PROGRESS IN NEUROSCIENCE PINS

Seminar Series of the
Brain & Mind Research Institute
Weill Cornell Medical College (WCMC)
&
The Graduate Program in Neuroscience of
WCMC and Sloan Kettering Institute

Thursday, 4/23/15, 4 PM, coffee at 3:45 PM
Weill Auditorium

"Gliomas alter glial-neuronal-vascular interactions"

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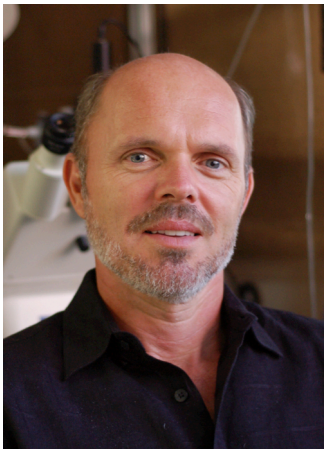

Abstract:

Gliomas rarely metastasize outside the brain but grow and invade exclusively with the brain and spinal cord. They invade along the abluminal side of blood vessels which they use as substrate for invasion. Invading gliomas displace astrocytic endfeet from the vasculature and cause focal breaches in the blood brain barrier. Satellite tumors, forming at vessel branch point release glutamate in excitotoxic concentrations to vacate space for the tumors expansion. Glutamate release also explains tumor associated epilepsy, which is often a presenting feature in newly diagnosed patients. Glutamate is released in conjunction with cysteine uptake via the system Xc, exchanger. It pharmacological inhibition suppresses seizures and slows tumor growth. Data from a early phase clinical trial data suggests feasibility of using an FDA approved system Xc inhibitor to reduce Glu release in glioma patients.

Recent relevant publications:

Buckingham, S. C., Campbell, S.L., Haas, B.R. Montana, V. Robel, S., Ogunrinu T. and Sontheimer, H., Glutamate Release by Primary Brain Tumors Induces Epileptic Activity, Nature Medicine, (2011) 17(10):1269-74. PMCID: PMC31992231

Watkins, S., Robel, S., Kimbrough I.K., Robert, S.M., Ellis-Davies, G. and Sontheimer, H. Disruption of astrocyte-vascula coupling and the blood-brain barrier by invading glioma cells. Nature Communications, 5: 4196. doi: 10.1038 (2014). PMID: 24943270

Campbell S.L., , Robel, S., Cuddapah, V.A., Robert, S., Buckingham, S.C., Kahle, K.T., and Sontheimer, H. GABAergic disinhibition and impaired KCC2 cotransporter activity underlie tumor-associated epilepsy. GLIA, 63(1):23-36 (2015). PMID: 25066727

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