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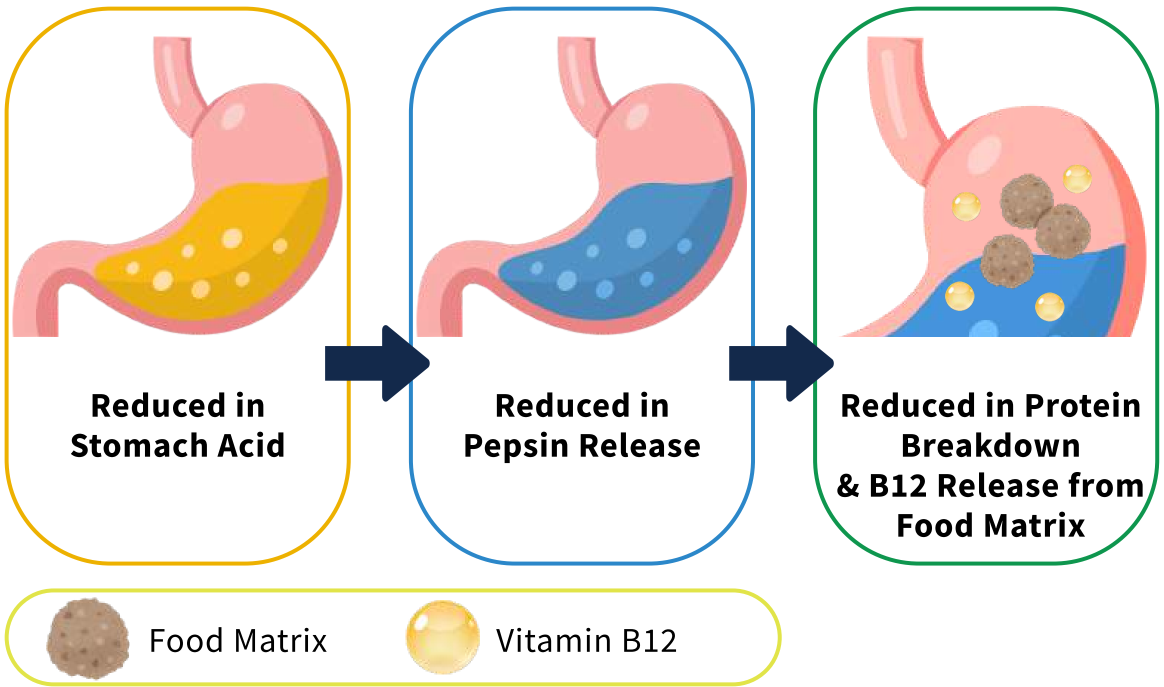
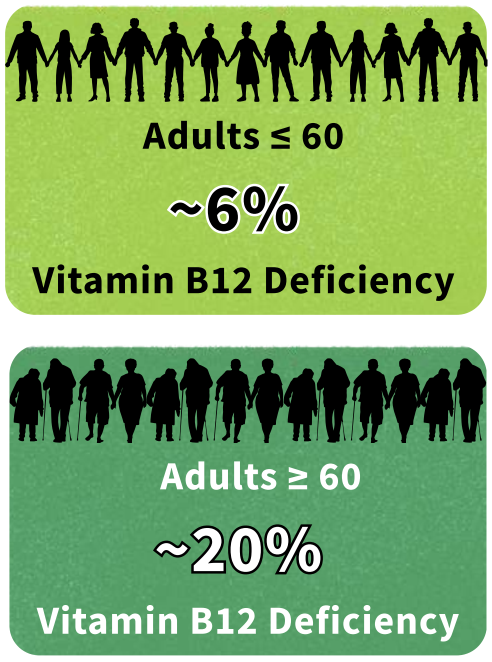
The Building Blocks of Micronutrients:
Vitamin B12 Production through Precision Fermentation

Why B12 Matters

Vitamin B12, also known as cobalamin, is a key micronutrient in humans for energy production, red blood cells formation, DNA synthesis, and the function and development of the brain and nerve cells. However, consuming enough B12 is increasingly challenging with aging and dietary shifts.





As people age, reduced stomach acid and pepsin release lead to a decrease in protein breakdown—less B12 is released from food. Deficiency in adults rises from 6% (under 60) to about 20% (over 60).

B12 Naturally Found in Animal Foods ✔

B12 Not Naturally Found in Plant Foods ✘

B12 can be found in many foods, but it is naturally found in foods of animal origin and not in plant foods, unless artificially fortified, or through microbial fermentation. With more people moving toward plant-based diets, B12 deficiencies could be further amplified.

When people are B12 deficient, fatigue, brain fog, low moods, or worse, even nerve damage could arise. Despite Singapore's thriving food culture, "hidden hunger" quietly emerges. People consume enough calories and feel full, yet they lack vital micronutrients. B12 is difficult to source sustainably. Neither plants nor animals can synthesize it—only bacteria can. It is naturally present in animal-derived foods rather than plants as B12 is produced by microorganisms present in their digestive tract and absorbed and stored in the muscle. Advances in metabolic engineering then make it possible to produce B12 in engineered microorganisms through precision fermentation on a large scale.

ILLINOIS ARCS ADVANCED RESEARCH CENTER AT SINGAPORE

PreFerS CENTRE FOR PRECISION FERMENTATION AND SUSTAINABILITY

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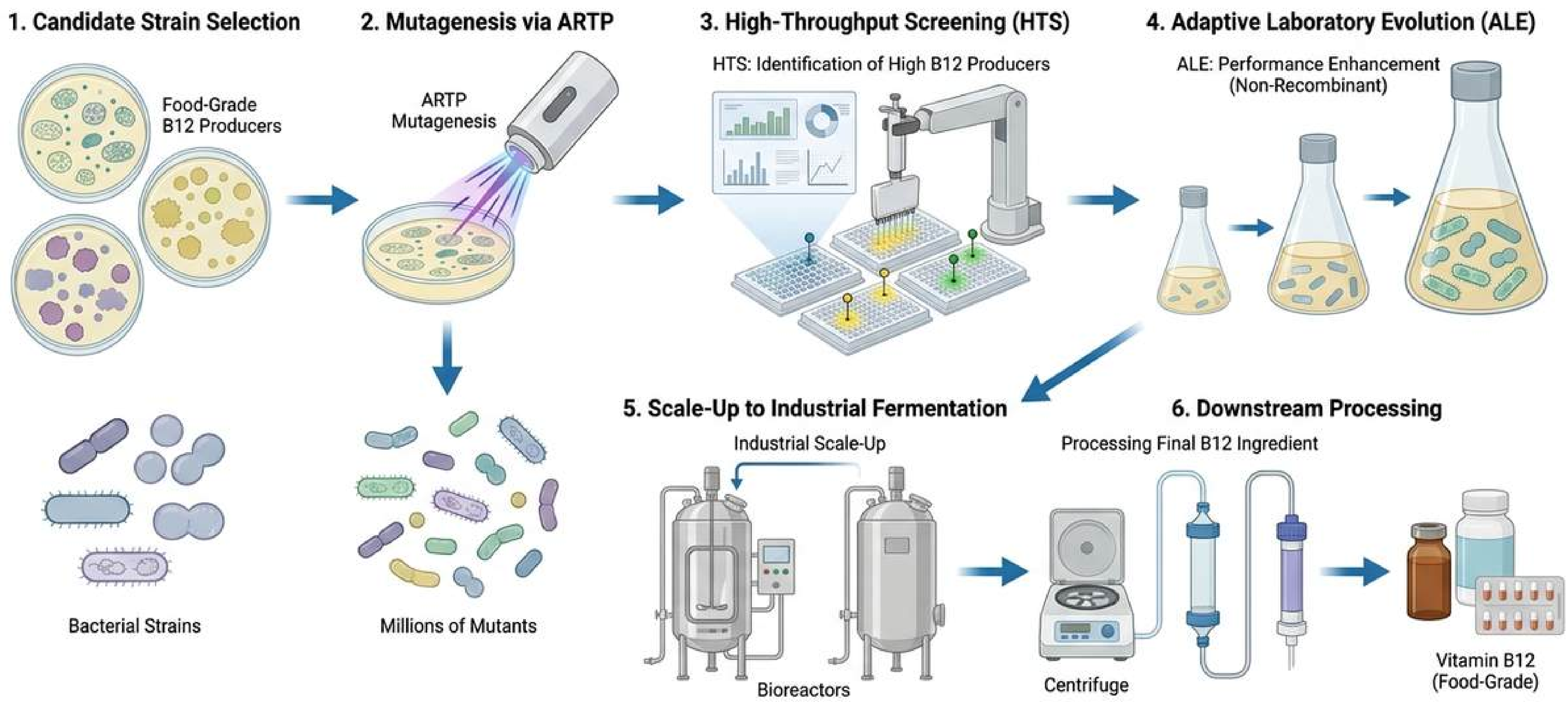
A Precision Fermentation Approach to Produce B12 Enriched Foods

Employing both non-genetically modified (non-GM) and GM approaches, PreFerS aims to use food-grade microorganisms to overproduce vitamins in fermented foods, ensuring economical and efficient vitamin production.

Non-Genetically Modified Approach



This approach begins with selecting candidate food-grade bacterial strains known to produce B12. High-throughput screening (HTS) is then used to efficiently manage and evaluate millions of mutants obtained from atmospheric and room-temperature plasma (ARTP) mutagenesis. Once promising high producing strains are identified using our HTS platform, the strains' performance will be further enhanced using non-recombinant technologies, such as adaptive laboratory evolution (ALE). The mutated and evolved strain will then be scaled up through an industrial framework, followed by downstream processing to process the final B12 ingredient.

Genetically-Modified Approach

Progressing from the selected and mutated strains from the non-GM workflow, metabolic engineering and ribonucleoprotein-(RNP)-based genome editing are applied to drive higher production of B12 in native B12 producing strains, or strains unable to produce B12. Key genes in the B12 biosynthesis pathway are overexpressed to boost precursor synthesis and product conversion. To maximize yield, combinatorial optimization of promoters and ribosome binding sites is conducted, utilizing only the genes and regulatory elements derived from food-grade microorganisms to streamline DSP and regulatory compliance.

This dual approach produces the essential vitamin while securing the micronutrients needed for a healthier future. As consumer preferences shift and populations age, hidden hunger remains a public health concern. Scaling up Vitamin B12 production through safe, food-grade biotechnology tackles these challenges sustainably without harming the environment.