Title:	Unraveling the molecular mechanisms underlying the cell death pathway induced by Vibrio parahaemolyticus Thermostable Direct Hemolysin, an atypical pore-forming toxin
Authors:	Verma, Pratima
Keywords:	Plasma membrane Cell death Ferroptosis
Issue Date:	Feb-2024
Publisher:	IISER Mohali
Abstract:	Thermostable Direct Hemolysin (TDH) is an atypical pore-forming toxin and a key virule nce factor secreted by Vibrio parahaemolyticus, a human gastrointestinal pathogen. Owing to its membrane-damaging pore-forming activity, TDH exerts several pathophysiological effects in the target cells. The manifestation of bloody mucous diarrhea during V. parahaemolyticus infections is attributed to the potent cytotoxicity of TDH, also reported against various nucleated mammalian cells. Nevertheless, the precise mechanism of TDH-induced cell death remains largely unexplored. The present work elucidates the mechanistic insights into the cytotoxic cell death responses elicited by TDH in the nucleated mammalian cells. The study reveals that TDH triggers features of apoptosis-like programmed cell death in the target cells. However, the involvement of caspases is not observed in TDH-mediated cell death. Therefore, TDH evokes a caspase-independent programmed cell death pathway, predominantly marked by mitochondrial damage. TDH prompts mitochondrial membrane permeability transitio n (MMPT), resulting in the release of mitochondrial factors like AIF and Endo G, responsible for the execution of caspase-independent cell death. Furthermore, this work documents ROS production, calcium influx, lysosomal membrane permeabilization and PARP-1 cleavage in response to TDH. Interestingly, a fraction of TDH and active Bax are found to translocate to the target cell mitochondria. TDH itself remains insufficient to induce mitochondrial damage, implying towards the Bax-mediated mitochondrial damage. Altogether, this study unravels significant executioners of the TDH-mediated caspase-independent programmed cell death. Furthermore, it provides critical new insights into the role of TDH in the context of host- pathogen interaction processes.
URI:	http://hdl.handle.net/123456789/5883
Appears in Collections:	PhD-2016

Files in This Item:

File	Description	Size	Format	
Thesis_Pratima_PH16072.pdf		4.64 MB	Adobe PDF	View/Open

Show full item record

Admin Tools

Edit...
Export Item
Export (migrate) Item
Export metadata