A Novel Mechanism of Chloroquine in Cancer Therapy

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Chloroquine (CQ) is a drug used to treat malaria, auto-immune disorders, and most recently, cancer. In ongoing clinical trials in cancer, CQ is used as an autophagy inhibitor. However, the underlying mechanisms of CQ's anti-cancer effects have yet to be understood. The goal of our research is to investigate the autophagy-related mechanism of CQ on cancer cell death. The current belief is that CQ functions solely as a lysosomotropic agent in the context of autophagy. We unexpectedly found that CQ acts as a potent autophagy inducer beyond its lysosome inhibition. The CQ-induced autophagic response is mTORC1 and Vps34 dependent and the proximal signaling molecule is v-ATPase. In contrast to the generally accepted concept that autophagy promotes cell survival under stress, the CQ-induced autophagy pathway enhances cancer cell death. Our research reveals a previously unknown mechanism of CQ in autophagy. This dual role of CQ in autophagy, i.e., an autophagy inducer and lysosome inhibitor, is unique to CQ and may be further explored in cancer therapy in vivo. In addition, our study sheds a new light into the mechanism of CQ on cancer cell death. These findings may establish the basis for new drug development (e.g., a single drug with multiple functions) and formation of a novel strategy for cancer therapy. Further, CQ's incredible cheapness (0.0084USD/dose) and anti-cancer effect in its singularity allude to the potential of CQ becoming the world's cheapest chemotherapeutic agent. CQ and its new derivatives could become viable cancer therapy options that can make cancer treatment available to patients all over the world.

Awards Won:

Third Award of $1,000