

Bankhead-Coley Cancer Research Program

El-Ashry, Dorraya

*Medicine
University of Miami*

*2009 Program
Florida Research Challenge
(2-year project)*

Project Title: Restoring ER Expression and Anti-Estrogen Response in ER-Negative Breast Cancer

Project Summary: The overall goal of the studies is to develop a novel therapy for estrogen receptor (ER)-negative breast cancer based on the re-expression of ER and restoration of anti-estrogen responses. Approximately 30-35 percent of breast cancer lacks expression of the estrogen receptor (ER). ER-negative breast cancer carries a worse prognosis, but more importantly, does not respond to hormonal therapies, must be treated with toxic chemotherapies, and frequently is resistant to these chemotherapies. The project has three specific aims. First, to perform a pilot clinical trial to determine if treatment with AZD6244 (a substance being studied in the treatment of several cancer types) increases ER protein expression in ER-breast cancer in humans. Second, to determine the frequency of ER re-expression and restoration of anti-estrogen sensitivity achieved and gene expression/phosphoprotein expression patterns associated with this in *in vitro* models with AZD6244. Third, to perform correlative analyses on specimens from both non-responding and responding clinical trial participants that will determine potential mechanisms underlying lack of re-expression of ER in non-responders and whether re-expression of ER in responders restores functional ER signaling and response to anti-estrogen therapy. Successful completion of this work will lead to a clinical trial testing a combination therapy in ER-breast cancer patients. If we determine this to be feasible, this could have a major impact on the treatment of ER-breast cancer.