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Pichia pastoris as One of the Best Choice for Expression of Biopharmaceutical Proteins

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Dear Editor,

Bioproducts such as vaccines, antibodies, antiviral peptides like interferon-γ, insulin, growth hormone (GH) and erythropoietin are models of biopharmaceuticals which are applied for therapeutic goals in modern medicine; In 2014, the global market has been estimated 44 billion $ for recombinant biopharmaceutical proteins which is predicted that extended to 70 billion $ in 2010 (1, 2). In the other hand, during last decades, the mammalian cell lines and *Escherichia coli* expression systems are available options for expressing and production of recombinant proteins; but there are serious problems such as slow growth rate replication, requiring to expensive synthetic media and susceptibility to viral contamination in mammalian cell lines, while bacterial expressing systems are associated with phage contamination, need to purification of bacterial toxins and limited in post modification translation (PMT) process (1-3). Beside these problems, increasing globally demands of biopharmaceutical proteins have been major reasons for developing genetic-manipulation process to introduction of new efficient expressing system which high-yield economical (2, 4).

Pichia pastoris (currently re-classified as *Komagataella pastoris*) is methylotrophic yeast that known as one of the great expressing machine in biotechnology works which is able to produce about more than 500 high titers heterologous proteins since 1750s until now (2, 5). This microorganism was first introduced by Phillips Petroleum as animal food-additive based on a high cell density fermentation process employing methanol as sole carbon source. This fermentative-yeast can be easily manipulated that successfully secret numerous heterologous proteins with high titers, while secreting low quantities of endogenous proteins (5).

P. pastoris expression systems are usually based on the methanol-induced alcohol oxidase (AOX1) promoter which control expression of foreign genes by oxidation of methanol to formaldehyde and hydrogen proxide. *P. pastoris* strains was classified in three different phenotypes according to utilizing methanol. (1) Mut^+ that have functional form of the both AOX genes (AOX1-2); this strains require large amounts of methanol and dependency of type Mut^+ to high concentration of methanol lead to serious problem to control of expressing level of foreign genes. (2) Mut^s strains with deletion in AOX1 gene (AOX1 expression constitute almost 90% of functional proteins in *P. pastoris*) which are low growth rate. (3) Mut^- strains that both AOX1 and AOX2 were deleted in this strains that cannot grow on methanol (2, 3). Moreover, methanol is toxic for human, flammable and hazardous substance; therefore, another promoter are introduced such as GAP, FLD1, PEX8, and YPT7 which are not required to methanol. for example, GAP (glyceraldehyde 3-phosphate) promoter is continuous promoter that expressed on glucose or glycerol contained growth media; according to literatures, there are opposed opinion in efficacy of GAP promoter compared with pAOX1-2 (2, 3, 6).

Pichia pastoris is an expert expressing system with more popularity due to (1) rapid growth rate on simple media, (2) expressing low quantities of endogenous protein, (3) prevention of viral or bacterial toxins contamination, (4) easily genetic engineering, (5) post modification translation consisting glycosylation, folding, disulfide bond, acylation, methylation, proteolytic and targeting process, (6) simple promoter inducing and (7) recombinant protein can easily extracted without harvesting of any yeast cells (2, 3) *Saccharomyces cerevisiae* is classic eukaryotic expressing system and more famous than *P. pastoris*; glycosylation patterns of these yeasts are different. Whoever, mannosylation and terminal a-1,3-mannose linkages are created by *S. cerevisiae*, this process cause of poor serum half-life or even allergenic and inducing immune-response against biopharmaceutical proteins. Also research approved that expression of secretory proteins in *P. pastoris* is better than *S. cerevisiae* (7, 8).

In summary, *P. pastoris* is methylotrophic yeast which has exclusive features (e.g. rapid growth rate, simple requirement, controllable promoter and post modification

translation process) to developed it as the best choice of eukaryotic expressing system; Review of the literatures show that *P. pastoris* is proper host for various industrial enzymes or biopharmaceutical product with efficient economically cost.

Footnotes

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