

ZEB1 deletions in brain cancer

Lincoln A Edwards

Weill Cornell Medical College, USA


Glioma stem cells (GSCs) drive the propagation of glioblastomas and can affect patient survival by imparting the virulence of unabated tumor growth through cancer stem cell self-renewal with a resistance to GSC differentiation. How GSCs achieve these characteristics are poorly understood. We have identified ZEB1 as a mediator of resistance to differentiation, and stem cell self-renewal. IFN- γ which causes ZEB1 induction aborts these GSC characteristics. We show that ZEB1 negatively regulates the stem cell self-renewal factor LIF, through newly identified E-box binding sites within the LIF promoter. Targeted suppression of ZEB1 resulted in the induction of LIF commensurate with GSC self-renewal and an inhibition to GSC differentiation. Interrogation of over 500 patient glioblastomas along with primary patient GSCs identified a significant number of glioblastoma patients harboring a ZEB1 deletion and frequent loss of heterozygosity (LOH). These findings are not in line with the present

literature, which suggests that ZEB1 expression increases tumorigenicity. Surprisingly, our findings illustrate that the loss of the ZEB1 gene is common in glioblastoma and that ZEB1 loss is associated with propagation of the glioma stem cell population. These findings link ZEB1 loss to stemness with important implications for prognosis and treatment.

Speaker Biography

Lincoln A Edwards completed his PhD at the University of British Columbia, (Canada) and his Post-doctoral studies from the National Institutes of Health, National Cancer Institute in the Department of Neuro-Oncology. He then went to the Department of Neurosurgery at Cedars-Sinai Medical Center serving as a Research Scientist before moving to New York where he is currently an Instructor of Neuroscience, Neuro-Oncology at Cornell University, Weill Cornell Medical College. He has been serving as a review board member for the journal *Frontiers of Oncology* and has published in journals like *JNCI*, *Cancer Cell*, *Scientific Reports* and *Molecular Cancer Therapeutics*. His work has led to the initiation of clinical trials for the treatment of brain cancer.

e: lae2011@med.cornell.edu

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