EDITORIAL

This inaugural supplement for The Open Toxinology Journal (TOTJ) contains articles of diverse-acting bacterial toxins. In our opinion, it is quite remarkable regarding the different intoxication methods that bacteria have evolved for enhancing their own survival. The bacteria that produce the various protein toxins found in this Bacterial Toxin supplement include multiple *Clostridium* species, *Shigella dysenteriae*, *Escherichia coli*, *Aeromonas hydrophila*, *Staphylococcus aureus*, and *Streptococcus pyogenes*. We hope the readers of TOTJ will enjoy this compilation of articles from contributors around the world.

Many of these articles delve into protein toxins produced by different *Clostridium* species. These anaerobic, Gram-positive, spore-forming bacteria are found throughout nature and can cause multiple diseases among animals and humans. Articles contributed by Just *et al.*, as well as Kaiser and Barth, investigate different *C. botulinum* toxins that affect the eukaryotic cytoskeleton directly (C2 toxin) or indirectly (C3 toxin alias C3 exoenzyme). The C2 toxin is a classic binary "A-B" toxin while C3 consists of a single protein, for which no cell-binding component has been identified to date. As with many of the other toxins in this supplement, the C2 toxin and C3 exoenzyme possess enzymatic activity targeting eukaryotic proteins. Other clostridia like *C. perfringens*, *C. spiroforme*, and *C. difficile* produce binary toxins very similar to *C. botulinum* C2 toxin. Each of these toxins directly prevent actin polymerization by mono-ADP-ribosylating a specific arginine residue (Arg-177) on globular actin. All of these proteins emanate from bacteria that can reside in the gastrointestinal tract and cause enteric disease. Discussions regarding the detection and relevancy to disease of the *C. perfringens* iota toxin, *C. spiroforme* S toxin, and *C. difficile* CDT are presented by Carman *et al*. Genth *et al.* nicely share their thoughts on *C. sordellii* lethal toxin and its effects upon the actin cytoskeleton and apoptosis. Rounding out the clostridial realm is a contribution by Uzal *et al.* They reveal the *in vivo* effects of various *C. perfringens* toxins in animal disease. In particular, these latter authors uniquely delve into the pathology of clostridial proteins in large animals that includes relevant discussion of animal models for more effectively studying countermeasures (i.e. therapeutics and vaccines).

Moving beyond clostridial toxins, the manuscript provided by Torgersen *et al.* discusses the shiga and shiga-like toxins respectively produced by *S. dysenteriae* and *E. coli*. These toxins are also "A-B" in nature, but unlike the clostridial binary toxins described above, each shiga or shiga-like holotoxin consists of five B subunits to one A subunit. The mode of action involves shutting down protein synthesis by N-glycosidase activity inherent to the A subunit, with ribosomal RNA being the targeted substrate. From an evolutionary perspective, this same mechanism is used by ricin, a plant-derived "A-B" type toxin derived from the beans of *Ricinus communis*. Like the clostridial toxins mentioned above, the shiga and shiga-like toxins are also associated with enteric disease.

Knapp *et al*. uniquely provide an extensive review of pore-forming proteins (aerolysin and aerolysin-like toxins) produced by many types of bacteria, with that from *A. hydrophila* being the prototype. These toxins are not of the "A-B" type and do not possess enzymatic activity, like so many others portrayed in this supplement. The aerolysin/aerolysin-like toxins are produced by Gram-negative and -positive bacteria, trees, and even aquatic animals. The mode of action is also unique versus many of the other toxins described in this supplement. These pore-forming proteins cause membrane perturbations, basically breaking down cell wall integrity and promoting leakage by forming large protein complexes on lipid bilayers. Again, conservation of the aerolysin/aerolysin-like toxins amongst such diverse organisms suggests a biological success story.

The final addition to this supplement includes structure and biology of staphylococcal and streptococcal superantigens as reviewed by Larkin *et al.* These toxins differ from those described above in that they indirectly harm the host. In essence,

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damage is elicited by an overly-sensitized immune system with subsequent release of various proinflammatory cytokines and chemokines that approach toxic levels. Too much of an inherently good thing (i.e. immunological messengers) proves to be bad for the host. The staphylococcal enterotoxins and streptococcal pyrogenic exotoxins are not "A-B" type toxins and do not damage the cell by membrane insertion or entry into the cytosol. Additionally, these toxins lack any known enzymatic activity.

Finally, it is our hope that this supplement to The Open Toxinology Journal spurs others to contribute their science to this new journal. Effective communications of not only bacterial toxins, but all biological toxins produced by various organisms, are welcomed. As evidenced by many of the articles in this supplement, common strategies exist for protein toxins shared by very diverse species. Such a realization should foster inter-disciplinary efforts that promote better science through collaborative efforts between laboratories from around the world.

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