SALK INSTITUTE
FOR BIOLOGICAL STUDIES

Office of Technology Management
10010 North Torrey Pines Road • La Jolla, CA 92037
Phone 858.453.4100 • Fax 858.450.0509
Web http://www.salk.edu/otm/techtran.html

Treatment of Disease States which Result from Neoplastic Cell Proliferation Using PPAR-gamma Activators and Compositions Useful Therefor

Inventors:

Ron Evans, Laszlo Nagy, and Peter Tontonoz

Applications:

Oncology, Drug Discovery and Development
Administration of PPAR-gamma agonists, optionally in combination with RXR specific agonists, can block neoplastic cell proliferation

Neoplastic cell proliferation is the underlying cause of a wide variety of diseases, e.g., breast cancer, leukemia, colon cancer, prostate cancer. Traditional approaches to treatment of neoplastic cell proliferation include surgery, chemotherapy and radiotherapy. Induction of terminal differentiation represents a promising alternative to conventional methods of treatment for certain malignancies. It has been discovered that PPAR-gamma is expressed consistently in tissues associated with a variety of disease states which result from neoplastic cell proliferation. Maximal activation of PPAR-gamma with exogenous ligand promotes terminal differentiation of primary cells which are otherwise subject to neoplastic cell proliferation. Thus, cells undergoing neoplastic cell proliferation can be induced to differentiate, thereby blocking further proliferation. It has also been discovered that RXR-specific ligands are potent agents for induction of differentiation of cells expressing the PPAR-gamma/RXR-alpha heterodimer and that simultaneous treatment of cells subject to neoplastic cell proliferation with a PPAR-gamma-selective ligand, in combination with an RXR-specific ligand, results in an additive stimulation of differentiation. The invention includes compounds and compositions which could be useful for the treatment of breast cancer, leukemia, colon cancer and prostate cancer.

References:
PNAS USA 1997 Jan 7; 94(1):237-41

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Contact: Anne-Marie Mueller, Director, OTM, 858.453.4100 x1275, amueller@salk.edu