

Public Abstract**First Name:**Matthew**Middle Name:**Thomas**Last Name:**Cook**Adviser's First Name:**Salman**Adviser's Last Name:**Hyder**Co-Adviser's First Name:****Co-Adviser's Last Name:****Graduation Term:**SS 2015**Department:**Biological Sciences**Degree:**PhD**Title:**THERAPEUTIC AND CHEMOPREVENTIVE POTENTIAL OF LUTEOLIN AGAINST GROWTH AND METASTASIS OF BREAST CANCER

Breast cancer is the second leading cause of cancer-related death in older women. Many postmenopausal women undergo hormone replacement therapy (HRT) to alleviate the symptoms of menopause. Recent studies implicate the progestin component of HRT as being most likely responsible for elevated breast cancer risk and increased mortality.

Using animal models and cell culture we explored the preventive and therapeutic potential of luteolin (LU), a naturally-occurring compound found commonly in fruits and vegetables, and examined its ability to both prevent the onset of breast cancer, and inhibit its growth and metastasis. LU effectively blocked progestin (P)-induced intratumoral vascularization in our animal models when given preventatively or therapeutically. LU blocked P-stimulated effects in cultured human breast cancer cells, including inhibiting the enrichment of a subpopulation of human breast cancer cells that are believed to be responsible for tumor initiation. Such cells are difficult to treat by conventional methods.

Progestins not only elevate the risk of breast cancer in postmenopausal women but have also been implicated in making tumor cells metastatic, increasing their ability to spread from the breast to distant sites around the body. With this in mind we utilized a hormone-independent model of lung metastasis, since most hormone-dependent cancer cells ultimately become hormone-resistant and lose therapeutic markers. LU significantly reduced the formation of lung colonies arising from these human breast cancer cells, with little or no animal toxicity. Overall, these studies provide compelling evidence that LU possesses chemopreventive, therapeutic, and anti-metastatic properties which might be harnessed to combat breast cancer.