Development of hydrophobic TRAP1 inhibitors

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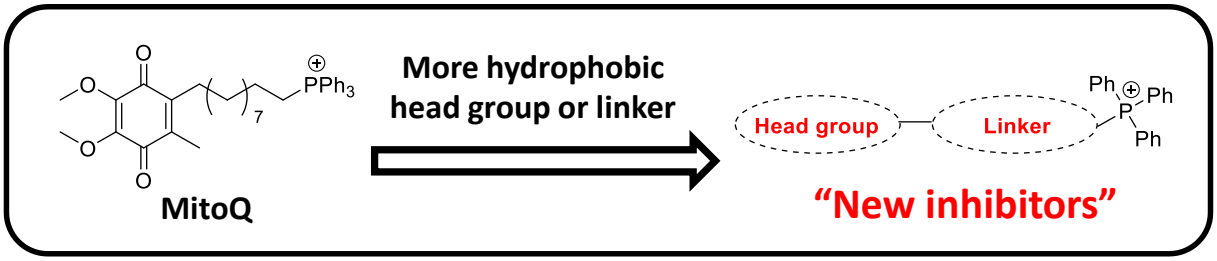
Hsp90 (Heat shock protein 90) family proteins are ATP-dependent molecular chaperones often related to tumorigenesis.[1] A mitochondrial Hsp90 paralog, TRAP1 (tumor necrosis factor receptor-associated protein 1), reprograms cellular metabolism and signaling pathways.[2,3] It allows tumor cells to adapt to various cellular stresses in rapid growth and to evolve into more aggressive.[4] Therefore, TRAP1 has been studied as a promising drug targets for cancer and other diseases.

Mitoquinone (MitoQ) is a recently reported TRAP1 inhibitor targeting the client binding site, not the canonical ATP-binding site.[2] Since misfolded TRAP1 clients would have nonpolar residues exposed on the surface, the client binding site of TRAP1 also has nonpolar residues. Therefore, more hydrophobic inhibitors are expected to have higher affinity toward TRAP1.



References

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