Second-Generation Estrogen Receptor Down-Regulators for Medical Therapy

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SUMMARY

UCLA researchers in the School of Medicine have developed a series of novel estrogen receptor antagonists for breast cancer therapy.

BACKGROUND

Breast cancer is the most common malignancy in women in North America. Each year, more than 210,000 new cases of breast cancer are diagnosed in the US. About 70% of breast cancers depend on estrogen for growth and progression. In the clinic, endocrine therapy has proven to be one of the most effective treatment strategies for breast cancer. However, a large number of patients with localized disease and all of the patients with metastatic breast cancer become resistant to current endocrine therapies such as tamoxifen and aromatase inhibitors. Moreover, recent data suggests that roughly 14% of metastatic breast cancer harbor estrogen receptor mutations that reduce sensitivity to the widely used tamoxifen and fulvestrant, so higher doses of these antiestrogens appear to be needed to achieve good antitumor effects. Therefore, there is an urgent need to develop alternative therapeutics to overcome endocrine resistance and to improve the long-term survival of patients afflicted with breast cancer.

INNOVATION

Researchers in UCLA School of Medicine have developed a series of novel estrogen receptor antagonists that are very effective in inhibiting the growth of breast cancer. These unique, selective estrogen receptor down-regulators optimally target the estrogen receptor for degradation and elimination, thereby blocking downstream growth-promoting signaling pathways induced by estrogen receptors in breast cancer. These never before reported compounds are more potent than fulvestrant and are effective in endocrine-resistant disease models. They exhibit the proper biologic and pharmacologic profile to be developed as therapeutics for endocrine-sensitive and -resistant cancers in the clinic.

APPLICATIONS

These selective estrogen receptor down-regulators (SERDs) can be used as therapeutics for endocrine-sensitive and -resistant breast cancers.

ADVANTAGES

- More effective than the first-generation commercial drug (Faslodex; fulvestrant) in suppressing tumor growth. Faslodex has poor bioavailability and must be administered by intramuscular injection. This is a significant barrier to achieving optimal therapeutic efficacy as an anticancer drug. Our second-generation SERD compounds are designed to have greater aqueous solubility and show more potent antitumor effects in preclinical experiments than Faslodex.
- May overcome endocrine resistance in breast cancer therapy. The estrogen receptor is often expressed in tumors with endocrine resistance to both antiestrogens (such as tamoxifen) and aromatase inhibitors. Hence, SERD compounds that can down-regulate estrogen receptors can be effective in overcoming endocrine resistance to both antiestrogens and to aromatase inhibitors.

STATE OF DEVELOPMENT

Researchers have designed, synthesized, and tested several selective estrogen receptor down-regulators (SERDs) using *in vitro* human breast cancer models.

PATENT STATUS

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OTHER INFORMATION

KEYWORDS

Breast cancer, Estrogen receptor, Endocrine therapy

CATEGORIZED AS

- **Medical**
  - Disease: Cancer
  - Disease: Women's Health
  - Therapeutics

RELATED CASES

2015-166-0

Country	Type	Number	Dated	Case
Canada	Issued Patent	3,063,834	05/06/2025	2015-166
Germany	Issued Patent	3463342	09/06/2023	2015-166
France	Issued Patent	3463342	09/06/2023	2015-166
United Kingdom	Issued Patent	3463342	09/06/2023	2015-166
United States Of America	Issued Patent	10,918,648	02/16/2021	2015-166
United States Of America	Issued Patent	10,400,006	09/03/2019	2015-166
United States Of America	Published Application	2022-013374	05/05/2022	2015-166

Additional Patent Pending

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- Novel Therapeutic Analogues of Metformin for the Treatment of Cancers

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