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## Specific Cytotoxic Effects of Parasporal Crystal Proteins Isolated from Native Saudi Arabian *Bacillus thuringiensis* Strains against Cervical Cancer Cells

By: [Aboul-Soud, MAM](#) (Aboul-Soud, Mourad A. M.)<sup>[1,2]</sup>; [Al-Amri, MZ](#) (Al-Amri, Mohammed Z.)<sup>[1]</sup>; [Kumar, A](#) (Kumar, Ashok)<sup>[3]</sup>; [Al-Sheikh, YA](#) (Al-Sheikh, Yazeed A.)<sup>[1]</sup>; [Ashour, AE](#) (Ashour, Abdelkader E.)<sup>[4,5]</sup>; [El-Kersh, TA](#) (El-Kersh, Talat A.)<sup>[1]</sup>

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### Abstract

Currently, global efforts are being intensified towards the discovery of local *Bacillus thuringiensis* (Bt) isolates with unique anticancer properties. Parasporins (PS) are a group of Bt non-insecticidal crystal proteins with potential and specific in vitro anticancer activity. However, despite the significant therapeutic potential of PS-producing Bt strains, our current knowledge on the effects of these proteins is limited. Hence, the main objective of this study was to screen Bt-derived parasporal toxins for cytotoxic activities against colon (HT-29) and cervical (HeLa) cancerous cell lines. Nine non-larvicidal and non-hemolytic Bt strains, native to Saudi Arabia, were employed for the isolation of their parasporal toxins. 16S rDNA sequencing revealed a 99.5% similarity with a reference Bt strain. While PCR screening results indicated the absence of selected Cry (Cry4A, Cry4B, Cry10 and Cry11), Cyt (Cyt1 and Cyt2) and PS (PS2, PS3 and PS4) genes, it concluded presence of the PS1 gene. SDS-PAGE analysis revealed that proteolytically-cleaved PS protein profiles exhibit patterns resembling those observed with PS1Aa1, with major bands at 56 kDa and 17 kDa (Bt7), and 41 kDa and 16 kDa (Bt5). Solubilized and trypsinized PS proteins from all Bt strains exhibited a marked and dose-dependent cytotoxicity against HeLa cancerous cells but not against HT-29 cells. IC50 values ranged from 3.2 (Bt1) to 14.2 (Bt6) with an average of 6.8  $\mu$ g/mL. The observed cytotoxicity of PS proteins against HeLa cells was specific as it was not evident against normal uterus smooth muscle cells. RT-qPCR analysis revealed the overexpression of caspase 3 and caspase 9 by 3.7, and 4.2 folds, respectively, indicative of the engagement of intrinsic pathway of apoptosis. To the best of our knowledge, this is the first report exploring and exploiting the versatile repertoire of Saudi Arabian environmental niches for the isolation of native and possibly novel Saudi Bt strains with unique and specific anticancer activity. In conclusion, native Saudi Bt-derived PS proteins might have a potential to join the arsenal of natural anticancer drugs.

### Keywords

**Author Keywords:** *Bacillus thuringiensis*; parasporin; delta-endotoxin; non-insecticidal inclusions; in vitro cytotoxicity; apoptosis

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### Author Information

**Reprint Address:** Aboul-Soud, MAM (reprint author)

+ King Saud Univ, Dept Clin Lab Sci, Coll Appl Med Sci, Chair Med & Mol Genet Res, POB 10219, Riyadh 11433, Saudi Arabia.

**Reprint Address:** Aboul-Soud, MAM (reprint author)

+ Cairo Univ, Cairo Univ Res Pk, Giza 12613, Egypt.

### Addresses:

+ [ 1 ] King Saud Univ, Dept Clin Lab Sci, Coll Appl Med Sci, Chair Med & Mol Genet Res, POB 10219, Riyadh 11433, Saudi Arabia

+ [ 2 ] Cairo Univ, Cairo Univ Res Pk, Giza 12613, Egypt

+ [ 3 ] King Saud Univ, Coll Med, Vitoligo Res Chair, POB 10219, Riyadh 11433, Saudi Arabia

+ [ 4 ] King Saud Univ, Coll Pharm, Dept Pharmacol & Toxicol, POB 2457, Riyadh 11451, Saudi Arabia

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