MDA-9/Syntenin-NF-κB-RKIP loop in triple negative breast cancers (TNBC) and human liver carcinoma

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We analyzed the presence of a regulation loop like that between MDA-9/Syntenin - NF-κB - RKIP in three TNBC cell lines (SUM 149, SUM 159 and MDA-MB-231) and in three cell lines of human liver carcinoma (HA22T/VGH, Hep3B and HepG2). Both these cancers are characterized by high aggressive phenotype, poor prognosis and few therapeutic possibilities.

Transient transfection was performed with siRNA anti-MDA-9/Syntenin. Expression of different factors was evaluated by Real time-PCR and Western blotting, while NF-κB activation by TransAM assay. Invasion capacity was analyzed by Matrigel Invasion Assay.

We observed that silencing of MDA-9/Syntenin expression by anti-MDA-9/Syntenin siRNA induced NF-κB downregulation and contemporary restored expression of an important metastasis suppressor like RKIP in all cancer models; interestingly, RKIP increase in liver cancer models occured only at mRNA levels. Lastly, in our cell models MDA-9/Syntenin downregulation caused a reduction of invasion ability.

Our data confirmed the key role of MDA-9/Syntenin in cancer biology and for the first time showed that is part of a regulation loop among NF-κB and RKIP in TNBC and in liver cancer cell lines. This loop could constitute a new potential pharmacological target and provide new therapeutic approaches.