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Essential Criteria for Use of Novel Microbial Hosts for Industrial Biotechnology Applications

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An efficient host microbial system that can meet industrial standards can be selected with defined substrate, product and bioprocess considerations with possibilities of strain improvement through Adoptive Laboratory evolution conditions for optimized industrial bioprocess.

With varied choices of suitability of microbial systems for the industrial use, some parameters are more relevant in all processes of industrial considerations. These include growth efficiency of microbes, availability of tools for manipulation, ease of handling, tolerance capability, and metabolic capacity of hosts. A strategy for exploitation of novel microbial system is presented in Fig.1.

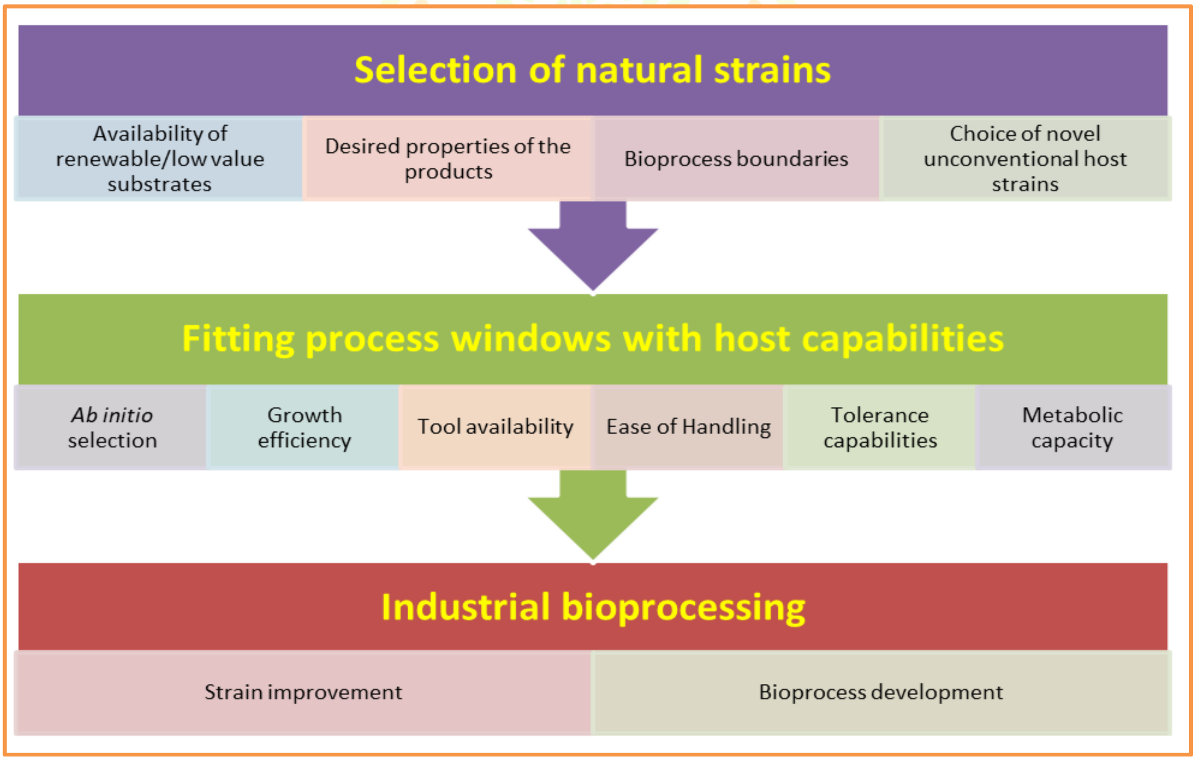

Fig.1. novel microbial host systems selection strategies for industrial biotechnology

Characteristics of novel hosts to reach industrial maturity

1. Growth efficiency: Growth efficiency is a key factor for in reducing the cost of production in all the biotechnological processes. So, a novel host must satisfy the choice of fast-growing capability with high growth rate (μ) and high specific substrate consumption rate (qS) under varied culture conditions. This parameter also considers low maintenance demand, viability, high biomass yield resulting in product formation uninfluenced by the growth perturbations. Yield and the growth rate of microbes serve as key performance indicators. These traits can be efficiently enhanced by using genome engineering tools (Wynands et al., 2019).

2. Tool availability: *E. coli* has been fully exploited for various industrial applications due to genomic engineering as a model organism. However, this cannot be extrapolated to non-model host systems as such due to several challenges; nevertheless, the intrinsic properties of the novel host systems open up possibilities for developing genetic engineering tool boxes for these host systems. Genetic manipulation deployed in manipulation of metabolism using synthetic biology tools and the design of CRISPR/Cas based systems has been remarkable tools for the strain improvement to make these novel hosts suit industrial capabilities. Time to market and the versatility of the tools to manipulate are key performance indicators.

3. Ease of Handling: Ability to handle any microbe in a laboratory scale or industrial environment makes no difference and easy of handling remains the choice. Growing microbes in a simpler media can cut down cost of production and helps widen the applicability of such hosts for use in several industrial applications. Handling of hosts is based on several factors including the robustness of the strain to grow under varied temperature, gas exchange gradients and recalcitrant substrate conditions (Ankenbauer et al., 2020). Novel hosts used in the pipelines should be safe to handle and be Generally Recognized as Safe (GRAS). The choice of host remains with lack of over-flow metabolism and by product formation with capability of scaling up being a key performance indicator.

4. Tolerance: A novel system should be capable of withstanding varied substrate and product concentrations that make them best choice for industrial applications. A key attribute that decides tolerance of novel hosts is how they perform well under fluctuating process conditions especially the dissolved oxygen concentration, pH regimes and salt concentrations under industrial scale production environments. This tolerance capability can be improved through the approach of adaptive laboratory evolution (ALE) (Mohamed et al., 2020) however this approach has certain limitations and can be detrimental at times(Cheng et al., 2019). ALE has been able to increase the temperature tolerance capability of model organism E. coli up to about 48°C, beyond which it's lethal considering the damages to the cellular metabolism leading to instability (Jarzab et al., 2020). However, microbes belonging to Bacillus or Thermus genera can grow and withstand much higher temperatures. Titer values and substrate flexibility are key performance indicators for the tolerance of host systems.

5. Metabolic capabilities: Metabolic capabilities of any host systems lie in their adaptability to various substrates and are a prerequisite to be considered for deployment in the industrial applications. Contrarily, valorization of the alternative carbon sources like C1 substrates needs use of more specialized microbial host systems. A key example is a thermophile, *B. methanolicus*, with ability to use limited alternative carbon sources, but can metabolize methanol more efficiently. Substrate and product flexibilities remain the key indicators for the efficient performance of the host systems.

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