

Large-Scale Fermentation and Purification of *rhLK8*, the Cryptic Apolipoprotein(a) Kringle Domain, Expressed in *Pichia pastoris*

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rhLK8, the cryptic apolipoprotein(a) kringle domain as an antiangiogenic protein, was expressed from *Pichia pastoris* and purified in large-scale. In a pressurized 300-L fermentor, a modified DO-stat fed-batch culture was performed to produce *rhLK8* using methylotropic yeast *Pichia pastoris* as a host. By regulating the vessel pressure, the limitation of dissolved oxygen associated with the feeding by DO-stat manner was overcome. *rhLK8* was captured directly from culture broth by batch type capturing method using cation exchanger. After capturing, *rhLK8* was further purified with cation exchanger and Lys-Affinity chromatography. The overall purification yield of *rhLK8* was approximately 50%. The finally purified *rhLK8* was free of endotoxin and was very stable at pH4.2.

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