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The role of ectopic human chorionic gonadotropin beta subunit in inducing epithelial mesenchymal transition in human keratinocytes and its possible pathways

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Background: The process of epithelial-mesenchymal transition (EMT) involves the trans-differentiation of epithelial cells to mesenchymal cells associated with high plasticity. It usually occurs when the cells acquire migratory and invasive characteristics due to the weakening or the loss of cell-cell adhesion. Human chorionic gonadotropin (hCG), a pregnancy hormone, consists of a common α subunit which is shared by three other hormones, thyroid stimulating hormone, luteinizing hormone and follicular stimulating hormone; and an unique β subunit (hCG β). Previous studies have demonstrated that hCG β was expressed by some epithelial origin cancers (1, 2, 3) and therefore it has been postulated as a possible epithelial cancer biomarker. Other studies have linked the presence hCG β to the aggressive and invasive behavior of certain cancers and their poor prognosis (3, 4).

Methods: This study was set out to investigate whether hCG β plays a role in inducing the EMT and to elucidate the possible pathways. Human keratinocytes (HK) were exposed to spent media collected from hCG β producing cancer cells (ScaBER cells) for 48 hours before the cells were either fixed for immunostaining or cells were lysed and protein extracts were collected for western blotting analysis. The expression of epithelial and mesenchymal markers was evaluated by both fluorescent immunocytochemistry and western blotting techniques.

Results: A trend of up-regulation of mesenchymal markers (Vimentin and β -catenin) and down regulation of epithelial marker (E-cadherin) in these treated HK cells was observed. There was 50% increase in cell number which was positively stained by anti-Vimentin antibody whilst 16% of the cells have lost E-cadherin expression (100% to 84%) following 48 hours' exposure to the hCG β containing media. These findings were in consistence with the results from HK cells that were exposed to recombinant hCG β (r-hCG β). It was also observed that the changes in the expressions of these markers were reduced when a combination of three anti-hCG β antibodies targeting different hCG β epitopes was added to the spent media. These results were confirmed by western blotting analysis.

Conclusion: The findings suggest that ectopic hCG β produced by cancer cells might be involved in EMT associated with the migratory and aggressive behavior of such cancers. Furthermore, the up-regulation of β -catenin also suggests its possible role in the Wnt pathway which offers an insight into EMT process at a molecular level. This could be valuable point in developing future novel anti hCG β therapies for such types of cancers.

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