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A Nanoparticle-forming Folding Enhancer with High-affinity Binding Site for the HSP70 Chaperone Dnak

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Contrary to the results of direct expression, various human proteins (ferritin light-chain, epithermal growth factor, interleukin-2, prepro-ghrelin, deletion mutants of glutamate decarboxylase and arginine deiminase, and mini-proinsulin) were all soluble in *E. coli* cytoplasm when expressed with the N-terminus fusion of ferritin heavy-chain (FTN-H). Through systematic investigations, we have found that a specific peptide motif within FTN-H has high affinity for HSP70 chaperone DnaK, and the peptide motif was composed of a hydrophobic core of three residues (I, F, and L) and two flanking regions enriched in polar residues (G, Q, and R). It was also observed that all the recombinant proteins expressed with FTN-H formed spherical nanoparticles. Upon the supra-molecule formation, the supra-molecule size is likely to be limited by the assembly properties of FTN-H thereby keeping the self-assembled particles soluble. This study reports the dual function of ferritin heavy chain used for fusion expression and solubility enhancement of heterologous proteins: 1) high-affinity interaction with DnaK and 2) formation of self-assembled supra-molecules with limited and constant size, thereby avoiding undesirable formation of insoluble macro-aggregates of heterologous proteins