Cross reactivity of the binary toxins Anthrax- and C2-toxin

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Binary toxins are among the most potent bacterial protein toxins. They perform a cooperative mode of translocation and exhibit fatal enzymatic activities in eukaryotic cells. Anthrax- and C2-toxin are the most prominent examples for this A-B type of toxins. To investigate the mechanism of translocation into target cells and the possible cross reactivity of toxin translocation we performed various in vitro and in vivo experiments by interchanging the different A-B components of Anthrax- and C2-toxins. The enzymatic components of one toxin were combined with the homologous binding component of the other toxin. Although the binding and translocation components protective antigen (PA_{63}) and C2II share a sequence homology of about 35%, the results indicate biochemical and functional differences between both binding proteins. *In vitro* measurements using the black lipid bilayer showed that Anthrax edema factor (EF) and lethal factor (LF) bind to channels formed by the binding component C2II of C2-toxin and that C2-toxin's enzymatic component C2I binds to PA_{63}-pores. Furthermore, we could demonstrate that *in vivo* the PA_{63}-channel has the ability to transport the enzymatic moiety C2I into target cells, causing actin modification and cell rounding, whereas C2II-channel are not able to transport EF or LF. Our findings support the commonly accepted mode of translocation of A-B toxins and, in addition, we present first-time evidence that a heterogenic combination of enzymatic and translocation components also exhibit toxicity to primary human endothelial cells (HUVECs).