

Neurotoxic reactive astrocytes in neurodegenerative disease

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- neurotoxic (A1) reactive astrocytes are induced by classically-activated neuroinflammatory reactive microglia

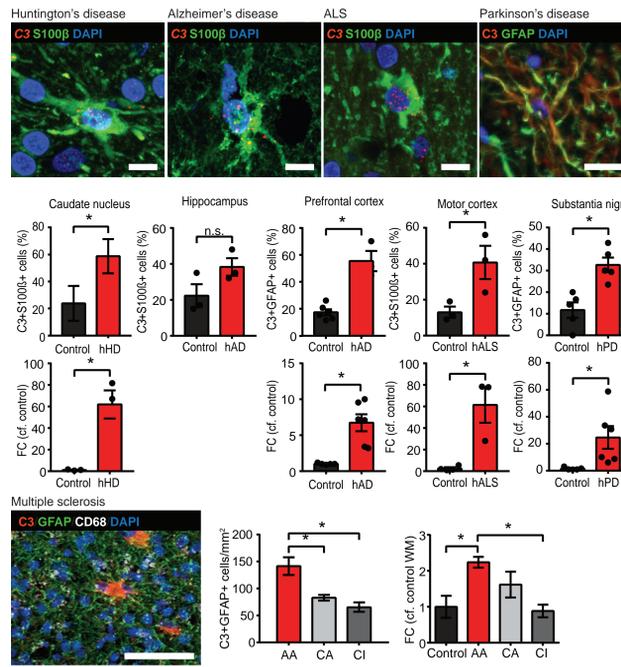
- microglia induce A1s by secreting IL1 α , TNF α AND C1q (both *in vitro* and *in vivo*)

- A1s are present in human neurodegenerative diseases including AD, HD, PD, ALS and MS

- death of axotomized CNS neurons *in vivo* is prevented when A1 formation is blocked

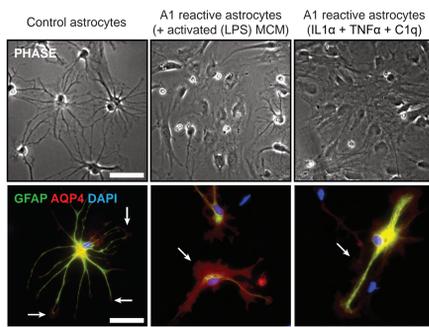
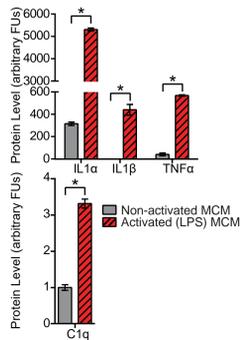
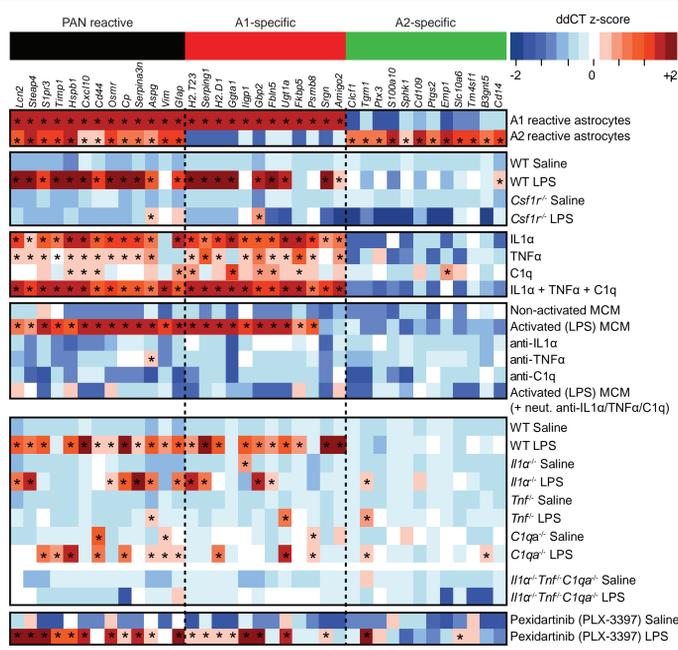
- in a mouse model of glaucoma, block of A1 astrocyte activation can stop death of RGCs

A1 reactive astrocytes in human disease



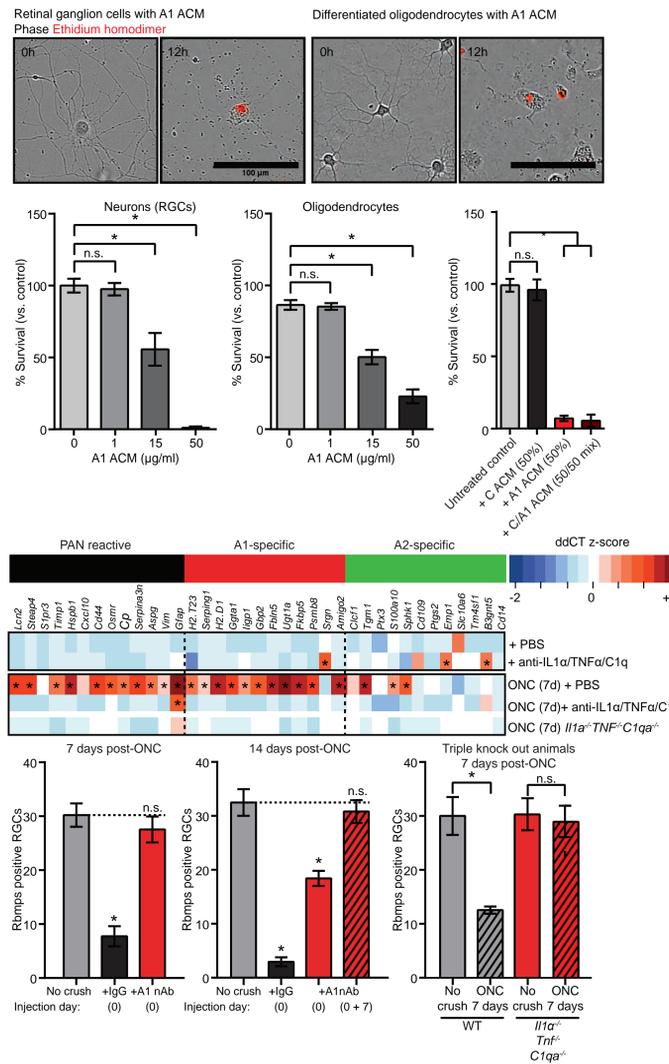
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microglia induce A1 reactive astrocytes *in vitro* and *in vivo*



A1s lose the ability to promote neuronal survival, outgrowth, synaptogenesis, and phagocytosis (see Liddelow et al. (2017) *Nature* 541:481-487)

A1 reactive astrocytes are strongly neurotoxic



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ACKNOWLEDGMENTS: This work was supported by grants from the National Institutes of Health (BAB, SAL), the Christopher and Dana Reeve Foundation (BAB), the Novartis Institute for Biomedical Research (BAB, SAL), Dr. Miriam and Sheldon G. Adelson Medical Research Foundation (BAB), the JPB Foundation (BAB), the Cure Alzheimer's Fund (BAB, SAL), the Glenn Foundation (BAB, SAL), The Glaucoma Research Foundation Catalyst for a Cure Initiative II (ADH), NYU School of Medicine (SAL, JS). The authors also acknowledge the support of our Anonymous donors and Vincent and Stella Coates.