Nuclear Receptor News

Dedicated to Nuclear Receptor Research and Researchers

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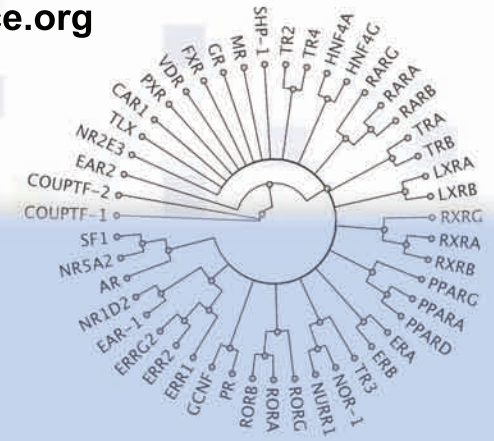

In This Edition

From:
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TO:

Nuclear Receptor News

Sponsored By: INDIGO Biosciences, Inc. The Nuclear Receptor Company™

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New Robust Ready-To-Use Nuclear Receptor Reporter Assay Kits

INDIGO Biosciences introduces a unique portfolio of cell-based, Nuclear Receptor Reporter Assay products for on-demand use in drug discovery and development. INDIGO Biosciences' assays enable sensitive screening of test compounds for agonist or antagonist activities for use in primary screening or secondary and toxicology screening. Kits are currently available for **PPARγ, LXRB, ERα, and MR**. Proprietary cryopreservation process, CryoMiteTM, permits overnight delivery for on-demand use. Stable-glow luciferase chemistry allows plates to be processed in batch, increases signal to noise ratios and yields excellent Z' scores. The assays are optimally configured for HTS or low throughput screening in 3x 32-, 96- and 384-well plate formats.

INDIGO Biosciences, 814-234-1919, www.indigobiosciences.com

NRN Nuclear Receptor News

Dedicated to Nuclear Receptors and Nuclear Receptor Research

Welcome

Welcome to the first issue of *Nuclear Receptor News*, a newsletter dedicated to this important family of proteins and to those researching in this fast-moving field. NRN is designed to provide a platform to share information and topics of interest. The website, www.nrresource.org will be up-and-running soon and will provide even more useful information and means of communication.

NRN will be published four times each year, and focus on a different receptor in each issue. We will keep you up to date with summaries of new journal articles and discussions of exciting research.

Please pass this correspondence to your colleagues, and ask them to sign up at info@nrresource.org. You are encouraged to send any additional material you'd like to see, links to valuable sites, and become a 'guest author.'

Cheers, Jack Vanden Heuvel, PhD

Visit my site on PPARs at http://ppar.cas.psu.edu/

PPARγ as an Important Drug Target

Peroxisome proliferator-activated receptors (PPARs) are members of the nuclear receptor (NR) superfamily of transcription factors, similar in both structure and function to the steroid, thyroid and retinoid receptors. In the systematic nomenclature for nuclear receptors[1], PPARs comprise the group C of subfamily 1 (NR1C). The subfamily has been defined as PPARα (NR1C1), PPARβ (also called PPARδ and NUC1, NR1C2) and PPARγ (NR1C3), each with a possibility of different ligands, target genes and biological role. The discovery of PPARγ as a target of insulin sensitizers, represented by thiazolidinediones (TZDs), has attracted significant scientific interest in this receptor and has had a great impact on the pharmaceutical industry (reviewed in [2]). The clinical and commercial success of the PPARγ agonists pioglitazone (Actos) and rosiglitazone (Avandia) has lead to accelerated development of novel anti-diabetic agents and treatments. Research into other therapeutic benefits of PPARγ activation related to inflammation and protection from various forms of cancer has also generated great enthusiasm (see Figure 1), and shows the breadth of PPARγ's biological niche. In addition to synthetic molecules, PPARγ is activated by both endogenous as well as dietary and environmental molecules, although the biological and pharmacologic ramification of this regulation is not always evident. Despite the plethora of beneficial effects observed for PPARγ ligands, there remains a few obstacles related to potential clinical toxicity of these agents, not the least of which is cardiovascular effects. Taken these factors into account, there is increasing need for addressing the activation of PPARγ by small molecules to determine on-target as well as off-target effects.

1.Committee NRN. A unified nomenclature system for the nuclear receptor superfamily. Cell 1999;97:161-3.

2.Vasudevan AR, Balasubramanyam A. Thiazolidinediones: a review of their mechanisms of insulin sensitization, therapeutic potential, clinical efficacy, and tolerability. Diabetes Technol Ther 2004;6:850-63.

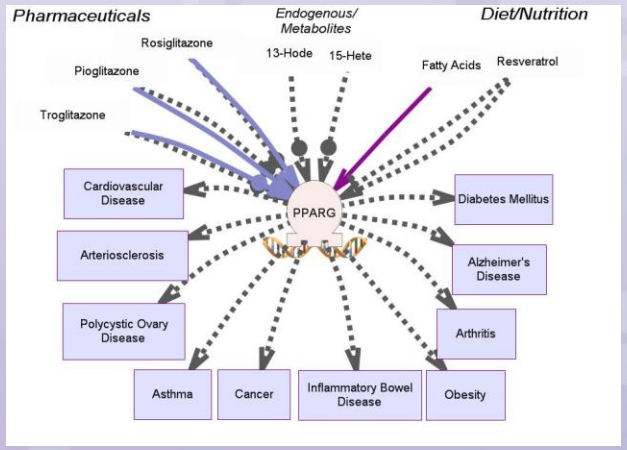

Figure 1. Clinical effects of PPAR-gamma ligands. Generated by Pathway Studio (Ariadne Genomics, Inc. Rockville, MD). An interactive version of this figure can be found on the NRN website.