773 Hormones and Cancer II Poster Session, Thursday, 6/22, Board 164 #198

Hermaphrodiol May Contribute Significantly to the Estrogenic/Androgenic Hormonal Milieu of Breast and Prostrate Cancer Cells. Rachel S Rosenberg Zand,[1] Eleftherios P Diamandis,[1] Frank Z Stanczyk,[2] [1]*Laboratory Medicine and Pathobiology, University of Toronto, Toronto, ON, Canada;* [2]*Obstetrics and Gynecology, University of Southern California, Los Angeles, CA*

There has been considerable interest in an unusual C_{19} steroid, namely, 5-androstene-3β, 17β-diol (Δ^5-diol), because of its possible involvement in the etiology and/or progression of breast cancer. This compound is unusual because it has an androgenic chemical structure, but possesses both androgenic and estrogenic activities; hence, Δ^5-diol is sometimes referred to as hermaphrodiol. In vitro studies show that Δ^5-diol stimulates tumor growth in MCF-7 human breast cancer cells. Also, we have previously shown a positive association between serum Δ^5-diol levels and breast cancer risk in postmenopausal women. Normal postmenopausal women have serum levels of Δ^5-diol that are at least 10 times higher than those of E_2 and estrone (E_1). Thus, Δ^5-diol may provide a constant estrogenic stimulus which, in postmenopausal women, would be unopposed by progesterone and may contribute to the risk of breast cancer. Although the dual estrogenic and androgenic activities of Δ^5-diol are well recognized, the strength of these activities relative to those of the potent hormones E_2 and dihydrotestosterone (DHT), respectively, has not yet been clearly established. To this end, we evaluated the estrogenic activity of Δ^5-diol through production of the estrogen-regulated pS2 protein and its androgenic activity via production of androgen-regulated prostate-specific antigen (PSA) in human breast and prostate cancer cells, respectively. Δ^5-Diol was added to BT-474 human breast cancer cells and PC3(AR)2 human prostate cancer cells containing transfected androgen receptors, at final concentrations of 1 x 10^{-5} to 1 x 10^{-10}M, and incubated for 7 days. E_2 and DHT at 1 x 10^{-7}M served as positive controls. The supernatants were harvested and analyzed for pS2 and PSA by use of our previously developed and validated ELISA-type competitive fluorometric immunoassay and ultrasensitive time-resolved immunofluorometric assay methods, respectively. The results are shown below:

			Δ^5-diol				E	DHT
	1 x 10^{-5}M	1 x 10^{-6}M	1 x 10^{-7}M	1 x 10^{-8}M	1 x 10^{-9}M	1 x 10^{-10}M	1 x 10^{-7}M	1 x 10^{-7}M
pS2(ng/ml)	1200	1600	1300	800	100	0	1000	
PSA (pg/ml)	600	550	900	1100	650	180		1000

We conclude that Δ^5-diol (1) has high estrogenic activity, similar to that of E_2, in BT-474 human breast cancer cells and substantial androgenic activity in prostate cancer cells; (2) may contribute significantly to the estrogenic/androgenic hormonal milieu of breast and prostate cancer cells; (3) should be included together with E_2 and E_1 in studies investigating the role of estrogens in the etiology of breast cancer.