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In silico analyses of several signal peptides for the excretory production of phenylalanine ammonia-lyase in *Escherichia coli*

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Statement of the Problem: Day by day, the demand for biotherapeutics and recombinant proteins is increasing. Herein, cytoplasmic expression in prokaryotic and eukaryotic hosts has been widely accepted. However, there are several obstacles in the large-scale production of recombinant proteins. Recombinant proteins might form inclusion bodies or be degraded by proteases. Endogenous proteins might also interfere with the folding of a recombinant secretory protein. These factors, as well as the complicated downstream purification process, will result in loss of protein yield. Moreover, the yield of recombinant protein is not only related to expression levels, but also to translocation efficiency. Thus, the translocation efficiency could be increased by using signal peptides. Phenylalanine ammonialyase (PAL), involved in the first step of the phenylpropanoid pathway, catalyzes the deamination of phenylalanine to cinnamate and ammonia. PALs are ubiquitous in plants and also commonly found in fungi; however, animal lacks it. They are of special interest in several medical and industrial applications, including preparation of low phenylalanine diet, treatment of phenylketonuria and certain neoplastic tumors. Although several methods have been applied in the production of PAL, the final titers of PAL are still low, thereby impeding considerable industrialization of this enzyme.

Objective: This study aims to evaluate a vast number of signal peptides, previously deposited in databases (1168 signal peptides), in order to select the most appropriate ones for secretory production of PAL.

Methodology & Theoretical Orientation: Herein, the SignalP tool was applied to determine the secretion efficiency as well as cleavage sites. Moreover, various physiochemical properties of signal peptides linked to the protein as well as secretory pathways were identified. Effects of signal peptide addition on antigenicity, allergenicity, and mRNA secondary structure of PAL were evaluated.

Findings: The appropriate candidates for high yield and efficient production of phenylalanine ammonia-lyse in *E. coli* were identified.

Recent Publications

1. Tsirigotaki A, De Geyter J, Šoštaric N, Economou A and Karamanou S (2017) Protein export through the bacterial sec pathway. Nature Reviews Microbiology 15(1):21–36.
2. Kong J-Q (2015) Phenylalanine ammonia-lyase, a key component used for phenylpropanoids production by metabolic engineering. RSC Advances 5(77):62587–603.
3. Cui J D, Qiu J Q, Fan X W, Jia S R and Tan Z L (2014) Biotechnological production and applications of microbial phenylalanine ammonia-lyase: a recent review. Critical Reviews in Biotechnology 34(3):258–68.
4. Ivankov D N, Payne S H, Galperin M Y, Bonissone S, Pevzner P A, et al. (2013) How many signal peptides are there in bacteria? Environmental Microbiology 15(4):983–90.
5. Low K O, Mahadi N M and Illias R M (2013) Optimisation of signal peptide for recombinant protein secretion in bacterial hosts. Applied Microbiology and Biotechnology 97(9):3811–26.

Biography

Hajar Owji completed her PharmD from Shiraz University of Medical Sciences. She is now working as a Research Pharmacist affiliated to the Department of Pharmaceutical Biotechnology. Her research interests are focused on Bioinformatics, Molecular Biology, and Biomolecular Pharmaceutical Sciences.

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