Crystal Structure of Botulinum Neurotoxin Type G Light Chain

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The seven serotypes (A-G) of botulinum neurotoxins (BoNTs) block neurotransmitter release through their specific proteolysis of one of the three proteins of the soluble N-ethylmaleimide-sensitive-factor attachment protein receptor (SNARE) complex, which is essential for membrane vesicle fusion. BoNTs have stringent substrate specificities that are unique for metalloprotease in that they require exceptionally long substrates. In order to understand the molecular reasons for the unique specificities of the BoNTs, it is essential to expose the molecular differences in their structures that give rise to their unique characteristic. Therefore, structures of all serotypes are required, and toward achieving this goal here is reported the crystal structure of the catalytic light chain of *Clostridium botulinum* neurotoxin type G (BoNT/G-LC) that has been determined to 2.35 Å resolution. The structure of BoNT/G-LC reveals a C-terminal β-sheet, which is critical for LC oligomerization, is unlike that seen in the other LC structures. Serotype structural differences observed in the pool of LC structures reveal residues in BoNT/G-LC that are likely to be involved in substrate recognition of the P1' residue and a second remote exosite for recognition of a SNARE motif.

Keywords: botulinum neurotoxin, light chain, substrate recognition