Glioblastoma multiforme targeted therapy: The Chlorotoxin story.
Cohen-Inbar O, Zaroor M.

Abstract
Glioblastoma multiforme (GBM) is the most common malignant primary brain neoplasm having a mean survival of <24 months. Scorpion toxins are considered promising cancer drug candidates, primarily due to the discovery of chlorotoxin, derived from the venom of the Israeli yellow scorpion. This intriguing short peptide of only 36 amino-acids length and tight configuration, possess the ability to bind to GBM cells in a grade-related manner with ~100% of GBM cells staining positive and no cross reactivity to normal brain. Chlorotoxin has an anti-angiogenic effect as well. Molecular targets for Chlorotoxin include voltage gated chloride channels (GCC), calcium-dependent phospholipid-binding protein Annexin-2, and the inducible extracellular enzyme Matrix Metalloproteinase-2 (MMP-2). Of all its targets, MMP-2 seems to bear the most anti-neoplastic potential. Chlorotoxin is a promising tumortargeting peptide. Its small size and compact shape are convenient for intracranial delivery. We present a short discussion on Chlorotoxin. The structure, biological activity, molecular targets and possible clinical role of Chlorotoxin are discussed. Chlorotoxin can be utilized as a targeting domain as well, attaching different effector functions to it. Clinical applications in GBM therapy, intraoperative imaging, nano-probes and nano-vectors based technology; targeted chemotherapy and immunotherapy are discussed as well. Chlorotoxin is likely to play a significant role in effective GBM immunotherapy in the future.

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