

#### Our Goal

1. Design a synthetic strain based on *E. coli* 1917 for the production of 5-HTP and GABA (gamma-aminobutyric acid).
2. Ingest probiotics to regulate the balance of human intestinal flora, and help groups with depression to recover with a gut-brain axis approach.

#### Motivation

1. Depression has become the fourth largest disease in the world, and its impact on human beings is self-evident. There are currently 322 million people with depression worldwide. Depression is also a serious problem in China. The incidence of depression in my country is 6.1%. Since 1990, the reported incidence of depression has increased by 10 to 20 times, and the prevention and treatment of depression has been included in the focus of national mental health work. Therefore, it is urgent to solve the problem of depression.
2. Today's drugs containing 5-HTP and GABA are not effective, there are many side effects, and the effect on patients with depression is not obvious.

Depression, as a disease with an increasing incidence in recent years, has gradually increased the attention of its patients. Because of this, the development of new treatment options for depression has become a top priority.

We decided to produce 5-HTP and GABA in our experiments by using a strain based on a modified *E. coli*, *E. coli* Nissle 1917 (EcN). 5-HTP, also known as 5-hydroxytryptophan, is the chemical precursor of serotonin, a neurotransmitter that regulates a series of metabolic and psychological functions in the human body. The human body produces serotonin through the following pathways: tryptophan  $\rightarrow$  5-HTP  $\rightarrow$  serotonin. 5-HTP is decarboxylated to serotonin (5-hydroxytryptamine or 5-HT) by the enzyme aromatic-L-amino-acid decarboxylase with the help of vitamin B6. This reaction occurs in nerve tissue and the liver. The human tryptophan hydroxylase 1 (TPH1) gene was overexpressed in Nissle 1917 (EcN) to encode tryptophan hydroxylase 1, which catalyzes the production of tryptophan in humans. Tryptophan hydroxylases catalyze the bipterin-dependent monooxygenation of tryptophan to 5-hydroxytryptophan (5-HTP), which is subsequently decarboxylated to form the neurotransmitter serotonin (5-hydroxytryptamine or 5-HT). It is the rate-limiting enzyme in the biosynthesis of serotonin.

We plan to produce  $\gamma$ -aminobutyric acid (GABA) by overexpressing the GadB (amino acid decarboxylase B) gene in EcN by converting glutamate to GABA. GABA is primarily synthesized from glutamate by glutamate decarboxylase (GAD) with pyridoxal phosphate (the active form of vitamin B6) as a cofactor. This process converts glutamate (the principal excitatory neurotransmitter) to GABA (the principal inhibitory neurotransmitter).

The current research has proved that gamma-aminobutyric acid has the effect of improving the quality of sleep, and serotonin, which is produced by 5-hydroxytryptophan, is also a messenger that can evoke pleasant emotions. Anti-depression drugs such as fluoxetine hydrochloride work by increasing serotonin levels in the brain. Therefore, our team believes that the introduction of the modified Nissle 1917 into the stomach and the successful operation will significantly ameliorate depression.

## LZU-HS-Pro-A

## Psychiatric Disorders Regulating Probiotics

#### Result

Our autonomous genetically modified *E. coli* can already autonomously produce 5-HTP and GABA neurotransmitters in the gut. Through the test of liquid chromatography, we can conclude that our genetically modified *Escherichia coli* has high efficiency and can play a role in the disease of patients with depression.

#### Safety

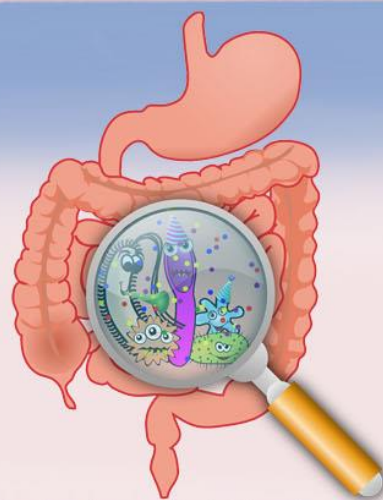
A system is designed to prevent strains from escaping suicide, control the production system, and control the death system, so as to avoid the pollution of the environment caused by genetic modification.

#### Perspective

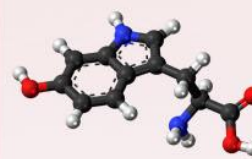
First of all, in the preparation of probiotics, we expect to use many innovative technologies, such as multi-layer coating technology, crystal ball probiotics, sustained release technology, suppository.

Second, we had the idea to reconstruct the biosynthesis and regeneration pathway of human tetrahydrobiopterin (BH4).

Finally, in addition to alleviating depression, the application of this strain can have other applications. Such as: senile dementia, microbial, aquaculture feed additives, etc.



From: <https://www.alexmanos.co.uk/psychobiotics-probiotics-for-mental-health/>



Molecular structure of 5-HTP, from: <https://en.m.wikipedia.org/wiki/5-Hydroxytryptophan>



Molecular structure of GABA, from: [https://en.m.wikipedia.org/wiki/GABA\\_receptor](https://en.m.wikipedia.org/wiki/GABA_receptor)