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Approaches to reduce immunogenicity of recombinant immunotoxins in order to have more efficient immunotherapy

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Recombinant immunotoxins (RITs) are proteins that contain a toxin fused to an antibody or small molecules being constructed by the genetic engineering technique. RITs can bind to and be internalized by cells and eliminate cancerous or non-cancerous cells by inhibiting protein synthesis. The clinical success of RITs in patients with a normal immune system is limited by their immunogenicity. Immunogenicity likely will be a major obstacle to the maintenance of therapeutic blood levels after multiple treatment cycles, as has been previously observed with several immunotoxins. To overcome this issue, scientists designed deimmunized RITs and developed a novel combination therapy to allow the deimmunized RITs to return to the bedside and be used for cancer treatment. In this paper, we briefly reviewed recent advances in the design of immunotoxins. There are various approaches including, humanization of the antibody fragment, elimination of immunodominant T- and B-cell epitopes of toxins, modification of immunotoxins with macromolecules like poly (ethylene glycol) and liposomes, and generation of immunotoxins with human endogenous cytotoxic enzymes like RNase, Granzyme B, and death-associated protein kinase 2 (DAPK2).

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