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Enhanced antitumor effect of TNF-related apoptosis-inducing ligand by using endogenous IgG as carrier

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TNF-related apoptosis-inducing ligand (TRAIL), a member of TNF superfamily, specifically induces apoptosis of tumor cells. It is cytotoxic to death receptor-expressing tumor cells *in vitro* at the low concentration of nanomole. However, owing to the short serum half-life, TRAIL exerts poor *in vivo* antitumor effect in the preclinical test as well as in clinical trials. IgG is one type of long-acting proteins in plasma. IgG-binding might prolong the serum half-life thus enhance the *in vivo* antitumor effect of TRAIL. To endow the IgG-binding ability to TRAIL, a IgG-binding domain (IgBD) was genetically fused to the N-terminus of TRAIL. The fusion protein IgBD-TRAIL was similar to TRAIL in cytotoxicity. IgBD-TRAIL could bind both human IgG and mouse IgG and IgG-binding did not reduce its cytotoxicity. The serum half-life of IgBD-TRAIL in mice was 50-60 times longer than that of TRAIL and the tumor uptake of IgBD-TRAIL was 4-7 times more than that of TRAIL. In the treatment of mice bearing COLO 205 tumor grafts with average tumor volume of 150 mm³, a single dose of intravenously injected IgBD-TRAIL (5mg/kg) eradicated all tumor grafts within one week. However, the same amount of TRAIL only suppressed the tumor growth. Moreover, in mice bearing HCT116 or LS174T tumor grafts, intravenous injection of a single dose (5mg/kg) of IgBD-TRAIL definitely suppressed the tumor growth. But TRAIL showed a little antitumor effect in these mice, demonstrating that intravenously injected IgBD-TRAIL exerted greater antitumor effect than TRAIL. These results indicated that binding to endogenous IgG could prolong the half-life thus enhance the antitumor effect of TRAIL. IgBD-mediated IgG binding might be a novel approach for drug delivery.

Biography

Feng Yanru is a PhD student of Sichuan University, China. His expertise is focused on Immune modulatory engineering proteins. He has done his Bachelor's degree in Southwest University and his research Focus on Plant Protection

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