Modulation of Progesterone Receptor Activity
Treated with Conjugated Estrogens and Bazedoxifene
Huh, Eunna, State University of New York at Fredonia, Class of 2014
Carolyn L Smith, ph.D. Department of Molecular & Cell Biology, Baylor College of Medicine

When Women reach menopause, they face dramatic changes which can include severe symptoms such as night sweats, vaginal dryness, depression, hot flashes, and osteoporosis. These symptoms have been treated by hormone therapy consisting of estrogen and progesterone, but this combined therapy is associated with an increase in the risk of breast cancer; thus another approach for control of menopausal symptoms is desirable. Selective Estrogen Receptor Modulators (SERM) are used for reducing breast tumor as well as increasing bone mineral density (BMD). Clinical studies showed that a combination of SERM and one or more estrogen can increase BMD, and relieve menopausal symptoms. This combination is referred as Tissue Selective Estrogen Complex (TSEC). As a TSEC, the combination of bazedoxifene and conjugated estrogens (CE) inhibited MCF-7 cell growth in vitro.

I tested the level of progesterone receptor (PR) activity was assessed by GRE-e1b-luc reporter gene which generates luciferase when it is activated. It was optimized the concentration of PR and the level of progesterone in dose response experiments. In HeLa cells transfected only with PR, and the luciferase reporter gene, the PR activity was not stimulated by CE, BAZ, and BAZ/CE, whereas showed modest inhibitory effect. On the other hand, in progesterone-treated cells expressing both PR and ER (estrogen receptor), BAZ and BAZ/CE stimulated PR activity while CE inhibited the receptor’s transcriptional activity.