HSP60

HSP60, a major chaperone for maintenance of mitochondrial proteostasis, is highly expressed in glioblastoma patients. To understand the effects of HSP60 on glioblastoma tumorigenesis and progression, we characterized the HSP60-knockdowned glioblastoma cells and revealed that HSP60 silencing markedly suppressed cell proliferation and promoted cell to undergo the epithelial-mesenchymal transition (EMT). Proteomic analysis showed that ribosomal proteins were significantly downregulated whereas EMT-associated proteins were up-regulated in HSP60-knockdowned U87 cells as confirmed by a distinct enrichment pattern in newly synthesized proteins with azido-homoalanine labeling. Biochemical analysis revealed that HSP60 knockdown increased reactive oxygen species (ROS) production that led to AMPK activation, similarly to the complex I inhibitor rotenone-induced AMPK activation. Activated AMPK suppressed mTORC1 mediated S6K and 4EBP1 phosphorylation to decrease protein translation, which slowed down cell growth and proliferation. On the other hand, high levels of ROS in HSP60 knockdowned or rotenone-treated U87 cells contributed to EMT. These results indicate that HSP60 silencing deactivates the mTOR pathway to suppress glioblastoma progression, suggesting that HSP60 is a potential therapeutic target for glioblastoma treatment [1)].

1)
Tang H, Li J, Liu X, Wang G, Luo M, Deng H. Down-regulation of HSP60 Suppresses the Proliferation of Glioblastoma Cells via the ROS/AMPK/mTOR Pathway. Sci Rep. 2016 Jun 21;6:28388. doi: 10.1038/srep28388. PubMed PMID: 27325206; PubMed Central PMCID: PMC4914999.