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of PX on tumor cells. By flow cytometry we confirmed that PX increased apoptosis (control:6.1±0.7%, PX:16.7±1.4%; p<0.05) in MDA-MB231 cells which was significantly reduced by NIC treatment (10.3±1.6%; p<0.05). In conclusion, the activation of nAChRs increases breast cell proliferation and could be responsible either of tumorigenesis or malignization; it should be considered that NIC reduces PX effectiveness in tumor treatment probably due to an increment in the resistance to chemotherapy.

452. (127) **INHIBITION OF HO-1 ENZYMATIC ACTIVITY IMPAIRS HEAD AND NECK CANCER CELL SURVIVAL**

Mascaró M[1], Alonso EG[1], Schweitzer K[1], Fernandez Chavez L[1], Ferronato MJ[1], Ibarra A[1], Coló GP[1], Giorgi G[2], Curino AC[1], Facchinetti MM[1]

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We have previously reported that, in human HNSCC samples, hemeoxygenase-1 (HO-1) mRNA expression is up-regulated and it is associated with worst survival. We also reported an up-regulation of HO-1 protein levels and that it is localized in the cytoplasmic and nuclear compartments. Moreover, we demonstrated that pharmacological activation of HO-1 by hemin and genetic full-length HO-1 (FL-HO-1) overexpression increases HN13 cells survival and cell cycle progression, suggesting a protumor role of HO-1 in HNSCC. However, whether byproducts of HO-1 enzymatic activity are involved in FL-HO-1 mediated-effects remains unknown. In this study, we aimed to elucidate if inhibition of HO-1 enzymatic activity impacts on head and neck cancer cells behavior. To that end, HO-1 activity was inhibited pharmacologically using ZnPP and an enzymatically inactive FL-H25A-HO1-overexpressing HN13 cell line was established. We evaluated HO-1 expression by western blot and indirect immunofluorescence, cell viability by crystal violet, cell proliferation by manual cell counting, cell cycle progression by propidium iodide staining and flow cytometry, and cell migration by wound healing assay. We found that 10 μM ZnPP impaired cell viability (p<0,001 vs DMSO) at 48h and 72h as well as it diminished cell number at 72h (p<0,01 vs DMSO). Also, in such conditions, ZnPP induces overexpression of HO-1, which is localized in the cytoplasm. In line with the previously mentioned, we found that FL-H25A-HO1 HN13 cells have a lower growth rate (p<0,001) than FL-HO1 HN13 cells. We also found that the population of FL-H25A-HO1 HN13 cells have an increase in Go/G1 phase (p<0,01) and a decrease in G2/M phase (p<0,05) compared with FL-HO1 HN13 cells. Related to cell migration, FL-H25A-HO1 failed to alter migratory capacity (p>0,05 vs FL-HO1). In conclusion, our results show that the enzymatic activity of HO-1 plays a role in the FL-HO-1-mediated effects on head and neck cancer cell survival.

453. (130) **ROLE OF RACOTUMOMAB IMMUNOTHERAPY AND N-GLYCOLYLNEURAMINIC ACID (NEUGC)-RICH DIET IN CYTIDINE MONOPHOSPHO-N-ACETYLNEURAMINIC ACID HYDROXILASE (CMAH) KNOCKOUT HUMANIZED MICE BEARING LUNG CANCER TUMORS**

Valeria Inés Segatori[1], Carla Sabrina Capobianco[1], Cynthia Antonella Gulino[1], Ignacio Demarco[2], Gabriel Fernández Graña[3], Geraldine Schlapp[3], Mariano Rolando Gabri[1], Martina Crispo[3], Daniel Fernando Alonso[1]

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NeuGc is a sialic acid molecule found in animal cell membranes as terminal components of glycoproteins and glycolipids. In most mammals including mice and apes, NeuGc synthesis is catalyzed by CMAH. However, humans lack such enzyme due to gene inactivation, being NeuGc obtained from dietary sources. Although healthy human tissues contain negligible levels, tumor cells are able to incorporate large amounts of NeuGc. Aggressive human neoplasms such as non-small cell lung cancer (NSCLC) can express NeuGc-containing gangliosides as cell surface neoantigens. The anti-NeuGc anti-idiotype monoclonal antibody racotumomab is approved for switch maintenance immunotherapy in patients with advanced NSCLC. We used CMAH knockout (CMAH-/-) mice to study the antitumor activity of racotumomab in the context of a humanized model and to further analyze the role of NeuGc-rich diet. CMAH-/- female mice were inoculated i.v. with 3LL Lewis lung carcinoma cells (10^5 cells/mouse) and surface lung nodules were counted 25 days later. Therapeutic immunization with weekly s.c. doses of racotumomab at 200 µg/dose formulated in aluminum hydroxide (racotumomab-alum) exhibited a significant antitumor activity against lung tumor nodules (Control: 14 ± 7 versus Racotumomab-alum: 6.5 ± 2.5, median lung nodules per mouse ± interquartile range; p<0.01, Mann-Whitney test) in CMAH-/- mice fed ad libitum with a NeuGc-rich diet, containing beef fat and cattle meat bone powder. On the contrary, no significant antitumor effects of racotumomab-alum immunization were observed in animals receiving a standard rodent chow with low NeuGc content. The present data suggest the importance of dietary intake of NeuGc-rich foods in the effectiveness of racotumomab immunotherapy using a humanized mouse model of NSCLC.

454. (132) **HEMEOXYGENASE-1 PLAYS A PROTUMORAL ROLE IN THYROID CANCER**

Alonso EG[1], Pichel P[2], Mascaró M[1], Schweitzer K[1], Fernandez Chavez L[1], Coló GP[1], Recio S[2], Rosemblit C[3], Facchinetti MM[1], Curino AC[1].

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3.- Instituto de Investigaciones Biomédicas (BIOMED), (CONICET), Facultad de Ciencias Médicas (UCA).

We have previously demonstrated that hemeoxygenase-1 (HO-1) mRNA is overexpressed in papillary (PTC) and anaplastic (ATC) thyroid tumor compared to non-malignant areas to the tumor (NMT). We also demonstrated that HO-1 protein levels are up-regulated in human PTC samples, showing cytoplasmic localization, and such HO-1 tumor expression correlates with histological subtype. Now, we aim to study the role of HO-1 in thyroid cancer (TC) biology. To that end, we evaluated HO-1 expression by indirect immunofluorescence, cell viability by crystal violet method, cell cycle progression by propidium iodide staining and flow cytometry, and cell migration by wound healing assay. We found that pharmacological activation of HO-1 using 80µM hemin increased cell viability in TPC-1 (p<0.001) and 8505c (p<0.001) cell lines at 72h. In TPC-1, we found that hemin increased cell number in S- (p<0,05) and G2/M (p<0,001) phases and diminished cell number in Go/G1 phase (p<0,001) at 48h. In 8505c, hemin increased cell number in S- (p<0,001) phase and diminished cell number in Go/G1 (p<0,01) and G2/M (p<0,001) phases at 48h. In Nthy-Ori-3-1, a normal thyroid cell line, we found that 80µM hemin decreased (p<0.001) cell viability at 72h. Also, we found that 80µM hemin increased cell migration (p<0.001) in TPC-1 and 8505c cell lines. On the contrary, inhibition of HO-1 activity using 16µM ZnPP decreased cell viability in TPC-1 (p<0.001) and 8505c (p<0.001) cell lines at 72h while no differences were observed in Nthy-Ori-3-1 cells. In TPC-1, ZnPP diminished cell number in Go/G1 phase (p<0,01) and increased cell number in G2/M (p<0,05) at 48h. However, in 8505c, cell cycle progression remained unaltered after ZnPP treatment. Also, 16µM ZnPP reduced TPC-1 cell migration (p<0.001), but in 8505c ZnPP failed to alter migratory capacity. In conclusion, our results demonstrate that HO-1 plays a protumoral role in TC cells by altering cell survival, cell cycle progression and cell migration.

455. (133) **ORAL TONGUE SQUAMOUS CELL CARCINOMAS CAN BE DIFFERENTIATED BY TWO PATHWAY- SPECIFIC**