Thyroid Receptors (TRs) belong to the family of the Nuclear Hormone Receptors. They are essential in regulation of growth, metabolic rate, cholesterol level and heart rate. In mammals four isoforms are present; TR alpha-1, TR alpha-2, TR beta-1 as well as TR beta-2. In this work we present the process of designing novel Maltose binding protein-Intein- Thymidylate Synthase:: Thyroid Receptor alpha-1 (pMIT::TR alpha-1) biosensor to detect potential TR alpha-1 agonists and antagonists. Resent results of computational analysis of binding modes of the compounds to the TR alpha-1 active side are also shown. In this study Shape Signatures method allowed for fast identification of the compounds which are similar to known TR antagonists and agonist such as NH3, T3 and Triac.