FOXO4

The results of a genomic analysis suggest that low FOXO4 expression is a significant risk factor for epileptic seizures in patients with LGGs and is associated with the seizure outcome. FOXO4 may be a potential therapeutic target for tumor-associated epilepsy [1].

Forkhead box protein O4 is a protein that in humans is encoded by the FOXO4 gene.

It is located on the long arm of the X chromosome from base pair 71,096,148 to 71,103,533.

FOXO4 is a member of the forkhead family transcription factors O subclass, which is characterized by a winged helix domain used for DNA binding.

There are 4 members of the FOXO family, including FOXO1, FOXO3, and FOXO6. Their activity is modified by many post translational activities, such as phosphorylation, ubiquitination, and acetylation.

Depending on this modified state, FOXO4 binding affinity for DNA is altered, allowing for FOXO4 to regulate many cellular pathways including oxidative stress signaling, longevity, insulin signaling, cell cycle progression, and apoptosis.

Two of the main upstream regulators of FOXO4 activity are phosphoinositide 3- kinase (PI3K) and serine/threonine kinase AKT/PKB.

Both PI3K and AKT modify FOXO4 and prevent it from translocating to the nucleus, effectively preventing the transcription of the downstream FOXO targets.

1)
Wang Y, Tang K, Zhao J, Liu L, Feng J. FOXO4 expression is associated with the occurrence and outcome of seizures: An RNA-sequencing analysis of low-grade gliomas. Seizure. 2017 Sep 21;52:41-45. doi: 10.1016/j.seizure.2017.09.012. [Epub ahead of print] PubMed PMID: 28963932.