Repurposing of choloroquine, as an inexpensive adjuvant for breast cancer therapy

Poly(ADP-ribose) polymerase inhibitors (PARPi) target tumors defective in homologous recombination (HR). Most breast cancers are intrinsically resistant to PARP inhibitors e.g. talazoparib. We have shown for the first time that autophagy plays key role in *de novo* resistance in breast cancer in response to PARP inhibitors (Fig. A). Targetting autophagy, by chloroquine (CQ), synergistically enhanced the therapeutic efficacy of talazoparib in breast cancer cells *in vitro* and *in vivo* xenograft tumor mouse model. Mechanistically, autophagy inhibition by chloroquine promoted deleterious NHEJ mediated DSB repair, leading to extensive genomic instability and mitotic catastrophe. Our research showed strategy to use PARP inhibitor and chloroquine (an inexpensive drug in India) for better therapeutic outcome.

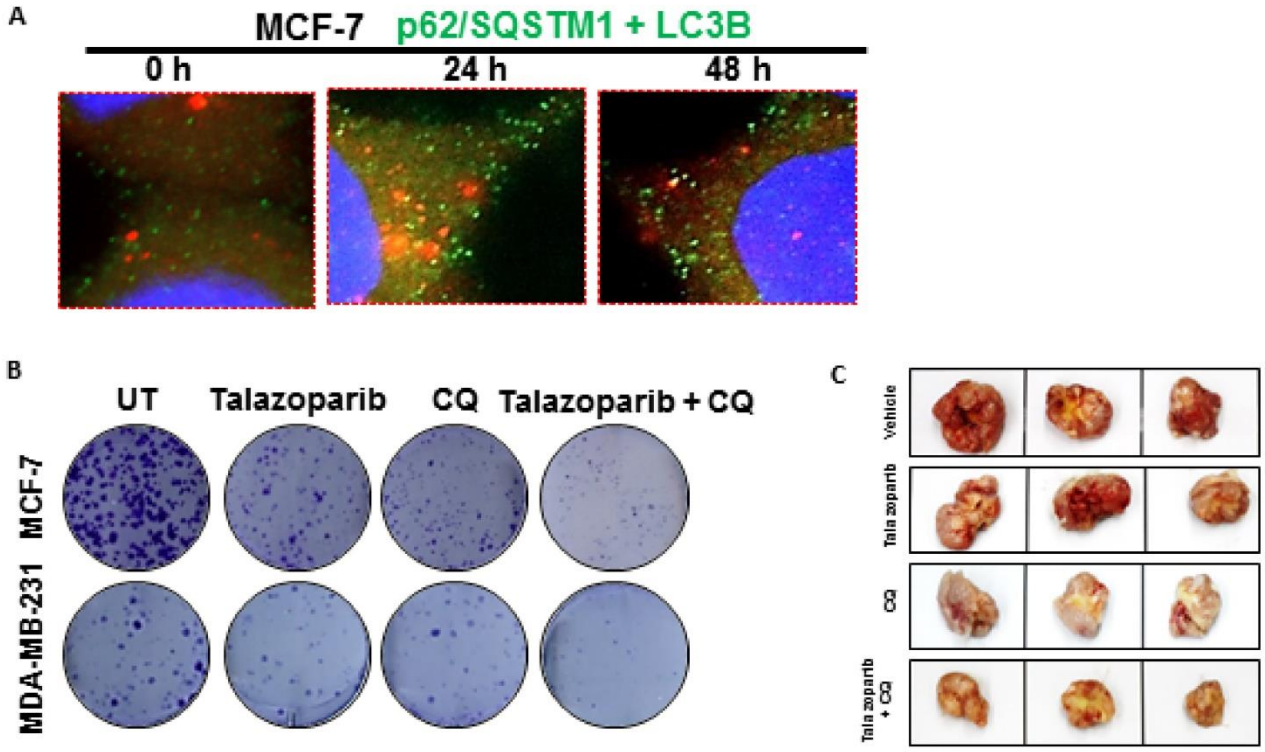

Figure (A) Talazoparib (PARP inhibitor) induces autophagy in breast cancer cells. **(B, C)** Co-treatment of talazoparib and chloroquine (CQ) sensitizes breast cancer cells in vitro and in vivo