

## Novel Compounds for Treatment of Liposarcomas

**INVENTION:** Researchers at Salk Institute have found that PPAR gamma is expressed consistently in each of the major histologic types of human liposarcoma. Maximal activation of PPAR-gamma with exogenous ligand (a thiazolidinedione or derivative thereof and RXR-specific retinoids) promotes terminal differentiation of primary human liposarcoma cells, thereby blocking further proliferation. It has also been discovered that RXR-specific ligands are potent adipogenic agents in cells expressing the PPAR-gamma/RXR-alpha heterodimer and that simultaneous treatment of liposarcoma cells with a thiazolidinedionyl moiety (a PPAR-gamma-selective class of compounds) and an RXR-specific ligand results in an additive stimulation of differentiation. The invention also includes compositions useful for the treatment of liposarcomas.

**APPLICATIONS:**

- Non-toxic alternative to conventional chemotherapy
- Therapeutic for liposarcomas

**ADVANTAGES:**

- Less systemic toxicity than current modes of therapy
- Induces growth arrest as a monotherapy

**STAGE OF DEVELOPMENT:** Preclinical, in vitro trials with human liposarcomas

**BACKGROUND:** Liposarcoma is a malignant tumor found in fat cells in deep soft tissue, such as those found inside the thigh or in the retroperitoneum. It is the most common soft tissue malignancy in adults, accounting for at least 20% of all sarcomas in this age group. Localized disease is treated primarily with surgery, often in combination with radiotherapy. Metastatic liposarcoma is associated with an extremely poor prognosis, with average five-year survival ranging from 70% to 25%, depending on the type of tumor. The development of effective, non-invasive methods for treating liposarcomas would fill a significant unmet need.

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