

TITLE: CHARACTERIZATION OF BRAZILIAN STRAINS OF *Corynebacterium diphtheriae* BY MULTILOCUS SEQUENCING TYPING (MLST)

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ABSTRACT:

Corynebacterium diphtheriae toxigenic (CTox) is the etiological agent of diphtheria, a serious disease whose symptoms are caused by diphtheria toxin. More than 7,000 cases of diphtheria occurred in 2016 in the world (WHO). A major epidemic in the 1990s in the Newly Independent States of the former Soviet Union with around 140,000 cases and 4,000 deaths is a warning for a possible resurgence of diphtheria in industrialized countries. Outbreaks have been reported in Latin America, and the migratory flows from Latin American countries to Brazil have been considered a threat to the increase of diphtheria cases in the country. A significant increase in non-toxigenic *C. diphtheriae* (CNTox) causing serious invasive infections, such as endocarditis, has been observed in recent years. Genetic studies have shown great heterogeneity of the circulating populations of CTox and CNTox. A total of 52 strains (38 CTox and 14 CNTox) isolated during the last two decades in Brazil were selected to investigate the population structure using whole genomic sequencing approach. Samples were isolated from nasopharyngeal and oropharyngeal swabs (diphtheriae cases and carriage) and blood (invasive infection). These strains were identified by biochemical methods and conventional PCR. In this report, we present the results of the Multi-Locus-Sequencing-Typing (MLST). The MLST types were obtained by the PubMLST website (<https://pubmlst.org/cdiphtheriae>). The isolates were assigned in 10 different STs: 176 (30%), 174 (21%), 317 (14%), 584 (11%), 212 (11%), 32 (5%), 67 (2%), 149 (2%), 172 (2%) and 175 (2%). We identified 2 new STs. The CNTox strains belonged to STs 176, 584 and 317, and to the new STs. All the ST317 strains were CNTox. All ST174 and ST176 strains were Ctox, but one ST176 strain that was CNTox. We identified the STs 149, 176, 317, 174, and a new ST among carriage strains, and the ST 176, 174, 317, 584, 67, 212, 172, 32, and a new ST among diphtheria cases. The only one strain from invasive infection was Ctox and was the exclusive representative strain of the ST175. These results show a great diversity of sequence types of *C. diphtheriae* in Brazil. The surveillance of *C. diphtheriae* can be improved through the molecular characterization of strains circulating in Brazil, in order to better understand the current epidemiological scenario of this important pathogen.

Keywords: *Corynebacterium diphtheriae*, MLST, diphtheria toxin, diphtheria.

Financial Support: This study was supported by grants from the Fundação de Amparo à Pesquisa do Estado de São Paulo.