

International Conference on

Cancer Biology & Drug Delivery

September 18-19, 2017 | Philadelphia, USA

Elucidating the mechanisms that underlie brain cancer stem cell regulation

Lincoln A Edwards

Weill Cornell Medical College, USA

Cancer stem cells are a small subset of cells that drive the propagation and the initiation of certain cancers. In glioblastoma multiforme (GBM), the most common and aggressive primary brain tumor, glioma stem cells (GSCs) can affect patient survival by imparting the virulence of unabated tumor growth through cancer stem cell self-renewal and the inhibition of GSC differentiation. The molecular mechanisms underpinning these properties of GSCs are poorly understood. Here, we show that *ZEB1* (Zinc Finger E-Box-Binding Homeobox 1) regulates stem cell self-renewal and differentiation (stemness) and its deletion negatively impacts patient survival. DNA pull down experiments confirmed novel E-box-*ZEB1* binding sites within the promoter region of the stemness promoting factor LIF, allowing *ZEB1* to repress LIF activation. We have identified that a majority of GBM patients (n>500) bear *ZEB1* deletion with frequent loss of heterozygosity, leading to LIF and subsequent stem cell activation. Mimicking *ZEB1* loss with *ZEB1* knockdown in GSCs resulted in the induction of LIF commensurate with GSC self-renewal and inhibition of differentiation. Exposure of GSCs to IFN- γ , which causes *ZEB1* induction, aborted these GSC characteristics. These findings run counter to the present literature, which would suggest that *ZEB1* expression increases tumorigenicity. Surprisingly, our findings illustrate that the loss of the *ZEB1* gene is common in glioblastomas and that *ZEB1* loss is associated with propagation of the glioma stem cell population. This implies a biologically selective role for *ZEB1* that when mutated or deleted favors propagation particularly of the cancer stem cell component. These findings link *ZEB1* loss to stemness with actionable implications for prognostication and treatment.

Biography

Lincoln A Edwards has 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 such journals as *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.

lae2011@med.cornell.edu

Notes: