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ISAC-1-1 Effect of Indirect Nonequilibrium Atmospheric Pressure Plasma on Anti-proliferative Activity against Chronic Chemo-resistant Ovarian Cancer Cells in vitro and in vivo

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[Objective] Nonequilibrium atmospheric pressure plasma (NEAPP) therapy has recently been focused on as a novel medical practice. Using cells with acquired resistance, we elucidated effects of indirect NEAPP-activated medium (NEAPP-AM) exposure on cell viability and tumor growth in vitro and in vivo.[Methods] Using chronic paclitaxel/cisplatin-resistant ovarian cancer cells, we applied indirect NEAPP-exposed medium to cells and xenografted tumors in a mouse model. Furthermore, we examined the role of reactive oxygen species (ROS) and mechanisms of NEAPP-AM therapy in the above -mentioned EOC cells.[Results] We assessed the viability of NOS2 and NOS3 cells exposed to NEAPP-AM, which was prepared beforehand by irradiation with NEAPP. In NOS2 cells, viability decreased by approximately 30% after NEAPP-AM 120-sec treatment (p < 0.01). The growth-inhibitory effects of NEAPP-AM were completely inhibited by N-acetyl cysteine treatment, while L-buthionine-[S, R]-sulfoximine, used with NEAPP-AM, decreased cell viability after NEAPP-AM treatment (p < 0.05). In the murine xenografted model, NEAPP-AM injection resulted in an average inhibition of the NOS2 cell -inoculated tumor by 66% (p < 0.05) and NOS2TR cell-inoculated tumor by 52% (p < 0.05) as compared with the control. [Conclusion] We demonstrated that NEAPP-AM also had an anti-tumor effect on chemo-resistant cells in vitro and in vivo.

ISAC-1-2 The role of GEP oncogenes, G12 and G13, in the progression of ovarian cancer

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[Objective] The GEP oncogenes, members of the Gl2 family of heterotrimeric G proteins (Gl2 and Gl3), are involved in the progression of human cancers including breast and prostate. This study is focused on evaluating the role of GEP oncogenes in human ovarian cancer (OVCA) progression.[Methods] The expression of GEP oncogene in human OVCA tissues and cells was examined by immunostaining, WB and real-time PCR. LPA-induced migration and activation of Akt, ERK and p 38 were evaluated by migration assay and WB, respectively. LPA-induced RhoA activation in OVCA cells was examined by pull-down assay. shRNAs and siRNAs were used to knock down the expression of GEP oncogene. The current study was approved by our institutional review board.[Results] Expression levels of G12 and G13 in human OVCA tissues were elevated compared to those in normal ovarian tissues. LPA, which binds to LPA receptors (LPARs) coupling with Gl2 and G13, induced cell migration of OVCA and activation of Akt, ERK, p38 and RhoA in OVCA cells. The migration induced by LPA was inhibited by knock-down of both G12 and G13. Knock down of G12 and G13 attenuated the activation of Akt, ERK and RhoA induced by LPA in OVCA cells.[Conclusion] Increased expression of GEP oncogenes, G12 and G13, can result in enhanced signaling downstream of LPARs, thereby influencing cell migration of OVCA.

ISAC-1-3 Role of SWI/SNF complex in Clear Cell Carcinoma of the ovary (CCC)

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[Objective] To study the expression of SWI/SNF subunits in CCC and their relation to CCC clinical &pathological features. [Methods] Specimens from 46 ovarian CCC cases were collected from ovarian cancer patients treated in our hospital in the period from 1995–2010. They were examined for SWI/SNF subunits by immunohistochemistry after an informed consent from all patients. The studied subunits include : ARID1A, ARID1B, BRG1, BRM, BAF170, BAF155, PBRM1, BCL11A and SNF5. Also, HNF1 β was stained as CCC marker and Ki67 as proliferation index. This study was approved by the Institutional Review Board.[Results] Expression of the tested subunits was lost in 63% (29/46). ARID1A was unstained in 45.7% representing the major subunit which is lost followed by BRM (19.6%) and BRG1 (10.9%). 55.2% of the 29 cases without complex expression showed loss of one subunit only, while the remaining showed loss of 2 subunits or more. Ki67 index was higher in loss of SWI/SNF subunits (p<0.0001). Complex loss has significantly less Overall and Progression free survival rates (p<0.05).[Conclusion] SWI/SNF complex is a major prognostic factor in CCC, which may be a good candidate for developing targeted therapy.