How may peptides increase antibody tissue selectivity and brain transport?

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Malignant brain tumors are severely impairing diseases and account for 4% of cancer-related deaths. The efficacy of current treatments is very limited and new therapies need to meet two main challenges: 1) overcoming the blood-brain barrier at the tumor periphery, and 2) selectively targeting tumor cells minimizing off-target toxicity. In our group (www.chemsynbio.iqs.edu), we combine chemical and synthetic biology to develop biotherapeutics aiming to meet these two challenges. One of the biggest issues in selectively targeting tumor cells resistant to chemotherapies is that the receptors they overexpress are also present on cells in healthy tissues. To address this issue, we have recently developed chemogenetic strategies to generate conditionally-active antibody mimetics that are able to engage the target receptor only when activated by tumor-specific proteases or other localized stimuli such as light.[1,2] In order to enhance BBB penetration of antibody derivatives we utilize brain shuttle peptides that can hijack endogenous transport mechanisms on brain endothelium. We have recently generated new efficient shuttle peptides that have high resistance to proteases and can enhance the transport of protein therapeutics.[3]

References:

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