
Nuclear Receptor Activation

Cytochrome P450 (CYP) induction occurs through nuclear receptor activation and increased gene expression of the CYP enzyme. Nuclear receptor activation can, therefore, be used as an early stage screen for assessment of CYP induction. Cyprotex offers nuclear receptor activation for PXR, AhR and CAR3 for the regulation of CYP3A4, CYP1A2 and CYP2B6, respectively. These assays are set up for rapid data delivery to feed into drug discovery programs and inform decision-making on potential CYP induction.

▶ Nuclear Receptors

- PXR (pregnane X receptor) for CYP3A4
- AhR (aryl hydrocarbon receptor) for CYP1A2
- CAR3 (constitutive androstrane receptor 3) for CYP2B6

▶ Method

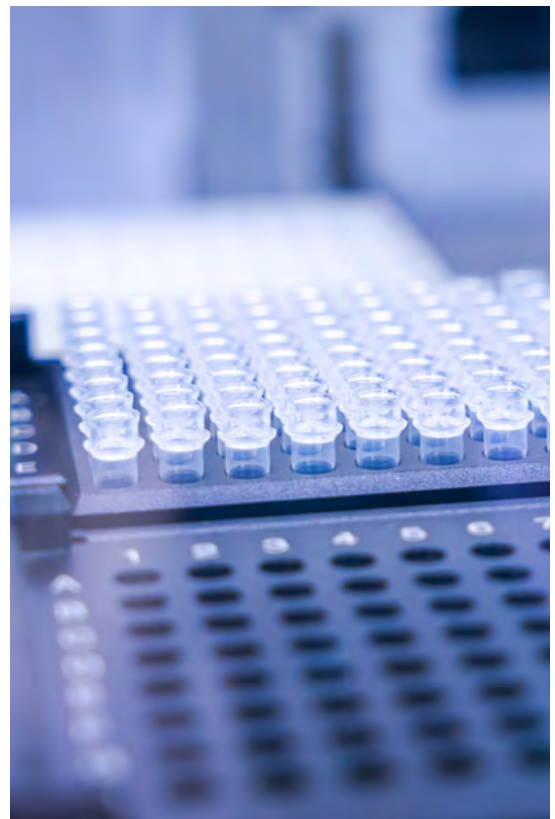
- luciferase reporter gene assay
- human cells engineered to provide expression of human nuclear receptor

▶ Positive Controls

- rifampicin (PXR)
- methylcholantrene (AhR)
- CITCO (CAR3)

▶ Data Delivery

- fold activation relative to vehicle control
- % cell viability
- % activation relative to the top dose of positive control
- EC₅₀ (if appropriate)





Benefits of using Cyprotex

- ▶ **Industry validated protocols.** Our protocols are based on industry-accepted protocols and are used routinely by our clients to assist them making decisions in drug discovery.
- ▶ **Designing screening strategies.** Our experienced ADME experts can guide you on tiered screening strategies based on your chemistry and intended target. You will be supported by a dedicated study manager for your project.
- ▶ **Rapid turnaround.** Standard turnaround is 10 business days. Regular screening contracts can benefit from < 5 business day turnaround.
- ▶ **Flexible approach.** For larger scale regular projects, customer-specific protocols can be designed and implemented on our high throughput platform.

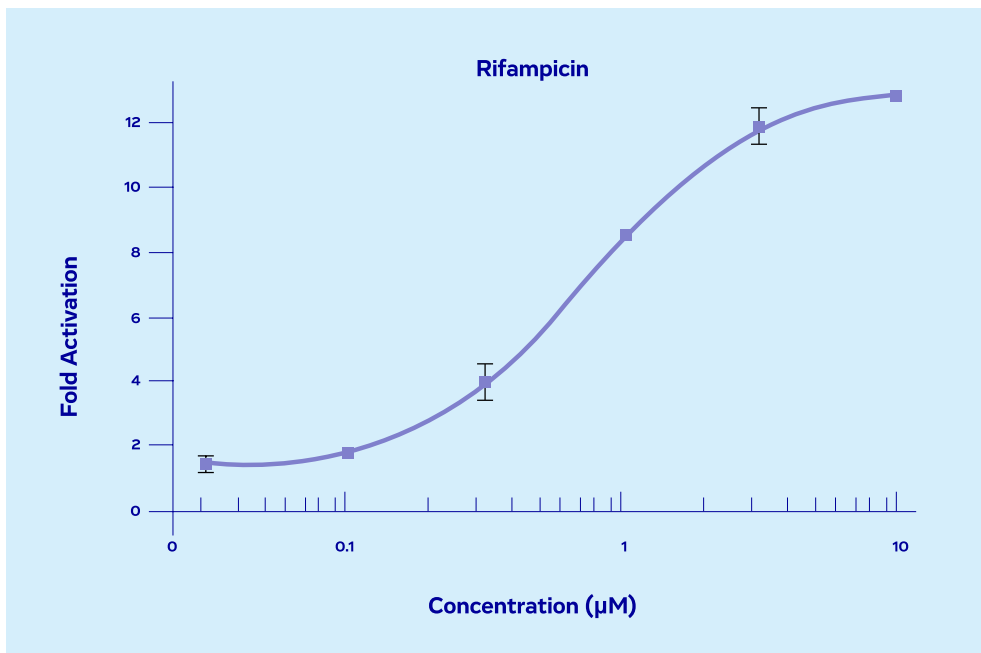


Figure 1: Graph illustrates PXR activation by rifampicin. Data show the mean fold activation to the vehicle control.

Related Services

- ▶ CYP induction using human hepatocytes with mRNA and/or catalytic activity analysis
 - Basic mRNA fold change
 - Correlation method: relative induction score
 - Mechanistic model: basic kinetic model
- ▶ Regulatory drug-drug interaction packages

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