High-level production of a C5aR antagonist by fed-batch cultivation of *Escherichia coli*

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Human complement fragment 5a (C5a) is a pro-inflammatory polypeptide with 74 amino acids produced during complement activation. C5a with elevated levels in the serum binds to a seven-transmembrane domain receptor, C5aR, and can induce the inflammatory disorders. Recently, a potent peptidic C5aR antagonist (C5aRA) was derived from the modification of the native C5a molecules but its production yield and solubility in cytoplasm of E. coli were not satisfactory. In this work, C5aRA was separately fused with three different fusion partners (MBP, NusA, Trx) at its N-terminus and then each fused gene was expressed in cytoplasm of E. coli. Among three fusion systems, fusion with MBP could give much higher production and solubility of the recombinant C5aRA in shake flask cultivation. After simple purification, it was successfully confirmed that a MBP-fused C5aRA has high binding activity to target C5aR. For the preparative scale production, fed-batch cultivation was also performed in 6.6 L jar bioreactor and the detailed results of fermentation will be presented.