Title: NMR Study of Mutations of Glycine-52 of the Catalytic Domain of Diphtheria Toxin

Authors: Simon Sauvé, Geneviève Gingras, Yves Aubin

PII: S0731-7085(17)31842-3
DOI: https://doi.org/10.1016/j.jpba.2017.11.056
Reference: PBA 11630

To appear in: *Journal of Pharmaceutical and Biomedical Analysis*

Received date: 18-7-2017
Revised date: 23-11-2017
Accepted date: 25-11-2017

Please cite this article as: Simon Sauvé, Geneviève Gingras, Yves Aubin, NMR Study of Mutations of Glycine-52 of the Catalytic Domain of Diphtheria Toxin, Journal of Pharmaceutical and Biomedical Analysis https://doi.org/10.1016/j.jpba.2017.11.056

NMR Study of Mutations of Glycine-52 of the Catalytic Domain of Diphtheria Toxin

Simon Sauvé[a], Geneviève Gingras[a] and Yves Aubin[a,b]*

a. Centre for Biologics Evaluation, Regulatory Research Division, Biologics and Genetic Therapies Directorate, Health Canada, 251 Sir Frederick Banting Driveway, Ottawa, Ontario K1A 0K9, Canada

b. Department of Chemistry, Carleton University, 1125 Colonel By, Ottawa, Ontario K1S 5B6, Canada

*Corresponding author: yves.aubin@hc-sc.gc.ca

Highlights:

- NMR study of mutants of the catalytic domain of diphtheria toxin
- Mutation of residue 52 destabilizes the conformation of DTA
- The lack of toxicity of CRM197 results from an unstable conformation of its catalytic domain.

Abstract

Cross-reacting-material 197 (CRM197) is a naturally occurring non-toxic mutant of diphtheria toxin (DT) that is one of the few carrier protein used in the manufacture of polysaccharide vaccines targeting bacterial pathogens such as *Neisseria meningitidis*, *Streptococcus pneumaniae* and *Haemophilus influenzae*. A detailed explanation in structural terms for the lack of toxicity has started to emerge with the report of the X-ray