Targeting the neural injury via astrocytic phenotypic alterations

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Over 1.7 million persons sustain a traumatic brain injury (TBI) in the U.S. alone. Current diagnostic techniques for TBI are excellent in detecting gross morphological alterations; however, they do little to detect the immediate molecular/cellular alterations. Therefore, there is a critical unmet need to develop targeting motifs that are sensitive to the heterogeneous molecular pathologies associated with TBI. The mechanical insult from TBI initiates immediate cellular death (i.e. primary injury) and stimulates a broad range of complex deleterious signaling cascades (i.e. secondary injury) including a phenotypic switch in astrocytes from basal to reactive phenotypes. This nuanced astrocyte phenotypic alteration is an ideal candidate to develop the next generation molecular targeting strategies diagnostic and therapeutic applications. In this study, we employed phage display biopanning with single chain variable fragment ('nanobody') libraries against viable basal and reactive astrocyte cultures (*in vitro*). Here, we report identification and characterization of novel nanobodies that (1) distinguish viable unfixed astrocytes over other cell types and (2) preferentially bind reactive astrocytes over basal astrocytes. Such targeting motifs will be critical in developing future diagnostic and therapeutic strategies for neural injury that are sensitive to the injury microenvironment.