Title:
EXPRESSION PATTERN OF SR AND HNRNP SPLICING FACTORS IN OVARIAN CARCINOMA CELLS AND PUTATIVE CORRELATION TO OSTEOPONTIN-C EXPRESSION LEVEL

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Introduction: It is well known that many genes implicated in ovarian carcinoma (OC) progression undergo alternative splicing events to produce isoforms with pro-cancer properties. Among them, osteopontin (OPN) primary transcript suffers alternative splicing generating OPNa, OPNb and OPNc isoforms. We have shown that OPNc activates OC tumor progression. There is now increasing evidence that the expression of splicing factors (SFs) SRs (SFRS1, SFRS3, SFRS4, SFRS5 and SFRS6) and hnRNPs (hnRNP A1, hnRNP B1, hnRNP A2/B1, hnRNP C2 and PTB) can modulate splicing control and the generation of oncogenic isoforms. Objectives: We aimed to compare the expression profile of main SFs between ovarian tumor and non-tumoral cells and then try to correlate this pattern to OPNc expression level. Material and Methods: We used tumoral (TOV, SKOV and OVCAR-3) and a non-tumoral cell line (IOSE 364) to evaluate the expression levels of SR and hnRNPs factors by using quantitative real time PCR. OVCAR-3 cells overexpressing OPNc and a corresponding cell sample in which this isoform has been silenced by using an anti-OPNc specific oligomer have also been analyzed. Results: Most SFs tested are downregulated in TOV and SKOV cell lines when compared to IOSE 364, except hnRNPK factor, which is highly upregulated in both OC tumor cell lines. Conversely, OPNc overexpression in OVCAR-3 cell line evokes an upregulation of all tested SFs. Conclusions: Our data evidence that SR and HnPNP factors have a general downregulated expression pattern when compared to a non-tumoral cell line. It also indicated that OPNc overexpression in OC cancer cells can induce an upregulation of most SR and hnRNPs SFs, probably disturbing molecular mechanisms that can favour aberrante splicing of OC cancer cells.

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