Cellular prion protein promotes glucose uptake through the Fyn-HIF-2α-Glut1 pathway to support colorectal cancer cell survival.


Abstract

Cellular prion protein (PrPc) is a glycosylphosphatidylinositol-anchored membrane protein that has various physical functions, including protection against apoptotic and oxidative stress, cellular uptake of copper ions, transmembrane signaling, and adhesion to the extracellular matrix. In this study, we show that PrPc is highly expressed in colorectal adenocarcinomas. Transcriptome profiling of PrPc-depleted DLD-1 cells revealed downregulation of glucose transporter 1 (Glut1). PrPc is shown to be involved in regulating Glut1 expression through the Fyn-HIF-2α pathway. As Glut1 is the natural transporter of glucose and is required for the high glycolytic rate seen in colorectal tumors, silencing of PrPc reduced the proliferation and survival rate of colorectal cancer cells in vitro. In vivo, knockdown of PrPc by hydrodynamic injection with a cocktail of PrPc-shRNA-encoding plasmids also inhibited tumorigenicity in a xenograft model in nude mice. In summary, our data characterize a novel molecular mechanism that links PrPc expression to the regulation of glycolysis. Targeting PrPc will therefore be a promising strategy to overcome the growth and survival advantage in colorectal tumors.


PMID:21265952