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Communication (heading)

Communication

Development of a potent peptide inhibitor of estrogen receptor α

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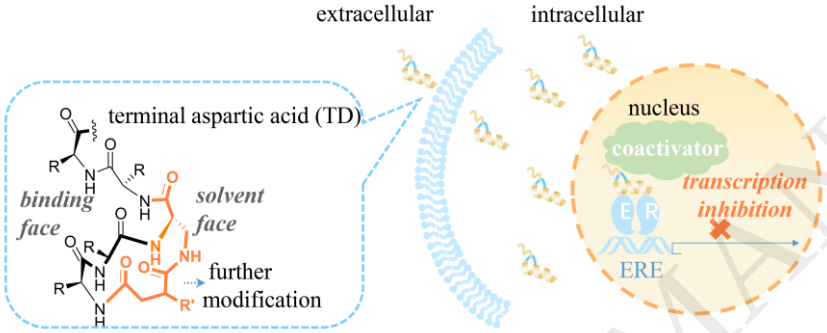
Graphical Abstract



A potent peptide inhibitor of estrogen receptor α (ER-α) with significantly increased cellular uptake and cellular distribution was developed by cell penetrating peptide attachment. The resulted peptide conjugate showed selective toxicity towards estrogen receptor positive cell lines and induced decreased transcription of estrogen receptor α downstream genes.

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ABSTRACT

We have developed a facile N-terminus helix-nucleating strategy using an unnaturally tethered aspartic acid (TD strategy). Relatively weak nuclear translocation efficiency of TD PERM limits its further biological applications. A potent peptide inhibitor of estrogen receptor α (ER-α) with significantly increased cellular uptake and cellular distribution was developed by cell penetrating peptide attachment. The resulted peptide conjugate showed selective toxicity towards estrogen receptor positive cell lines and induced decreased transcription of estrogen receptor α downstream genes.

Overexpression of estrogen receptors (ER-α and ER-β, nuclear receptor superfamily members) is observed in over 70% of all breast cancer cases [1]. Upon the stimulation of estradiol, ER-α regulates many genes to prompt cell proliferation and metastasis [2]. Selective estrogen receptor modulators (SERMs) designed as competitive inhibitors to target estradiol binding pocket, such as tamoxifen and raloxifen, are broadly used as efficient ER positive breast cancer therapeutics [3]. However, in addition to increasing