

Novel Targeted Therapy for Depression and Cancer (Hadasit)**code:** 8-2011-173[Bernard Lerer](#), Hadassah Ein Kerem, Psychiatry**Investigators: Bernard Lerer, MD; Osnat Ashur-Fabian, PhD****Market Need**

High-grade serous (HGS) ovarian cancer is the most lethal gynecologic cancer with a global market size valued at >\$1B in 2016. It is expected CAGR of 23.7% at least until 2022, with the U.S. at the forefront. The rising incidence of ovarian cancer seems to be due to growing geriatric population and unhealthy lifestyles. In 2016, approximately 235,200 new cases and 140,000 deaths were reported worldwide. A better understanding of the molecular basis of this aggressive disease is merited to find novel treatments. It is known that tumors have evolved a strategy of eliminating and avoiding the local differentiating activity of the biologically active thyroid hormone (T3), via re-expression of the T3-catabolizing enzyme, DIO3, which makes DIO3 inhibition a potential approach for treatment of tumors it has a role in, and specifically in ovarian cancer.

Innovation

Novel DIO3 inhibitors, generated based on a unique DIO3-mimic, for the treatment of ovarian cancer and depression.

Findings

- ◆ DIO3 protein levels were significantly elevated in several HGS ovarian cancer cell lines, as well as in tumor tissues from an ovarian cancer mice model and human patients.
- ◆ Using a synthetic DIO3-mimic the group generated several novel putative DIO3 inhibitors. Screening experiments in ovarian cancer cells indicated a marked reduction in cell density, deformed cell morphology and a reduction in cell viability by several lead compounds.
- ◆ Toxicology experiments confirmed low toxicity profile for these selected molecules.
- ◆ DIO3 knockdown in ovarian cancer cells reduced cell proliferation in parallel to an increase in apoptosis.
- ◆ In vivo POC showed that tumor growth was attenuated in the DIO3KD cells, compared to control cells.

Indications/Applications:

The first indication suggested here is ovarian cancer, although other types of cancer in which DIO3 plays a role in.

Competitive Advantage

A novel mechanism for treatment of ovarian cancer and potentially other types of cancer, using small molecules with a defined target.

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