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Engineering of a tri-functional antioxidant enzyme with CuZn SOD, catalase and cell-permeable activities

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Oxidative stress has been recognized as an important factor contributing to progression of many diseases. Superoxide dismutase (SOD) and catalase (CAT) are two main antioxidant enzymes that function to balance the oxidative status. Synergistic action of these two enzymes which catalyze sequential reactions has been suggested to be more effective than either single one. To increase such synergy and improve cell permeable activity for intracellular application, in this study, a tri-functional protein bearing CuZn SOD, CAT and TAT cell penetrating peptide was genetically engineered. Co-expression of chimeric CAT-CuZn SOD and chimeric 6His-CuZn SOD-TAT resulted in a novel protein complex (CS/S-TAT) with 61% SOD and 100% catalase activities comparing to native enzymes. Treatment of L929 fibroblast cells with 0.1 μ M of the protein complex for 1 hour showed efficient protein transduction into the cells. Protection against paraquat-induced cell death by the transduced protein was also investigated. L929 cell viability was brought up to 88% upon pretreatment with 0.2 SOD units of the protein complex. Moreover, pre-treatment with the protein resulted in superior restoration of paraquat-induced L929 migratory dysfunction to native enzymes fused with TAT (6His-CuZn SOD-TAT and 6His-CAT-TAT). This study not only provided a novel strategy to produce multi-functional protein complexes which have multimeric nature but also provided an insight into the development of protective and therapeutic proteins against oxidative stress-related conditions.

Biography

Piriya Luangwattananun has completed her Bachelor's degree in Medical Technology with first degree of honor from Faculty of Medical Technology, Mahidol University in 2013. She has then joined fast track program offered by the faculty to pursue her PhD degree in the same major. She has been working on the thesis entitled "Engineering of Novel Tri-functional Antioxidant Proteins". Her works on genetic and protein engineering of antioxidant enzymes have shed light on new therapeutic approaches and also novel strategy to produce protein chimeras.

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