

**New Jersey State Commission on Cancer Research  
LAY ABSTRACT OF RESEARCH PROJECT**

NAME OF PRINCIPAL INVESTIGATOR/PROGRAM DIRECTOR: **Celine Gelinas**

Project Title: **Role of CAPER in ER and NF- $\kappa$ B activity in breast cancer**

Description: **This project is to characterize the role of coactivator CAPERa in breast cancer cell survival, chemoresistance and invasion and, to investigate its contribution to the negative cross-talk between Era- and NF- $\kappa$ B in these cells and the mechanisms involved.**

Breast cancer is the second leading cause of cancer death in American women between ages 40-55. It is expected that 211,240 new cases of invasive breast cancer will be diagnosed in 2005 with an additional 58,490 cases of *in situ* breast cancer, and that 40,410 patients will die from the disease. In New Jersey, the incidence of breast cancer in Caucasian and African-American women between 1998- 2002 was 140.7 and 115.2 per 100,000 respectively, with mortality rates of 29.5 and 34.3 per 100,000.

It is therefore important to identify the factors involved in the development and progression of this disease. A hallmark of many breast cancers is the hyperactivation of the Rel/NF- $\kappa$ B transcription factors that are required for the survival of tumor cells and their resistance to chemotherapy. Importantly the expression status of estrogen receptor alpha (ERa) is a critical prognostic indicator for breast cancer and is inversely correlated with the activity of Rel/NF- $\kappa$ B. That is, NF- $\kappa$ B becomes strongly activated as breast cancer cells progress to a more aggressive, chemoresistant and estrogen-independent status. In this regard, we recently isolated the CAPERa protein as an interacting factor for NF- $\kappa$ B. Importantly, CAPERa strongly potentiates the ability of NF- $\kappa$ B to activate gene expression and was previously implicated as a coactivator for ERa. We hypothesize that CAPERa is an important mediator of the effects of ERa and NF- $\kappa$ B on gene expression in breast cancer cells, and that it may be involved in the negative cross-talk between ERa and NF- $\kappa$ B in ERa-positive breast cancer. In this application, we will: 1) characterize how the role of CAPERa in breast cancer cell survival, chemoresistance, proliferation, anchorage independence and invasion, and 2) address CAPERa's contribution to ERa- and NF- $\kappa$ B-mediated gene expression, the negative interplay between these factors and the mechanisms involved. Overall these studies will help to clarify the contribution of these factors to breast cancer progression and will reveal if CAPERa should be further evaluated as a possible molecular target for therapeutic intervention, as small molecules capable of selectively inhibiting the interaction of CAPERa with NF- $\kappa$ B might be of clinical relevance. Given the high incidence of breast cancer in New Jersey and in the United States, the discovery of novel targets for therapeutic treatment is highly significant.