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Piperlongumine induces G2/M phase arrest and apoptosis in brain cancer cells through the ROS-JNK-ERK signaling pathway**Kyung Jin Lee**

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Brain Cancer Cell (BCC) is an aggressive, metastatic bile duct cancer. BCC is difficult to diagnose, and responds poorly to current radio- and chemo-therapy. Piperlongumine (PL) is a naturally-occurring small molecule selectively toxic to cancer cells by targeting Reactive Oxygen Species (ROS). In this study, we demonstrated the potential anticancer activity of PL in BCC. PL markedly induced death in BCC cell lines in a dose and time-dependent manner through the activation of caspase-3 and PARP. PL also stimulated ROS accumulation in BCC. Co-exposure of PL with the ROS scavenger N-acetyl-L-cysteine or GSH completely blocked PL-induced apoptosis in BCC. Increased p21 *via* the p53-independent pathway in PL-treated BCC led to G2/M phase arrest and cell apoptosis. In addition, the study showed that PL trigger BCC death through JNK-ERK activation. Furthermore, the different antioxidant capacity of BCC also indicates the susceptibility of the cells to PL treatment. Our findings reveal that PL exhibits anti-tumor activity and has potential to be used as a chemotherapeutic agent against BCC.

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