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### **Astrocytic contributions to chronic methamphetamine induced neuroinflammation and disease**

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Chronic inflammatory disease is recognized as the most significant cause of death in the world, where drug misuse has been a key correlative factor. In the central nervous system, this inflammation has been characterized in part by changes in astrocytes. Astrocytes provide critical support for neurons but become reactive in response to neuroinflammation. Reactive astrocytes (RAs) are defined by proliferation, enlarged cell bodies and processes, and changes in function. A longstanding and unresolved issue is whether RAs contribute to, or help alleviate, disease progression. Chronic abuse of psychostimulant methamphetamine is a public health problem worldwide. Notably, psychostimulant abuse has become a leading cause of overdose deaths in California, closing the gap between opioid substance abuse. Utilizing flow cytometry to analyze integrin expression, we determined there is inflammation-induced astrocyte heterogeneity based on astrocytic expression of CD51, CD63, and CD71 throughout methamphetamine exposure in mice. Furthermore, we identified and characterized previously undescribed astrocyte subsets. To determine functional changes, single cell RNA sequencing was conducted to investigate the transcriptional profile of astrocyte populations. Considerable cohesiveness in the subsets were observed between protein and transcriptional data. Gene ontology and STRING analysis revealed roles astrocytes gain and/or lose throughout meth exposure. Using a novel inducible Cre knock-in mouse line driven by the lipocalin 2 promoter, we plan to sort and isolate RAs to track resolution of astrocyte reactivity throughout chronic inflammation. This research contributes has broad implications for astrocytic contributions to drug-induced neurological disease progression, aiding in potential therapeutics for inflammation-related CNS diseases.