OSTEOPONTIN SPLICING ISOFORMS EXPRESSION IS MODULATED BY EPITHELIAL MESENCHYMAL TRANSITION INDUCED BY TGF-β IN OVARIAN CARCINOMA CELLS

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Introduction: In ovarian carcinoma (OC), invasive cell properties are supported by a process named epithelial mesenchymal transition (EMT). We showed that OPNc, one of the glycosphosphoprotein osteopontin splicing isoforms (OPN-SI), activates OC progression. However , the involvement of these OPN-SI in EMT in OC has not been addressed. Objectives: We aimed to evaluate the expression of OPN-SI in OC cells induced to EMT by TGF-β. Material and Methods: ES2 and A2780 OC cell lines were treated with 10ng/ml of TGF-β in order to induce EMT. The expression of OPN-SI and EMT epithelial (E) (Claudin-3, Claudin-4 and E-cadherin) and mesenchymal (M) (slug, vimentin and N-cadherin) markers were tested by quantitative real time PCR. Results: In both cell lines, OPNa is overexpressed in relation to OPNb and OPNc. Upon treatment with TGF-β, in A2780 cells we observed an upregulation of OPNc. Conversely, OPNa and OPNb are downregulated. In ES2 cells, TGF-β also induced OPNc upregulation, but OPNb expression is activated as well, while OPNa expression is inhibited. To validate EMT induction by TGF-β , we tested the expression of E and M markers. In A2780 cells, TGF-β induce the downregulation of E-cadherin, but Claudin-3 and Claudin-4 are upregulated. In ES2 cells, Claudin-3 expression is downregulated in this condition. After TGF-β treatment, in A2780 cells all M markers are downregulated, while in ES2 cells, only N-cadherin expression has been inhibited. Conclusions: Our data indicate that the expression of OPN-SI is modulated by TGF-β-induced EMT and that mostly the oncogenic OPNc is upregulated in this condition. Our results evidence that TGF-β induce a partial EMT phenotype, which is cell-type specific. In summary, our data suggest that the expression of OPN-SI is modulated by a partial EMT induced by TGF-β and that isoforms could contribute to this key step on tumor progression in OC cells.

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