Cationic amino acids tags inhibit profer folding of glucagon-like peptide-1 fused with ubiquitin expressed in recimbinant *Escherichia coli*

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Human glucagon like peptide 1 (GLP-1) is an incretin hormone that promotes biosynthesis and secretion of insulin. The GLP-1 fused with 6 lysines tag and ubiquitin (K6UbGLP-1) was mainly expressed as form of inclusion body in recombinant *Escherichia coli*. However, the elimination of 6 lysines tag from K6UbGLP-1 induced soluble expression of ubiquitin fused GLP-1. GLP-1 has 4 anionic amino acids, 3 glutamic acids and 1 aspartic acid, in the GLP-1 sequence of 31 amino acids. The electrostatic interaction between 6 lyinses tag and 4 negative charged amino acids of GLP-1 might hinder proper folding of K6UbGLP-1 and induce formation of insoluble aggregates during in vivo folding. 3 glutamic acids and 1 aspartic acid of GLP-1 were substituted to 3 glutamines and 1 asparagine, respectively, to eliminate negative charges in GLP-1. The mutation in GLP-1 suppressed the formation of insoluble aggregate as the fused form of GLP-1 mutant with 6 lysines tag and ubiquitin. Likewise, 6 arginines tag, 4 arginines tag and 6 histidines tag fused with ubiquitin and GLP-1 were aggregated in recombinant *E. coli*.