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Diphtheria Toxin

1. List Labs' products in the Diphtheria toxin group:

LIS149 - CRM_{197}, non-toxic mutant
LIS150 - Diphtheria Toxin, un-nicked
LIS151 - Diphtheria Toxoid

2. Key Attributes

Diphtheria toxin (DT) is a potent cytotoxin produced by the native organism *Corynebacterium diphtheriae* and purified to > 95% purity. This 58-kDa toxin has the ability to bind, enter and destroy cells carrying the diphtheria toxin receptor (DTR). Diphtheria toxin receptor is also known as heparin-binding EGF-like growth factor precursor (pro HB-EGF). Diphtheria toxin inhibits protein synthesis by modifying a key part of the cell's protein synthesis machinery, elongation factor 2 (EF-2), resulting in inhibition of protein synthesis, eventually leading to the death of affected cells.

Diphtheria toxoid is produced by chemically treating purified toxin and when prepared carefully, toxoid has many of the characteristics of the toxin with a much-reduced toxicity to animals. Appropriate dosages of toxoid will initiate formation of antibodies in animals. Peptides and polysaccharides may be conjugated to diphtheria toxoid and the conjugate used to vaccinate, producing antibodies to the conjugated material as well as to the toxoid.

Cross Reacting Material, CRM_{197} is a naturally occurring mutated toxin produced by *Corynebacterium diphtheriae* carrying a mutation, changing a single amino acid in the toxin gene which eliminates enzyme activity, making it less toxic. CRM_{197} has been used extensively in vaccines to carry and present attached peptides and polysaccharides to the immune system. Presentation by CRM_{197} generally increases the antibody titer to conjugated ligands and induces a beneficial memory T cell response.

3. Specific Requirements

These products can be handled in a laboratory setting using good laboratory techniques. They are not for use in humans and are not approved for diagnostic development.

4. Technical information

Immune carriers

Diphtheria toxoid and CRM_{197} are of great interest as reagent which stimulate a robust immune response. Fukushima et al evaluate a vaccine made by conjugating four meningococcal polysaccharides to diphtheria toxoid.

- Fukushima S *et al* A Safety and immunogenicity Study of a SingleDose of a Meningococcal (Groups A, C, W, and Y) PolysaccharideDiphtheria Toxoid Conjugate Vaccine (MEN-ACWY-D) in HealthyJapanese Participants (2018) Jpn J Infect Dis 71:402-407. **PMID:29962480**

Tobias *et al* describe the use of a peptide representing B cell epitopes conjugated to CRM197 to induce anti-tumor antibodies in mice.

Tobias J *et al* Enhanced and long term immunogenicity of a Hwe-2/neu multi-epitope vaccine conjugated to the carrier CRM_{197} inconjunction with the adjuvant Monanide (2017) BMC Cancer 17:118.**PMID: 28183282**.

Transgenic mice

Mice lack a receptor for DT and as a result are not sensitive to the toxin. Several mouse lines have been genetically engineered, adding DT receptors to specific cell types, allowing with the injection of DT, elimination of receptor-carrying cells. Data from studies with these mice provide significant information about the function of specific cell types within a living organism.

A review by Ruedl and Jung provides a list of nineteen DTR transgenic mouse strains developed to study just myeloid immune cells.

- Ruedl C and S Jung (2019) DTR-mediated conditional cell ablation-Progress and challenges European J of Immunology 48: 1114-1119.**PMID: 29974950**