Improved TRAIL-based Therapeutics with Protein Nanoparticle

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TNF-related Apoptosis inducing ligand(TRAIL) is the member of TNF-superfamily discovered in 1995. It has attracted considerable attention as an anti-tumor agent due to Its characteristic of inducing apoptosis only in cancer cells, not in normal cells. However There are limitations such as low stability, low apoptotic activity of monomeric soluble TRAIL and the presence of resistant cancer cell populations. In this study, We designed the protein nanoparticle that can mimic the native trimeric form of TRAIL and simultaneously deliver doxorubicin, a chemical drug that can overcome TRAIL resistance. The ecto-domain of TRAIL was genetically fused to 3-axis of ferritin N-termini which created a trimeric TRAIL complex. The recombinant protein was expressed and self-assemble into nanoparticles with a diameter of ~25 nm in *Escherichia coli*. Also, using iron storage ability of the ferritin, doxorubicin was successfully loaded into inner cavity of ferritin nanoparticle using Cu(II). This designed protein nanoparticle could be a drug delivery platform that can improve therapeutic efficacy of TRAIL by mimicking its native trimeric form and overcoming TRAIL resistance.