

Tumor Suppressor p53 and Glutamine Metabolism

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The tumor suppressor p53 has been shown to control energy balance and metabolic homeostasis, concerning its role in Warburg effect and cancer stemness. Importantly, cancer cells often depend on the two major energy source, catabolism of both glucose and glutamine- glycolysis and glutaminolysis- and mitochondria is a key organelle involved in this altered metabolism. In this context, we first found that p53 controls glutamine metabolism through GLS2, a key enzyme in mitochondria to convert glutamine to glutamate, whereas GLS1, which mainly localizes in cytoplasm, was upregulated by c-MYC through miRNA23. Metabolome and biochemical analysis revealed that GLS2 associates with mitochondrial supercomplex and downregulates ROS through glutathione synthesis as well as facilitates energy supply via oxidative phosphorylation, counteracting Warburg effect. Indeed, mouse NASH model and GEO database analysis showed that GLS2 expression is correlated to the prognosis of breast cancer and HCC patients. Thus p53 regulates mitochondrial glutamate-dependent metabolic pathways through GLS2 to exert antioxidant and bioenergetic function, profound linking to tumor suppressor function in early-onset of tumor.

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EDUCATIONS/TRAINING

1992	Chiba University School of Medicine, Japan, MD.
1992-1993	Chiba University Hospital, Japan, Clinical Resident
1993-1995	Funabashi Central Hospital, Japan, Clinical Resident
1999	Chiba University Graduate School of Medicine, Japan, MD & PhD.

POSITIONS AND HONORS

1999	Research Resident, National Cancer Center Research Institute, Japan
1999-2002	CREST Research Fellow, National Cancer Center Research Institute, Japan
2002-2004	Research Fellow, Columbia University, USA
2004-2006	Research Associate, Columbia University, USA
2006-Present	Assistant Professor, Graduate School of Medicine, Chiba University, Japan
2002	JSPS Postdoctoral Fellowship for Research Abroad
2007	Japan Endocrine Society Research Award
2008	Chiba Medical Society Award

RECENT PUBLICATIONS

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