

## Cytolethal distending toxin (CDT) from *Aggregatibacter actinomycetemcomitans*

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A variety of Gram negative pathogenic bacteria, i.e., *Salmonella enterica*, *Haemophilus ducreyi*, *Escherichia coli*, *Campylobacter* sp., *Shigella* sp., and *Aggregatibacter actinomycetemcomitans*, produce cytolethal distending toxins (Cdt). In the last decade much attention has been paying to *A. actinomycetemcomitans* (*Aa*), inhabiting human oral cavity and being associated with periodontal diseases (gingivitis, aggressive juvenile and chronic periodontitis) and endocarditis. Besides *Aa* leukotoxin and other virulence factors, Cdt is considered to be a crucial factor promoting damage of tissues, and immune cells in particular, by causing DNA damage in the target cells. Cdt is thus a genotoxin that blocks cell cycle progression resulting in eukaryotic cell senescence, and apoptotic or non-apoptotic cell death. Cdt is a heterotrimeric protein consisting of CdtA, CdtB, and CdtC subunit. These proteins are encoded by the *cdtABC* operon including adjacent *cdtA*, *cdtB*, and *cdtC* genes. CdtABC acts as an A-B<sub>2</sub> - type toxin: CdtB (283 amino acids) is an active subunit exhibiting endonuclease (DNase) activity while CdtA and CdtC are necessary for a dynamin-dependent CdtB translocation into susceptible cells. In addition to be an endonuclease, CdtB has been shown to exhibit phosphatidylinositol 3,4,5-triphosphatase (PIP3) activity that presumably potentiates its genotoxic effect in lymphocytes.

Our recent PCR-analysis of 15 clinical *A. actinomycetemcomitans* isolates from patients suffering from chronic periodontitis revealed that all examined strains code for CdtABC toxin. Here we will discuss the structure and function of Cdt toxin and its potential application.