

LAY ABSTRACT

TITLE: Identification of Estrogen-Related Receptor α Agonists in the Tox21 Compound Library

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The female hormone estrogen works in the human body by binding to and activating a receptor protein called estrogen receptor (ER). The estrogen-related receptor α (ERR α) was named as a receptor protein whose structure is similar to ER, but estrogen cannot bind to it. Its biological function is different from ER. This is important because ERR α regulates the production of energy for various functions in our body, however it is not yet known whether any steroid hormone can bind to this receptor. It is known that many environmental chemicals can bind and affect the activity of ER, therefore, increasing breast cancer risk. The goal of this study was to determine whether similar or different environmental chemicals could affect the activity of ERR α .

A cell line system was developed to screen 10,000 chemicals (known as the Tox21 10K collection). A group of these chemicals related to statin, which lowers the level of cholesterol in the blood, was found to bind and activate ERR α . Several sets of experiments were performed to confirm the ability of these statin-like chemicals to activate ERR α . Our novel finding suggest that environmental chemicals with structures like statin may affect the energy production pathways in our body through an interaction with ERR α .

