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"DT56a (Femarelle®); Contrary to Estradiol-17β; is Effective in Human Derived Female Osteoblasts in Hyperglycemic Condition"

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Abstract

We have reported previously, that female-derived cultured osteoblasts (hObs) responded to DT56a (Femarelle®) measured by the stimulation of creatine kinase specific activity (CK), which is a marker for hormone responsiveness and (3)[H] thymidine incorporation into DNA (DNA synthesis). Since the skeletal protective effects of estrogens are not discernable in hyperglycemic diabetic women, we sought to analyze the effect of estrogenic compounds on CK and DNA synthesis in hObs when grown in high glucose concentration (HG). Cells were grown either in normal glucose (NG) (4.5g/L; 22mM) or HG (9.0g/L; 44mM) for 7 days. HG increased constitutive CK but, the response of CK activity and DNA synthesis to estradiol-17β (E_2) treatment was reduced. In contrary, DT56a was found to be active (as measured by CK activity and DNA synthesis) in both NG and HG. HG decreases the hormonal responsiveness and might block important effects of estrogenic compounds, most likely contributing to their decreased skeletal preserving properties in hyperglycemic women. In hObs from post-menopausal women grown in HG, ERs mRNA expressions were unchanged. On the other hand, in hObs from pre-menopausal women HG increased ERs mRNA expressions. Since DT56a unlike E_2 is active in HG environment as well as in normal glucose, it may be an effective bone restoring agent in diabetic post-menopausal women.