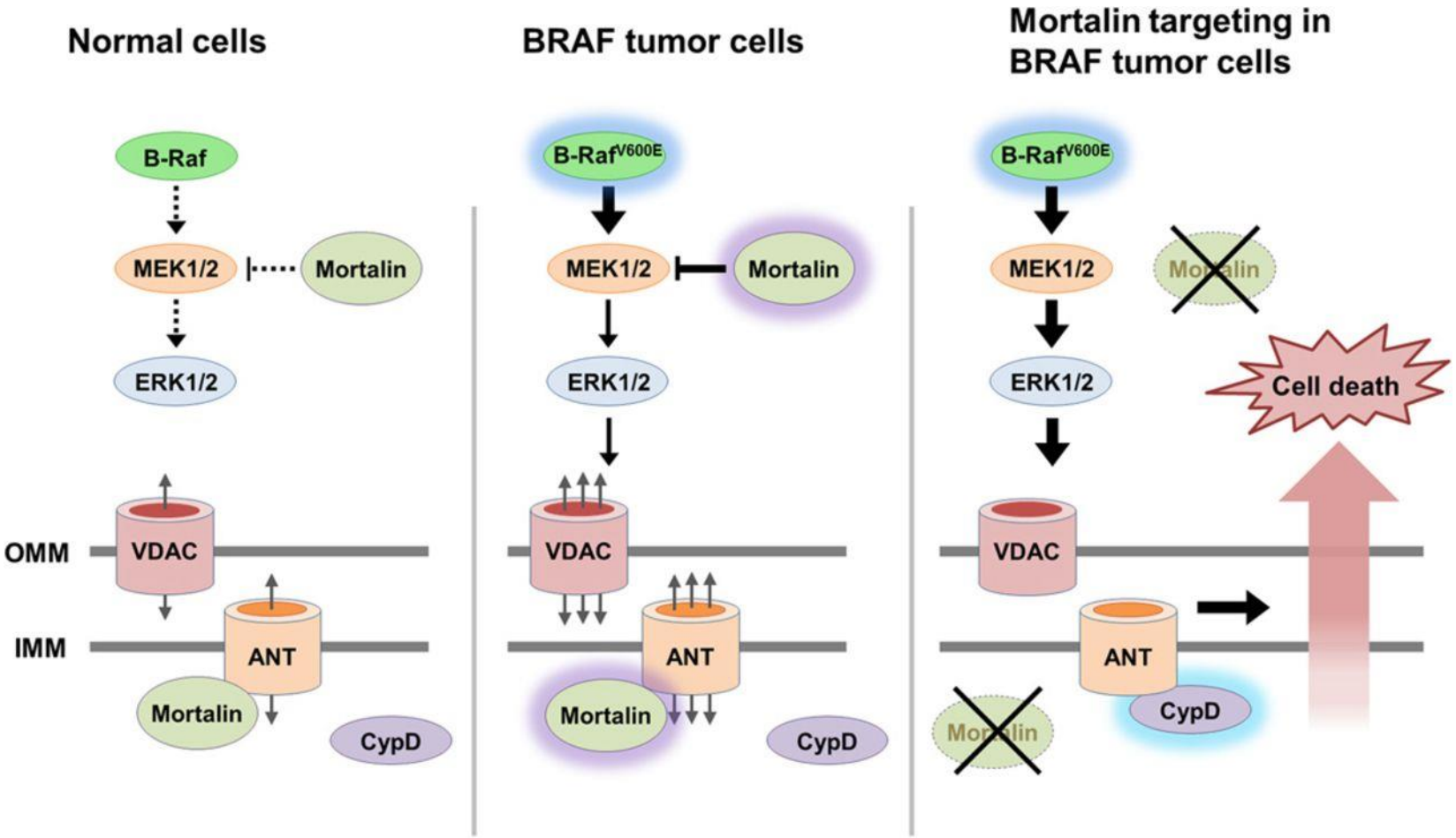
Blocking the heat shock chaperone mortalin kills BRAF-mutant and MEK-ERK pathway–driven tumor cells.



ANT is a mitochondrial channel that maintains cellular bioenergetics in collaboration with VDAC. However, ANT can also interact with CypD, the gatekeeper of MPTP, and cause cell death by perturbing mitochondrial membrane permeability. Deregulated MEK/ERK activity in *BRAF*-mutant tumor cells increases this lethal risk, but mortalin counteracts it by inhibiting ANT-CypD interaction and by modulating MEK1/2 activity. These processes may be exploited to selectively suppress *BRAF*-mutant tumor cells.

Science Signaling 10 Mar 2020: Vol. 13, Issue 622, eaay1478