

Effect of transforming growth factor- β 1, insulin-like growth factor-I and insulin-like growth factor-II on cell growth and oestrogen metabolism in human breast cancer cell lines

ABSTRACT

Oestrogens play an important role in the development of breast cancer. Oestrone sulphate (E1S) acts as a huge reservoir of oestrogens in the breast and is converted to oestrone (E1) by oestrone sulphatase (E1STS). E1 is then reversibly converted to the potent oestrogen, oestradiol (E2) by oestradiol-17 β hydroxysteroid dehydrogenase (E2DH). The aim of this study was to assess the effects of transforming growth factor- β 1 (TGF β 1), insulin-like growth factor-I (IGF-I) and insulin-like growth factor-II (IGF-II) on cell growth, E1STS and E2DH activities in the MCF-7 and MDA-MB-231 human breast cancer cell lines. TGF β 1, IGF-I and IGF-II alone or in combination inhibited cell growth of both cell lines but no additive or synergistic effects were observed. The treatments significantly stimulated E1STS activity in the MCF-7 cell line, except for TGF β 1 alone and TGF β 1 and IGF-I in combination, where no effects were seen. Only TGF β 1 and IGF-II acted synergistically to stimulate E1STS activity in the MCF-7 cells. There was no significant effect on E1STS activity in the MDA-MB-231 cells with any of the treatments. In the MCF-7 cells, TGF β 1 and IGF-I, IGF-I and IGF-II, and TGF β 1, IGF-I and IGF-II acted synergistically to stimulate the reductive E2DH activity, while only TGF β 1, IGF-I and IGF-II synergistically stimulated the oxidative E2DH activity. There were no additive or synergistic effects on both oxidative and reductive E2DH activities in the MDA-MB-231 cells. In conclusion, TGF β 1, IGF-I and IGF-II may have effects on oestrogen metabolism, especially in the MCF-7 cell line where they stimulated the conversion of E1S to E1 and E1 to E2 and, thus, may have roles to play in the development of breast cancer.

Keyword: Transforming growth factor- β 1; Insulin-like growth factor; Oestrogen metabolism; Estrogen metabolism; Breast cancer