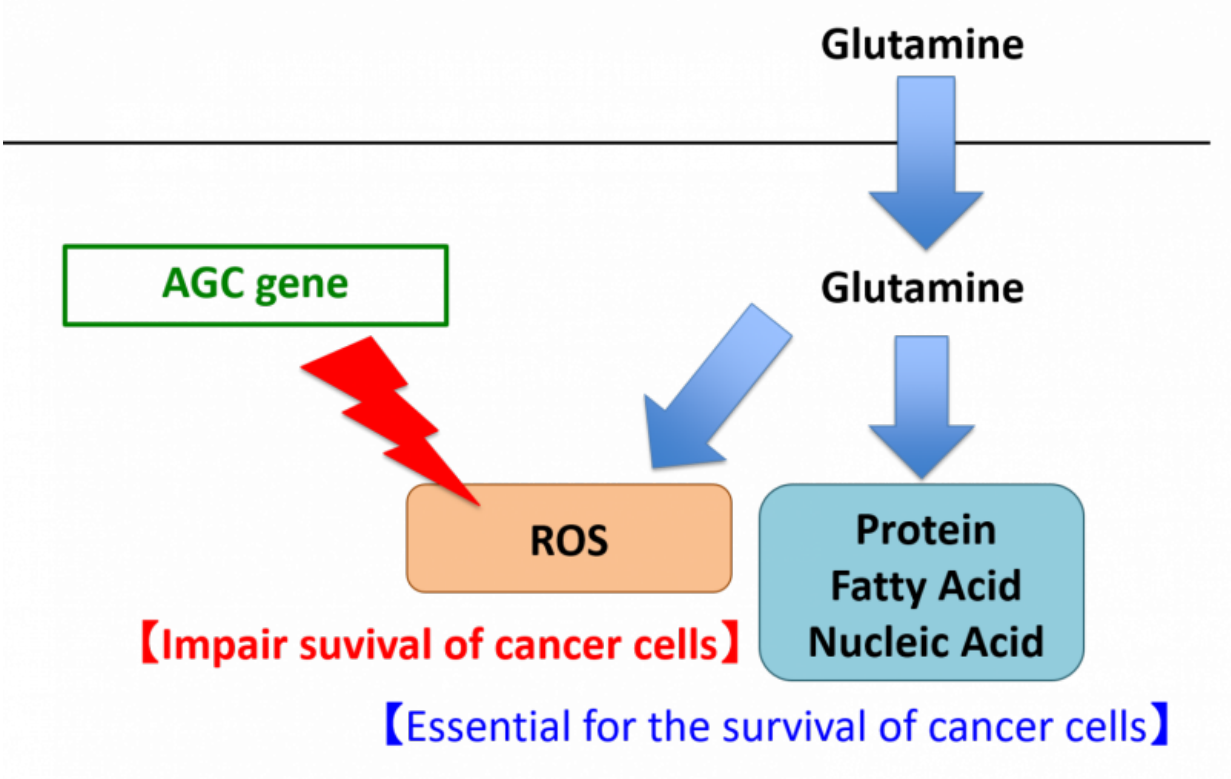
The importance of the glutamine metabolism in colon cancer

January 10 2017



Colon cancer cells produce proteins, fatty acids, nucleic acids and reactive oxygen species (ROS). Proteins, fatty acids, and nucleic acids are essential factors for cell survival using glutamine metabolism. On the other hand, ROS is a factor for cellular disorder. Colon cancer cells up-regulate the expression AGC gene. Then AGC reduce ROS. Credit: Osaka University

The importance of glutamine was made clear as a colon cancer specific metabolism. It is known that glutamine metabolism is important for pancreatic cancer, but the importance of glutamine metabolism for colon cancer has been unclear. In this study, we showed the importance of glutamine metabolism.

The importance of glutamine metabolism for colon cancer was revealed by Masamitsu Konno Ph.D, Masaaki Miyo M.D. Ph.D, Masaki Mori, M.D. Ph.D and Hideshi Ishii M.D. Ph.D. The aim of this study is to elucidate metabolic adaptation to nutritional stress and the role of the involved oncogenes in human colorectal cancer. The present study showed that the metabolism of colorectal cancer, distinct from that of pancreatic cancer, depended on genomic alterations, which previously have been uncharacterized, and was not restricted to KRAS mutation alone. Colorectal cancer can survive under the condition of glucose depletion while retaining TCA cycle activity. The cells' survival relies on a delicate balance between energy and reactive oxygen species (ROS) production. Glutamate dehydrogenase 1 (GLUD1) and SLC25A13 have pivotal roles under glucose-deprived conditions and are associated with tumor aggressiveness and colorectal cancer prognosis.

GLUD1 and SLC25A13 have pivotal roles in nutritional stress and are associated with tumor aggressiveness and poorer prognosis of colorectal cancer. These proteins may serve as new targets in the treatment of refractory colorectal cancer.

"We found that colorectal cancer cells survived under the condition of glucose depletion, and their resistance to such conditions depended on genomic alterations rather than on KRAS mutation alone. Metabolomic analysis demonstrated that those cells maintained TCA cycle activity and ATP production under such conditions. Furthermore, we identified pivotal roles of GLUD1 and SLC25A13 in nutritional stress. ", says Hideshi Ishii. "GLUD1 and SLC25A13 were associated with tumor

aggressiveness and poorer prognosis of colorectal cancer. GLUD1 and SLC25A13 may serve as new targets in treating refractory colorectal cancer, which survives in malnutritional microenvironments."

More information: Masaaki Miyo et al. Metabolic Adaptation to Nutritional Stress in Human Colorectal Cancer, *Scientific Reports* (2016). DOI: 10.1038/srep38415

Provided by Osaka University