

PanVera Corporation

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Project Title: HTS Assays for Selective Steroid Receptor Modulators

Technology Developed

Recombinant human steroid hormone receptors including estrogen, androgen and glucocorticoid receptors have been produced and purified. Fluorescent steroid ligands that bind to each of the receptors have been identified and used to develop single addition "mix and read" assays for identification of novel ligands from pharmaceutical chemical libraries or environmental samples. The assay measures the difference in fluorescence polarization of the fluorescent ligand when it is bound to a steroid receptor and when it is displaced by a competing test ligand.

Uses of Technology

The steroid receptor superfamily is a class of ligand activated transcription factors that are involved in regulation of almost all aspects of cell growth and metabolism. Thus it is not surprising that from a pharmaceutical perspective they are considered key targets for therapeutic intervention for a wide range of diseases and metabolic disorders; these include breast and prostate cancers, osteoporosis, inflammation, and diabetes. To enable these drug discovery opportunities, simple, robust assay methods that can be used to assess large diverse chemical collections for identification of novel steroid receptor ligands are needed. In addition, the ability to assess manmade and naturally occurring chemicals found in soil and water for potential disruption of endocrine functions has become an important priority for environmental agencies and industrial manufacturing groups.

Previous to PanVera's efforts in this area, investigators relied on impure preparations of rodent receptors and cumbersome radioactive assay methods to assess binding of test compounds to steroid receptors. Screening the hundreds of thousands of compounds typical of pharmaceutical compound collections was not practical using these methods. Using the purified recombinant receptors and fluorescent ligands developed by PanVera, pharmaceutical scientists can now test tens of thousands of compounds for in a single day using any one of a number of commercially available fluorescence plate readers typically used for automated high throughput screening. Thus, this technology should accelerate the development of more selective steroid receptor modulators to address a wide range of diseases and metabolic disorders.

Cumulative sales/ revenues to date from SBIR/STTR-developed technology

Approximately \$1 million for sales of recombinant steroid receptors and fluorescent assay probes.

National Institutes of Health Awards

R43/R44 DK54619