Targeting the Gut-Brain Axis: A Multi-Pathway Engineered Yogurt for Mild Depressive Symptoms

Depression affects an estimated 332 million people globally, yet current treatments like Selective Serotonin Reuptake Inhibitors (SSRIs) offer limited efficacy by failing to address underlying physiological factors such as gut inflammation and microbiome imbalances. This project proposes a functional yogurt containing an engineered probiotic to mitigate mild, subclinical depressive symptoms via the gut-brain axis. Yogurt provides a nutrient-dense matrix that supports gut health and reduces inflammation. The probiotic *Bacillus subtilis* (BS50) will be genetically modified to produce bile salt hydrolase (bsh). By inserting the bsh1 gene from *Lactobacillus plantarum* RK21, the engineered BS50 will decrease gut inflammation through interruption of interleukin-6 (IL-6), an inflammatory cytokine elevated in depression. Additionally, native BS50 contains the trp operon for tryptophan synthesis, providing the essential precursor to serotonin, a neurotransmitter whose dysregulation is linked to mood disorders. Following successful modification, the engineered BS50 will be incorporated into a yogurt culture for fermentation, ensuring delivery within a familiar and accessible food matrix. This food-based intervention integrates synthetic biology, nutrition, and microbiome science to offer a promising, sustainable alternative to traditional pharmacotherapies for managing milder depressive symptoms.