# Editorial: Joining the billion year old journey of botulinum

## Bal Ram Singh

Botulinum Research Center, University of Massachusetts Dartmouth, 285 Old Westport Road, Dartmouth, MA 02747, USA Fax: 508-999-8451 E-mail: bsingh@umassd.edu

**Biographical notes:** Bal Ram Singh, Professor of Biophysical Chemistry at the University of Massachusetts Dartmouth since 1990 has been working with structure and function aspects of botulinum neurotoxins and associated proteins for the past 21 years. He is the Director of the National Botulinum Research Center established at UMass Dartmouth in 2003, which has over three dozen national and international botulinum researchers associated with it. He received his PhD in Chemistry from Texas Tech University in 1987, and received his post-doctoral training at University of Wisconsin – Madison, where he began his research with botulinum neurotoxins.

*The Botulinum Journal* is the result of both long-term thinking and a need in the field since the time I edited a book on Natural Toxins II (Plenum Press, 1996). I had initially realised that, although protein toxins in general represent extremely active biological molecules, due consideration must be given when examining them as a biological system. These aspects are generally catalogued under 'other proteins', which does not allow examination of their special features, such as their smart nature of utilising host cellular machinery, dual solubility in both aqueous polar and lipidic non-polar solvents, and survival in the host cellular milieu, at times for long periods of time.

My second realisation came during review processes at several federal funding agencies in the USA, either while serving on review panels or reading reviewer comments. For most people not working in the protein toxin area, these molecules just represent another group of proteins with membrane destabilising or enzymatic activities which they think could be modelled after other membrane proteins or enzymes. While there is so much to borrow from the knowledge of other proteins, to utilise in creating a better understanding of protein toxins, these have in general evolved to multitask; specific and selective binding, crossing of a membrane barrier, and finally interference with intracellular biochemical processes.

Botulinum neurotoxins are even more unique amongst protein toxins, and have defied many of the generalisations at microbiological, biochemical, biophysical, medical and clinical levels. The most dramatic observation has been their very long lasting effects reportedly due to survival of the biologically-active domain within the cell for months, a feature virtually unheard of in any other biological system. Botulinum neurotoxins are currently the only biological molecules which are relevant for their toxicity as a biothreat

#### 2 B. Ram Singh

agent and, simultaneously, for their therapeutic and aesthetic utilities attracting researchers, physicians, policy makers and business groups alike.

Botulinum neurotoxins produced by anaerobic bacteria billions of years ago have targeted the most advanced biological system, the nervous system, in animals and humans. This presents a fascinating scientific curiosity as to how these bacteria evolved to target the nervous system. Genetically, botulinum neurotoxins are produced as part of a group of genes which has a common regulatory factor for the expression of the gene cluster as a whole. The proteins collectively form a stable complex, which is critically important to their role in food poisoning and to the bioweapon role of this agent. This complex is also used as the therapeutic product because of its naturally stable formulation. Overall, these topics provide an important coalescence of interest in fundamental research, applied technology development and major business and health concerns.

Consequently, botulinum neurotoxins have become a tremendous target of research and subsequent publications within the past 25 years. A data mining study (Chennamaraju, A., 2005, A generic data acquisition tool to build a data warehouse, MS Thesis, UMass Dartmouth) has shown dramatic enhancement of botulinum-related publications in the USA, particularly since the mid-1990s. An obvious connection of this enhancement in publications is the approval of botulinum neurotoxin as a therapeutic drug against several neuromuscular disorders. Data mining exercises of Pubmed, a service of the US National Library of Medicine and the US National Institutes of Health (www.pubmed.gov) suggested that while articles referring to food poison and detection were predominant in the 1970s and early 1980s, mode, mechanism and receptor studies dominated the 1990s. Research with therapeutic products like Botox<sup>®</sup> and Dysport<sup>®</sup> started to increase in the mid 1990s; in 2007 about half of the articles were related to therapeutic products. A small number of botulinum articles have started appearing since 2000 with terms like 'bioweapon' and 'antidotes'.



#### Editorial

This wide range of topics related to botulinum provides a strong base of scholarship in the field, which is expected to be served by The Botulinum Journal (*TBJ*).

While a journal's success totally depends on the kind of researchers who are willing to associate their work with it, the editors can play a major role in promoting scholarship in a creative way. The Editorial Board of *TBJ* is very strong, consisting of international scholars from academia, government agencies and industry, which is expected to bring out creative ways to promote interactions amongst different constituencies.

In consultation with the members of the *TBJ* Editorial Board, we have charted out plans for the journal that will allow interactive communication amongst clinical and scientific researchers, industry and government agencies.



*TBJ* will publish original and review papers, commentaries, technical reports, analytical models, mathematical simulations, case studies, conference reports, book reviews, scientific notes, managerial and policy issues and news. Based on experiences of many people on the Editorial Board and also of the botulinum research community at large, considerable small yet significant information related to assays, solubility, stability, etc. of the neurotoxins or growth, strain variation, genetic make-up, etc. of the bacterial cultures does not get reported in research articles, either because of negative results or small amount of experimental data. *TBJ* would like to address this issue by encouraging short reports on techniques, observations, commentaries, hypothesis, letters and perspectives.

Each issue of *TBJ* will carry a section on Perspectives, which will include policy, technical, historical and personal perspectives. Although most of these essay-type articles will be invited from people in the field, unsolicited submissions will also be considered. We hope this series will create a space for those who may not be carrying out bench or clinical works, yet have ideas to share with the botulinum community.

From my personal perspective, the journal provides an avenue to promote botulinum research for which I have developed huge passion over the past 21 years, and I hope *TBJ* will become a useful and invaluable resource to others who have either developed their own passion already or may just be getting into the field.

### 4 B. Ram Singh

The botulinum field offers tremendous opportunity not only to the health and business community, but also to basic researchers in biochemistry, biophysics, evolutionary science, microbiology, neurology and neuroscience, pharmacology and toxicology. I invite the botulinum community to make *TBJ* a choice for their voice.