manner. The changes in the cell morphology, viability and protein expressions such as p53 and ERK were examined after the exposure of hyperoxia (90% O_2). In addition, to investigate whether hyperoxia condition affects the production of ROS and cell cycle regulation, cells were analyzed by a flow cytometry.

Results: Exposure to the hyperoxia caused morphologic changes such as atypical nuclei and numerous mitotic figures which inhibited the cell viability in a time-dependent manner in A549 ($p < 0.01$). In addition, the colony formation was suppressed selectively in A549 exposed to hyperoxia. Although not statistically significant, A549 exposed to hyperoxia showed increases in the ROS levels compared with Beas-2b. Also, the hyperoxia condition caused a progression delay in the G2/M cell cycle significantly in A549 ($p < 0.01$). In hyperoxia exposed A549 cells, the phosphorylation of ERK 1/2 (p-ERK 1/2) was reduced while the phosphorylation of p53 was increased.

Conclusion: This study showed that hyperoxia may have anti-cancer effect by decreasing cell viability and the colony forming ability. ROS generation by hyperoxia may cause to suppress the p-ERK, it related with the activation of p53 and G2/M cell cycle arrest. In conclusion, our data suggests that the anti-cancer effect of hyperoxia may relate to the ROS through oxidative stress mediated ERK signaling and cell arrest.

Keywords: hyperoxia, oxidative stress, lung cancer

P3.01-042
Lung Cancer Cells Can Stimulate Functional and Genotypic Modifications in Normal Bronchial Epithelial Cells

Topic: Functional Biology in Lung Cancer

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Background: Normal lung epithelium cells may act in concert with tumor cells, given that bystander effects may exist between the two. This interaction may lead to inappropriate activation of pro-oncogenic signaling pathways, which may result in high mutational load and tumor heterogeneity. The aim of this project is to evaluate the effects of non-small cell lung cancer (NSCLC) cells on an immortalized normal bronchial epithelial cell line.

Methods: A normal bronchial epithelial cell line (HBEC4) was exposed to A549 (adenocarcinoma), H460 (large cell carcinoma) and SK-MES-1 (squamous cell carcinoma) NSCLC cell lines in a trans-well co-culture system. Cellular characteristics were examined using a Cytell Cell Imaging System (cell number, viability, apoptosis, cell cycle). The gene expression profile was also determined in terms of inflammatory mediators, stem cell markers (RT-PCR) and miRNA profiling (Nanostring). The proliferative effect of NSCLC cancer exosomes was also examined (BrdU ELISA) on the HBEC4 cell line.

Results: A number of functional and gene modifications were observed in the HBEC4 cell line after seven days of co-culture. While patterns were similar amongst all NSCLC subtypes, SK-MES-1 elicited the most significant effects in terms of cell number, viability, cell cycle progression and proliferative potential of isolated cancer exosome fraction. Promotion of both inflammatory mediators and stem cell marker expression was evident at the mRNA level. There was no apparent consensus between NSCLC subtypes and miRNA expression, as exposure to each cell line resulted in distinct profiles of miRNAs in HBEC4 cells. Bioinformatic analysis of miRNA target genes, demonstrated that pathways such as p53, MAPK, VEGF, TLR and Wnt were amongst those altered.

Conclusion: Cancer cells may promote significant genotypic and phenotypic alterations within the normal lung epithelium though multiple mechanisms. These modifications may, in part, contribute to the heterogeneity of lung cancer tumors and influence response to both chemotherapeutics and targeted agents.

Keywords: HBEC, non-small cell lung cancer, miRNA, inflammation

P3.01-043
Inhibition of Ornithine Decarboxylase Facilitates Pegylated Arginase Treatment in Lung Adenocarcinoma Xenograft Models

Topic: Functional Biology in Lung Cancer

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