

Unraveling the role of RNA Binding Protein with Multiple Splicing (RBPMS) in Ovarian Cancer Cells

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To date the most effective treatment for patients with ovarian cancer has been a combination of surgery and platinum-based chemotherapy. It has been effective in the reduction of incidence and deaths. Unfortunately, ovarian cancer remains one of the most aggressive and malignant gynecological cancers. Therefore, it is imperative to understand and identify molecules that could be related to platinum resistance/sensitivity-related mechanisms. Previous research for our laboratory suggest that MicroRNAs (miRNAs) such as miR-21 (both miR-21-5p and miR-21-3p) are overexpressed in most cancers and it has been implicated in ovarian cancer initiation, progression, and cisplatin resistance. Luciferase assays identify three direct target genes of miR-21-3p: *RBPMS*, *Enolase-1*, *RCBTB1* and *ZNF608*. Fu, *et al.* 2015 recently implicated RBPMS in the inhibition of the proliferation and migration of breast cancer cells. They observed that RBPMS block the formation of c-Jun-c-Fos or c-Jun-Smad3 complexes.

RNA-binding protein with multiple splicing (RBPMS) belongs to a family of RNA-binding proteins characterized by the presence of an N-terminal RNA-recognition motif (RRM) sequence RBPMS is member of a family of proteins which bind to the nascent RNA transcripts and regulate their processing, including the pre-mRNA splicing and transport, localization, and stability of the RNA molecules. Alternative splicing results in multiple transcript variants encoding different RBPMS isoforms. RBPMSA, RBPMSB, and RBPMSC are the best described isoforms in the literature; and previous studies suggest that RBPMS is a critical repressor of AP-1 signaling. These transcription factor activator protein-1 as multiple roles in cellular behavior, including cancer cell growth, migration, invasion, and metastasis. Molecules in this pathway can be proposed as a strategy for cancer treatment.

Until now, little is known about the biological function of RBPMS proteins in ovarian cancer and less is known about which isoform is related with cisplatin resistance. Based in our performing data and previous report we **hypothesized** that the decreased expression of RBPMS protein levels in high-grade serous ovarian cancer cells is associated with the increase of ovarian cancer progression and platinum-based drug resistance on *in vitro* cell growth and *in vivo* tumors. The

objective of this doctoral dissertation is to unravel the role of RBPMS in ovarian cancer cells and identify which isoform is involved in platinum-based drug resistance.