

## Effect of CeONP co-treatment in tobacco exposed lung stroma cells

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Cerium oxide nanoparticles (nanoceria; CeO<sub>2</sub>NP) have been proposed as a new promising agent in the treatment of oxidant induced diseases, including cancer, due to its known and well demonstrated antioxidant properties. However, our previous data indicate that CeO<sub>2</sub>NP were unable to protect cells from the carcinogenic effects of tobacco smoke condensate after long-term exposure in lung BEAS-2B cells. In fact, results rather support a synergistic role of CeO<sub>2</sub>NP in the tobacco-induced tumor secretome.

Since lung stroma cells would better reflect the tumor secretome than epithelial cells, in this work we aim to assess the effects of tobacco smoke condensate and CeO<sub>2</sub>NP co-treatment in lung MRC5 fibroblasts. Thus, MRC5 cells long-term exposed to 5 µM of tobacco smoke condensate alone or in combination with 5 and 7.5 µM CeO<sub>2</sub>NP for 5 weeks were monitored for changes in the fibroblast differentiation program and signals of fibroblasts trans-differentiation. Also, we analyzed the influence of MRC5 secretome from the different treatments over the anchorage independent cell growth capacity of previously exposed BEAS-2B lung epithelial cell line.

Results evidence no protective role of CeO<sub>2</sub>NP in MRC5 cells exposed to tobacco smoke condensates. The crosstalk between lung MRC5 stroma cells and BEAS-2B epithelial cells via secretome demonstrated that CeO<sub>2</sub>NP co-exposure exacerbate the effects of tobacco exposure.