 severity. Additional studies are ongoing to clarify the mechanisms that mediate SARS-CoV-2 spike protein increased TYMP expression as well as the potential effect of TYMP in long COVID-19.

More information: W. Li et al, SARS-CoV-2 Spike Protein Enhanced Thrombosis is inhibited by Tipiracil in Mice [abstract], (2022). abstracts.isth.org/abstract/sa … y-tipiracil-in-mice/

Provided by Marshall University Joan C. Edwards School of Medicine