PICHIA PASTORIS, A PROMISING MICROBIAL CELL FACTORY FOR CONTINUOUS BIOMANUFACTURING

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Such other industries did in the past, currently, the Industrial Biotechnology is involved in the transition from batch to continuous manufacturing in order to exploit the benefits of the continuous production. Among them, some are considered specially relevant such as; flexibility in operations, higher productivity and quality, decreased cost, smaller facilities as well as the integration and the simplification of the bioprocesses. However, the use of these cultivation mode in large scale biomanufacturing processes is still infancy and several drawbacks need to be addressed in the next future.

The cell factory Pichia pastoris, recently reclassified as Komagataella phaffii, is currently considered to be one of the most effective and versatile systems for the production of heterologous proteins and metabolites of interest. As a yeast, it combines the advantages of the microbial expression systems, such as fast and robust growth in defined media, and the ability to perform typical eukaryotic post-translational modifications. Furthermore, this host is able to target proteins extracellularly while secreting very low levels of native proteins.

One of the main feature of this cell factory is that P. pastoris is a metilotrophic yeast, and thus has the ability to grow on methanol as a sole carbon source, which leads to a achieve very high expression rates of an enzyme involved in the methanol metabolization (Aox1). This fact made that this cell factory was used in large scale to produce single-cell protein (SCP), then adapted to host from recombinant protein production. Up to date, over 5.000 proteins have been produced in Pichia. The excellent results obtained attracted the scientific community, which have continuously implementing relevant improvements in the expression system becoming into an excellent alternative to produce both recombinant biopharmaceutical and industrial enzymes, as well as metabolites, which its interest is increasing during the last years towards achieving a sostenible biocircular economy.

Currently, in the market are available different alternative expression systems that allows to regulate the expression of the target protein by the selection of the carbon source and/or the cultivations conditions. By the understanding of this regulation from the strain engineering point of view, is essential to develop efficient culture strategies from a bioprocess engineering approach. In this sense, continuous cultures based on alternative strategies have been implemented with Pichia producing different products of interest. For its application in large-scale production processes, is essential to develop stable and robust strains and bioprocesses which assure to maintain high production rates, product quality and bioprocess repdroducibility over long operation times.