The thyroid hormone receptor (THR) is an important member of the nuclear receptor family that can be activated by endocrine disrupting chemicals (EDC). Quantitative Structure-Activity Relationship (QSAR) models were developed to facilitate the prioritization of THR-mediated EDC for the experimental validation. The largest database of binding affinities available at the time of the study for ligand binding domain (LBD) of THRβ was assembled to generate both continuous and classification QSAR models with an external accuracy of $R^2 = 0.55$ and CCR = 0.76, respectively. In addition, for the first time a QSAR model was developed to predict binding affinity of antagonists inhibiting the interaction of coactivator with AF-2 domain of THRβ ($R^2 = 0.70$). Furthermore, molecular docking studies were performed for THRβ ligands (57 agonists and 15 antagonists of LBD, 210 antagonists of AF-2 domain, supplemented by putative decoys/non-binders) using several THRβ structures retrieved from the Protein Data Bank. We found that two agonist-bound THRβ conformations could effectively discriminate their corresponding ligands from presumed non-binders. Moreover, one of the agonist conformations could discriminate agonists from antagonists. Finally, we conducted virtual screening of a chemical library screened by EPA as part of the Tox21 program to identify potential THRβ-mediated EDCs using both QSAR models and docking. We concluded that the library is unlikely to have any EDC that would bind to THRβ. Models developed in this study can be employed to either identify environmental chemicals interacting with THR or, conversely, eliminate the THR-mediated mechanism of action for chemicals of concern.