**Serine/Threonine kinase MLK4 determines Mesenchymal**

**Identity in Glioma Stem Cells in an NF-κB-dependent manner**

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**Abstract**

Proneural (PN) and mesenchymal (MES) glioma stem cells (GSCs) represent two mutually-exclusive, and biologically distinct GSC subtypes. GBM patients with the MES GSC signature belong to the poorer prognosis subclass and are resistant to irradiation. Identification of regulatory mechanisms that regulate MES trans-differentiation is therefore critical for developing GSC-targeted therapy. Here we find that silencing MLK4 inhibits de novo and acquired (radiation-induced) MES GSCs both in vitro and in vivo. In addition, we present the first evidence of IKKα as a direct molecular target of MLK4 that drives NF-κB pathway activation, thereby promoting MES trans-differentiation of GSCs. Targeting the MLK4-driven NF-κB signaling axis could be a therapeutic strategy for GBM patients with a MES signature.

**Short Bio**

Sung-Hak Kim is an associate professor of Department of Animal Science in Chonnam National University. He received his B.S in Animal Science from Chonnam National University, the M.S. in Agribiotechnology from Seoul National University, and the Ph.D in Tumor Biology from Seoul National University College of Medicine. He was an instructor of Neurosurgery Department of University of Alabama at Birmingham, Ohio State University and Korea University. The purpose of his study is to pursue a better understanding of the molecular mechanism of brain tumorigenesis and its treatment. When he was a research professor in Korea University, he has focused on the characterization of cancer stem cells and understanding how they are generated during tumorigenesis. He discovered the role of IRF7 on promoting brain tumor aggressiveness by regulating self-renewal activity in response to inflammatory microenvironments, published in *Brain* in 2012. This study provided a mechanistic framework to the well-accepted observation that cancer stem cell population is important for therapeutic resistance and tumor recurrence. At the Ohio State University in the Department of Neurological Surgery, he has been carrying out the establishment of glioma stem cells from human brain tumor tissues and making clinical relevant models such as PDX (patient-derived xenograft). As a result of these experiences, he published 10 peer-reviewed research and review articles. Specifically, I determined two mutually-exclusive subtypes of cancer stem cells which clinical relevance, focusing on the elucidation of molecular mechanism, published in *PNAS* in 2013 and 2016. In addition, he found serine/threonine kinase, MLK4, which is significantly activated in distinct subtypes by kinome-shRNA screening and transciptome microarray analysis, published in Cancer Cell at 2016. His final goal is to reveal new insight into brain tumorigenesis to find a novel therapeutic target.