

# Chloroquine

Chloroquine (CQ) is a quinoline-based drug widely used for the prevention and treatment of malaria. More recent studies have provided evidence that this drug may also harbor antitumor properties, whereby CQ possesses the ability to accumulate in lysosomes and blocks the cellular process of autophagy.

Therefore, Golden et al. set out to investigate whether CQ analogs, in particular clinically established antimalaria drugs, would also be able to exert antitumor properties, with a specific focus on glioma cells.

Toward this goal, they treated different glioma cell lines with quinine (QN), quinacrine (QNX), mefloquine (MFQ), and [hydroxychloroquine](#) (HCQ) and investigated [endoplasmic reticulum](#) (ER) stress-induced cell death, autophagy, and cell death.

All agents blocked cellular autophagy and exerted cytotoxic effects on drug-sensitive and drug-resistant glioma cells with varying degrees of potency (QNX > MFQ > HCQ > CQ > QN). Furthermore, all quinoline-based drugs killed glioma cells that were highly resistant to [temozolomide](#) (TMZ), the current standard of care for patients with glioma. The cytotoxic mechanism involved the induction of apoptosis and ER stress, as indicated by poly(ADP-ribose) polymerase (PARP) cleavage and CHOP/GADD153. The induction of ER stress and resulting apoptosis could be confirmed in the in vivo setting, in which tumor tissues from animals treated with quinoline-based drugs showed increased expression of CHOP/GADD153, along with elevated TUNEL staining, a measure of apoptosis.

Thus, the antimalarial compounds investigated in this study hold promise as a novel class of autophagy inhibitors for the treatment of newly diagnosed TMZ-sensitive and recurrent TMZ-resistant gliomas <sup>1)</sup>.

<sup>1)</sup>

Golden EB, Cho HY, Hofman FM, Louie SG, Schönthal AH, Chen TC. Quinoline-based antimalarial drugs: a novel class of autophagy inhibitors. *Neurosurg Focus*. 2015 Mar;38(3):E12. doi: 10.3171/2014.12.FOCUS14748. PubMed PMID: 25727221.

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