The shortage of oxygen, termed as hypoxia, plays critical roles in many cancers. So far, however, very limited is known about the mechanism of hypoxia stress on the tumorigenesis. Understanding the mechanism can help the clinical treatment to many tumors. Recently, LIU Jiang’s lab from the Beijing Institute of Genomics (BIG), CAS in collaboration with the University of Chicago, revealed that speckle-type POZ protein (SPOP) acts as the key regulatory hub in hypoxia-induced tumorigenesis in kidney cancer.

Under normal physiological conditions, hypoxia stress can promote the expression of PDGF and EGF, which in turn can promote the angiogenesis. Therefore, many investments have been focused on inhibiting the receptors of PDGF and EGF to treat the cancer. However, the clinical outcome is very limited, suggesting that more important targets are required to be identified.

Hypoxia-induced factors have been found elevated in nearly 50% of kidney cancers. Surgical operation is the major treatment to kidney cancer, but it is not suitable for patients with metastasis. Such patients need drugs to cure their cancers.

Unfortunately, the clinical outcome from existing drugs is very poor. To address this plight, the BIG scientists used kidney cancer as the model to understand the mechanism of the tumorigenesis under hypoxia stress. Their study unravels that hypoxia stress can elevate the expression of SPOP, and drive the cytoplasmic accumulation of SPOP, which is sufficient to induce the tumorigenesis. Scientists further revealed that SPOP, an E3 ligase adaptor, can degrade the tumor suppressor PTEN, ERK phosphatases and many other proteins, which can contribute to the kidney tumorigenesis.

Since the accumulation of SPOP in the cytoplasm plays crucial roles in kidney cancer, scientists are interested whether the inhibition of SPOP can kill the tumor. Their studies show that the deletion of SPOP can only kill cancer cells, but not the normal cells, suggesting that SPOP could be a promising therapeutic target specific to cancer. In the future, it is envisioned that the success in identifying drugs target to SPOP will benefit many cancer patients, not limited to kidney cancer patients.

The work was supported by CAS, the Ministry of Science and Technology, and the National Natural Science Foundation of China. The article was published online in Cancer Cell on Mar 20, 2014.