Structure of Parasporin-1, a Novel Bacterial Cytotoxin against Human Cancer Cells

Toshihiko Akiba[a], Tokio Ichimatsu[b], Hideki Katayama[b], Tetsuyuki Akao[b], Osamu Nakamura[b], Eiichi Mizuki[b], Michio Ohba[c], Kazuaki Harata[a], *[a]BIRC, AIST, Tsukuba. [b]BFRI, FITC, Kurume. [c]Grad. Sch. Agric., Kyushu Univ., Fukuoka, Japan.* E-mail: k-harata@aist.go.jp

The crystal structure of parasporin-1 from *Bacillus thuringiensis* strain A1190 has been determined at 1.76 Å resolution. Parasporin-1 belongs to the Cry protein family, which includes insecticidal pore-forming toxins successfully utilized in agriculture; however, the protein is not insecticidal but specifically toxic to particular types of cultured human carcinoma cells. This strict selectivity suggests its potential use as an anti-cancer drug.

Parasporin-1 has a three-domain architecture common to available structures of other insecticidal Cry proteins; the main chain of each domain is superimposed reasonably well with their counterparts in spite of low sequence homology. Significant deviations are found in a few limited regions. Of particular interest is the N-terminal extension upstream of domain 1, which clamps the domain to domain 2 and which presumably disable the transformation of the domain necessary for pore formation. Among the available Cry protein structures, only the inactive Cry2Aa protoxin has an analogous structure. These observations along with biochemical results [1] suggest that parasporin-1 may act as a simple ligand to activate an unidentified signaling pathway leading to malfunction of membrane channels rather than as a pore-forming toxin.

[1] Katayama H., et al., *J. Biochem.*, 2005, **137**, 17.

Keywords: pore-forming toxins, anticancer biochemistry, receptor recognition