Award ID:
DP150055

Project Title:
Druggable Targets that Regulate the Antitumor Activity of ER-beta

Award Mechanism:
Bridging the Gap: Early Translational Research Awards

Principal Investigator:
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Entity:
The University of Texas Health Science Center at San Antonio

Lay Summary:

Estrogen Receptor beta (ER-beta) is often viewed as the “Cinderella sister” of ER-alpha with just the “opposite personality”. Unlike ER-alpha that has the known tumor-promoting activity, ER-beta has an antitumor activity in breast cancer. Because ER-beta is present in as many as half of all breast cancer cases, rallying its tumor-inhibitory activity is an attractive therapeutic strategy. However, this therapeutic potential of ER-beta has been largely untapped.

The current proposal, which is aimed at mobilizing the antitumor activity of ER-beta, is based on two recent exciting developments in ER-beta research. First, a highly potent ER-beta-specific activator was shown recently to be clinically safe and well tolerated in humans. Second, our pioneer discovery of a molecular switch for the antitumor activity of ER-beta enables us to mobilize ER-beta function with unprecedented precision.

To rapidly maximize the translational potential of our novel findings, we have assembled a highly interactive multidisciplinary team that includes expertise in breast cancer biology, drug discovery and development, clinical oncology, and pharmaceutical partnership. This group of investigators will identify small-molecule compounds that, when acting alone or combined with the clinically safe ER-beta activator, can inhibit triple negative breast cancer (TNBC), an aggressive subtype of breast cancer that currently lacks any targeted therapies.

When successfully executed, the proposed work promises to have far-reaching and transformative impact on breast cancer treatment. Because the ER-beta activator is well tolerated in humans, our studies promise to inform accelerated development of new strategies for TNBC treatment. Furthermore, uncovering new small-molecule compounds that can synergize with the ER-beta activator will help development of novel combinational therapies.