

In Silico Evaluation of Different Signal Peptides for the Secretory Production of Human Growth Hormone in *E. coli*

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Abstract Various advantages of protein secretion have prompted scientists to search for secretory production of heterologous proteins. Signal peptides are one of the most important factors for prosperous secretion of the recombinant proteins. The aim of this study was to evaluate 23 different signal peptides and theoretically determine suitable ones for secretory production of the human growth hormone (hGH) in the *E. coli* host. The signal peptide sequences and the precise location of their cleavage sites were predicted using SignalP 4.0 server. Accordingly, six of the signal peptides, including hGH, major outer membrane lipoprotein, protease VII, protein TolB, periplasmic protein TorT and beta-lactamase TEM were excluded from the further study, due to their inappropriate cleavage scores. Different physico-chemical properties, which are essential for selecting a proper signal peptide, were evaluated using ProtParam and Solpro as the most accurate and reliable servers. Computational analysis of the above-mentioned factors, indicates that outer membrane protein C, fimbrial chaperone SfmC, outer membrane protein F and disulfide interchange protein DsbA can theoretically be suitable signal peptides for hGH secretion.

Keywords Signal peptide · Human growth hormone · *E. coli* · Bioinformatics

Introduction

Human growth hormone (hGH) or somatotropin is a single-chain polypeptide, which is synthesized in the pituitary gland and contains 191 amino acid residues with a molecular mass of 22 kDa (Isaksson et al. 1985; Tritos and Mantzoros 1998). A mature form of hGH is derived from the 217 amino acid precursor, after the signal peptide (26 amino terminal residues) has been removed. Due to its fundamental role in a variety of biological functions, hGH has a broad range of therapeutic applications such as treatment of hypopituitary dwarfism, bone fractures, skin burns, HIV wasting syndrome and genetic disorders such as Turner's syndrome and Down's syndrome (Hahm and Chung 2001; Özdamar et al. 2009; Roehr 2002). The enteric bacterium *Escherichia coli* (*E. coli*) is considered to be the powerhouse for the recombinant production of the hGH, since this protein does not require post-translational modifications like glycosylation (Baneyx and Mujacic 2004; Ramanan et al. 2010; Soares et al. 2003). Despite several advantages of *E. coli*, including convenient growth on inexpensive substrates, rapid biomass accumulation (Arora and Khanna 1996; Baneyx and Mujacic 2004), and well-characterized genetics and physiology (Marr 1991), there are some problems in obtaining considerable yields of correctly folded proteins. Failure of protein to rapidly reach a native conformation causes degradation into insoluble aggregates or inactive proteins called inclusion bodies (Baneyx and Mujacic 2004; Choi and Lee 2004; Ventura and Villaverde 2006). One approach to solve these problems is to transfer the protein into the periplasmic space of

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