Shiga Toxin as a Select Agent

Andy Kouse

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Shigella dysenteriae is a gram-negative facultative anaerobe first isolated in 1898. After isolation, S. dysenteriae has been attributed to several diseases including shigellosis, hemolytic uremia syndrome and Reiter’s syndrome. Because of the lack of a vaccine and low infectious dose, S. dysenteriae was a good candidate for a bio-weapon; being weaponized as early as 1943 and used in warfare and bioterror attacks. The main virulence factor of S. dysenteriae is shiga toxin, an AB-5 toxin specific for the Gobotriaosylceramide receptor found on neurons, renal epithelial and intestinal endothelial cells. Once shiga toxin is endocytosed it travels through retrograde transport to the ER and the cytoplasm where it can inhibit protein synthesis and induce apoptosis. The mechanism of protein inhibition has been well characterized and results from removal of adenine-3723 from the host’s 28S rRNA, inhibiting peptide elongation. Apoptosis induced by shiga toxin has not been well studied. Recent studies have shown that while in the ER, shiga toxin is able to induce the ER stress response through an unknown mechanism. The ER stress response activates three stress sensors, IRE-1, ATF6 and PERK, that upregulate factors to reduce ER stress. If stress is not reduced after prolonged stress sensors activation, apoptosis occurs through the caspase cascade.

Lee, Moo-Seung. "Bcl-2 Regulates the Onset of Shiga Toxin 1-Induced Apoptosis in THP-1 Cells." Infection and Immunity. 77.12 (2009): 5233-44.
