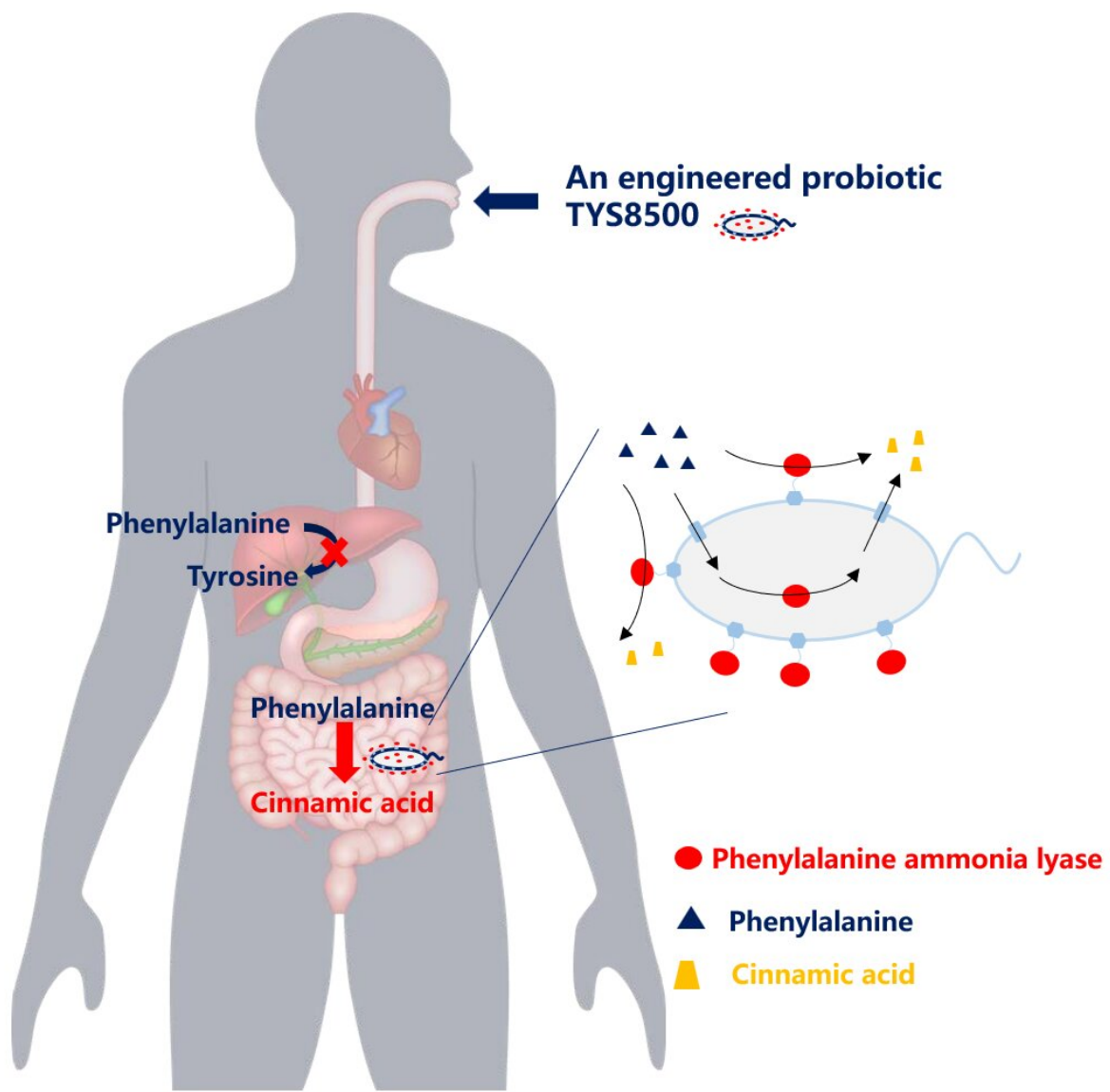


Phenylalanine degrading probiotics are a more effective live biotherapeutic for phenylketonuria

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Patients with phenylketonuria are unable to metabolize phenylalanine in the liver as healthy people do. They metabolize phenylalanine in the intestine through oral administration of the engineered probiotic TYS8500. Credit: Science China Press

Research published recently in *Science China Life Sciences* led by Prof. Sheng Yang from the Key Laboratory of Synthetic Biology, Chinese Academy of Sciences and a collaborating company, developed an engineered probiotic with better efficacy in a mouse model of phenylketonuria.

Phenylketonuria, a disease resulting in the disability to degrade phenylalanine is an inborn error with a 1 in 10,000 morbidity rate on average around the world which leads to neurotoxicity. The prevailing and predominant treatment is restricting [dietary intake](#) supplemented with specifically designed medical foods.

Oral administration of recombinant phenylalanine ammonia lyase-expressing probiotics can degrade phenylalanine in the patient's intestine into a non-toxic and urinary excreted metabolite, which has advantages of safety and high accessibility for [phenylketonuria](#). The challenge is whether the activity of the engineered [probiotic](#) on phenylalanine is high enough to reduce the patient's blood phenylalanine level below the safety line.

The novelty of the reported engineered probiotic is that in addition to enhancing the phenylalanine transport protein to intake intestinal phenylalanine into the probiotic for degradation, the phenylalanine ammonia lyase is also displayed on the surface of the probiotic so that it directly accesses phenylalanine in the intestine, thus overcoming the

[phenylalanine](#) transport bottleneck. For the researchers, these results indicated that developing similar live biotherapeutic products for displaying enzymes on the surface of probiotics is an effective strategy to enhance the drug efficacy.

More information: Yu Jiang et al, Expression of phenylalanine ammonia lyase as an intracellularly free and extracellularly cell surface-immobilized enzyme on a gut microbe as a live biotherapeutic for phenylketonuria, *Science China Life Sciences* (2022). [DOI: 10.1007/s11427-021-2137-3](#)

Provided by Science China Press

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