Genomic Signature Induced by r-hCG as a Marker of a Preventive Effect in a Woman at Risk to Develop Breast Cancer
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Background

One of the established risk factors for breast cancer is a BRCA1 and BRCA2 germ line mutations, that confer a lifetime risk of up to 70%. Carriers of these mutations therefore constitute a cohort with the highest risk. Breast cancer prevention in these women is challenging. To date, bilateral mastectomy remains the most effective means of reducing the incidence of BRCA-associated breast cancer. Chemoprevention with selective estrogen receptor modulators such as tamoxifen and aromatase inhibitors have been used to reduce breast cancer development for women at high risk, but it has not been validated as a chemopreventive method for primary breast cancer in BRCA1 mutation carriers.

Although there is an association between early full term pregnancy and a reduction in the lifetime risk of developing breast cancer, the mechanism providing this protection is still being determined. Chorionic gonadotropin (hCG) is a glycoprotein hormone, typically produced early in pregnancy after implantation, it is also upregulated in certain cancer tumors in both males and females. Thus, compositions and methods that attenuate hCG production within cancer microenvironments and ultimately improve patient outcomes are needed.

Summary of the Invention

hCG is a heterodimeric protein composed of two non-covalently linked (α and β) subunits. While the α-subunit is ubiquitous among the other glycoprotein families, the β-subunit is limited to hCG. In particular, overexpression and secretion of β-subunit in various cancer cell types has been observed independent of α-subunit gene expression. Researchers from Fox Chase Cancer Center and Ghent University developed methods of treating a nulligravid females having a high risk of developing breast cancer. Application of recombinant hCG (r-hGC) and monitoring of genomic signature of the breast induced by r-hCG in BRCA1/2 carriers can be successfully combined with regimens for preventive or therapeutic breast cancer treatment. Effectiveness of such application for breast cancer prevention was successfully tested in cell culture, animal studies and clinical trial as well. Thereby, monitoring the efficacy of treatment of patient with developed breast cancer or having a high risk of developing breast cancer with a panel of genes from the biological sample can ultimately improve patient outcomes.