Microbial Cell Factories

Poster Presentation

Production of human α_1 proteinase inhibitor from *Aspergillus niger*

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Background

α_1 proteinase inhibitor (α_1PI) belongs to the serin protease inhibitor (serpin) family; it is responsible for 90% of the trypsin inhibitory capacity of human plasma. Its primary physiological role is to inhibit neutrophil elastase that degrades elastin, collagen and proteoglycan and can cause extensive lung damage. α_1PI deficiency can result in lung emphisema in adults, liver disease in children and is also associated with cystic fibrosis, arthritis and other malignant conditions [1-3]. Human plasma-derived α_1PI is a licensed product used for replacement therapy. Although viral inactivation measures are taken, products derived from human plasma carry the risk of contamination with blood-borne pathogens, and therefore recombinant is an attractive alternative.

α_1PI exhibits a molecular mass of approximately 52 kD, has 394 amino acids, a single cystein residue and three carbohydrate attachment sites at asparagine residues 46, 83 and 247 [4,5]. Significant research effort was directed to produce recombinant human α_1PI in *E. coli* [6], yeast [7], transgenic mice and sheep as well as plant cells [3]. *E-coli* produced an unglycosylated product, the yeast produced incorrect glycosylation and the transgenic animals pose the same threats as plasma derived product.

Results

Human α_1PI was cloned and expressed in *Aspergillus niger*, filamentous fungus that can grow in defined media and had the ability to perform glycosylation. Submerged culture conditions were established: using starch as carbon source, 30% dissolved oxygen concentration, pH 7.0 and 28°C; 10 mg per liter of active α_1PI were secreted to the growth media in 40 hours. Controlling the protein proteolysis was found to be an important factor in the production from the *fungus*. The effect of carbon sources and growth conditions on the production and stability of the protein will be presented and evaluated.

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