

NODAL REGULATES CELLS METABOLISM THROUGH HIF-1A IN GLIOMA CELLS

Jing-Huei Lai², Hsun-Jin Jan¹, Li-Wen Liu¹ and Horng-Mo Lee¹

¹ Graduate Institute of Medical Sciences, College of Medicine, Taipei Medical University, Taiwan;

²Graduate Institute of Life Sciences, National Defense Medical Center

Metabolism plays an important role in tumor growth. Hypoxia inducible factor-1 α (HIF-1 α) is a major regulator of cell metabolism mechanisms. Our previous studies showed that Nodal expression correlated with glioma cell proliferation and invasion. We ask whether Nodal may affect HIF-1 α and cell metabolism mechanisms. We investigated how Nodal protein expression affect endogenous HIF-1 α expression, glucose transporter-1 (Glut-1) expression, glucose uptake and lactate accumulation in glioma cells. The knockdown of Nodal expression with specific shRNA decreased HIF-1 α and Glut-1 expressions. Nodal knockdown reduced glucose uptake and lactate accumulation. Conversely, the addition of recombinant Nodal to glioma cells increased Glut-1 and HIF-1 α expressions, and increased glucose uptake and lactate accumulation. These results were similar with the ectopic expression of Nodal in low-expressing Nodal glioma cells. The knockdown of HIF-1 α by specific shRNA reduced Glut-1 expression, and decreased glucose uptake and lactate accumulation. Furthermore, HIF-1 α -knockdown also increased mitochondria membrane potential, MMP-2 activity and expression, and cell invasiveness. These results are similar to those of Nodal knockdown published previously. In conclusion, we show that changes in Nodal expression can directly affect HIF-1 α expression. Furthermore, we show that Nodal expression and HIF-1 α expression can affect measures of cell metabolism such as glucose uptake, lactate accumulation, and mitochondria membrane potential assays in the same manner. Interestingly, changes in HIF-1 α can also affect tumorigenic activity such as MMP-2 activity and cell invasiveness. Finally, these results imply that Nodal affect cell metabolism through HIF-1 α .

Key word:

glioma;Nodal;HIF-1 α ; Glut-1