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Novel signal peptides improve the secretion of recombinant *Staphylococcus aureus* Alpha toxin$_{H35L}$ in *Escherichia coli*

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Secretion of heterologous proteins into *E. coli* cell culture medium offers significant advantages for downstream processing over production as inclusion bodies; including cost and time savings and reduction of endotoxin. Signal peptides play an important role in targeting proteins for translocation across the cytoplasmic membrane to the periplasmic space and release into culture medium during the secretion process. Alpha toxinH35L (AT_{H35L}) was selected as an antigen for vaccine development against *S. aureus* infections. It was successfully secreted into culture medium of *E. coli* by using bacterial signal peptides linked to the N-terminus of the protein. In order to improve the level of secreted AT_{H35L}, we designed a series of novel signal peptides by swapping individual domains of modifying dsbA and pelB signal peptides and tested them in a fed-batch fermentation process. The data showed that some of the modified signal peptides improved the secretion efficiency of AT_{H35L} compared with *E. coli* signal peptides from dsbA, pelB and phoA proteins. In particular, one of novel signal peptides improved the yield of secreted AT_{H35L} by 4-fold in the fed-batch fermentation process and at the same time maintained the expected site for signal peptide cleavage. Potentially, these new novel signal peptides can be used to improve the secretion efficiency of other heterologous proteins in *E. coli*. Furthermore, analysis of the synthetic signal peptide amino acid sequences provides some insight into the sequence features within the signal peptide that influence secretion efficiency.

Biography

Soo Jin Han has completed her PhD from both KIST and Hanyang University in Korea and Post-doctoral studies from University of Alabama and University of Florida in USA. She has been working as a Scientist of the Department of Cell Culture and Fermentation Sciences at MedImmune, a Maryland based biotechnology development enterprise owned by AstraZeneca. She has much experience and great knowledge in mAb and non-mAb production in prokaryotic and eukaryotic expression platforms and published several papers in reputed journals.

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