

# NUCLEAR HORMONE RECEPTOR SCREENING

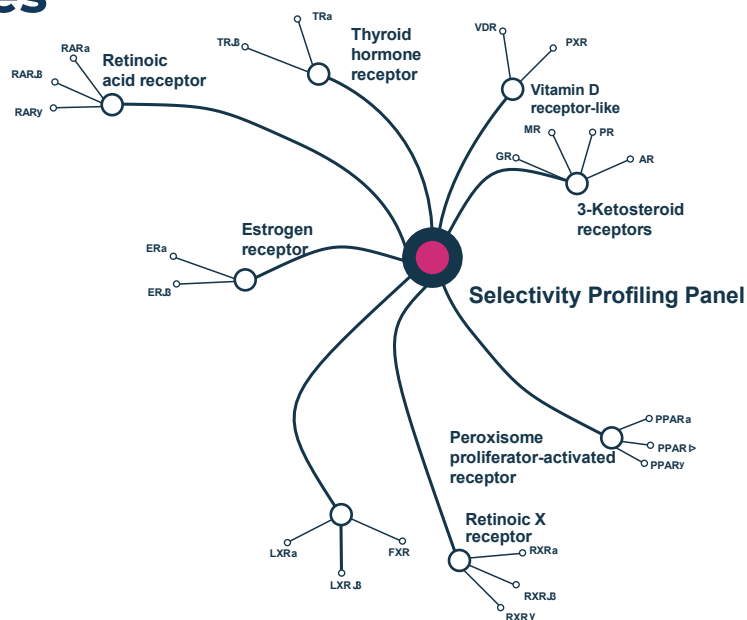
## Overview of Capabilities

### Multiple Assay Platforms

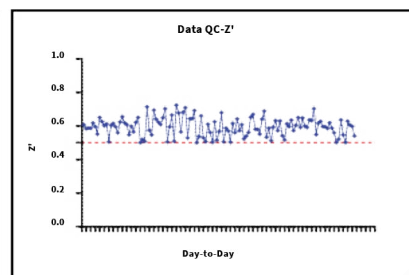
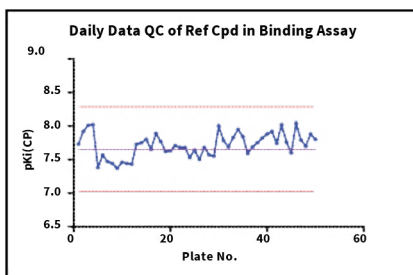
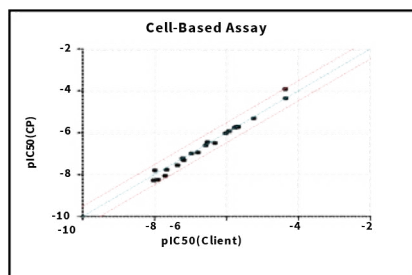
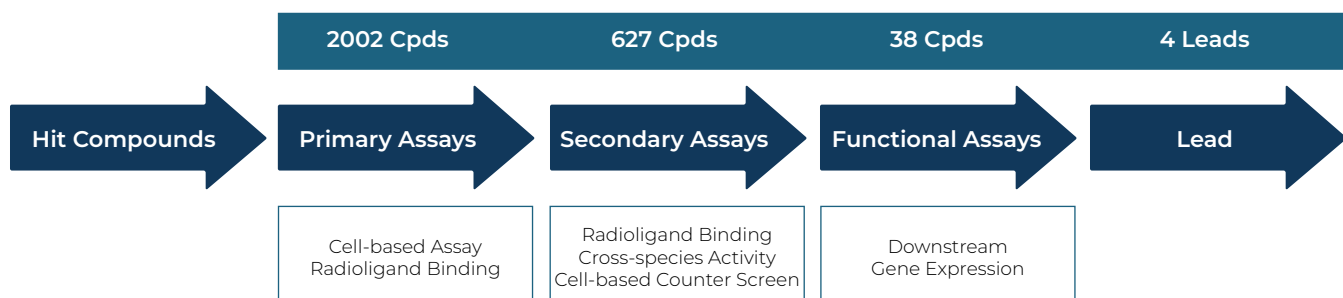
- Cell-based Assays
  - Gal4 DBD-NHR LBD reporter assay
  - Full-length NHR reporter assay
- Biochemical Assays
  - TR-FRET co-activator recruitment assay
  - Radioligand binding assay

### Broad Service Scope

- High-throughput screening
- Lead optimization
- Selectivity panel
- IC50 determination
- Compound mode of action



## Drug Discovery Project: Hit-to-Lead



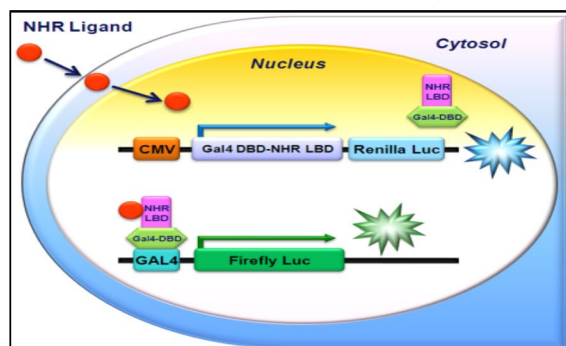
# Selectivity Profiling Panel

3-Ketosteroid Receptors	Estrogen Receptor	Liver X Receptor-like	Peroxisome Proliferator-Activated Receptor
GR	ER $\alpha$	LXR $\alpha$	PPAR $\alpha$
MR	ER $\beta$	LXR $\beta$	PPAR $\delta$
PR		FXR	PPAR $\gamma$
AR			

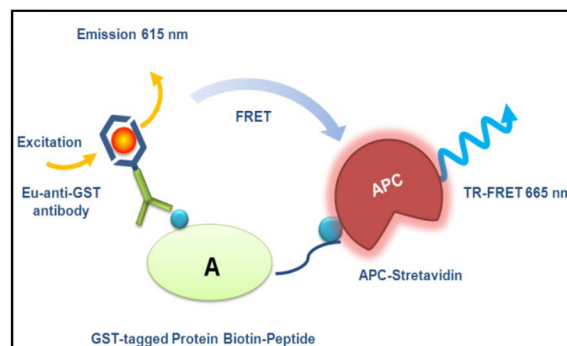
  

Retinoic X Receptor	Retinoic Acid Receptor	Thyroid Hormone Receptor	Vitamin D Receptor-like
RXR $\alpha$	RAR $\alpha$	TR $\alpha$	VDR
RXR $\beta$	RAR $\beta$	TR $\beta$	PXR
RXR $\gamma$	RAR $\gamma$		

## Cell-based Reporter Assay

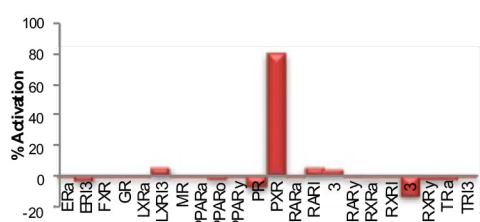


## TR-FRET Coactivator Recruitment

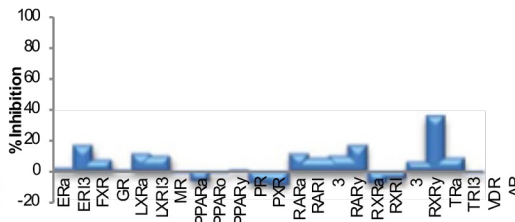


# Compound Selectivity Profiling on 22 NHRs

## Agonist Mode



## Antagonist Mode



Cell-based luciferase reporter assay on 22 NHRs provides the information of compound selectivity for SAR guidance.