



# *In Vivo* and *In Vitro* Anti-tumor Effect of a Unique Nutrient Mixture on Lung Cancer Cell Line A-549

M.Waheed Roomi, Vadim Ivanov, Tatiana Kalinovsky, Aleksandra Niedzwiecki, and Matthias Rath

*Experimental Lung Research*, 2006, 32:1-13.

## **Introduction:**

The high incidence of lung cancer and ineffective toxic action of current mono and doublet chemotherapy approaches result in poor patient survival. Enzymes called matrix metalloproteinases (MMPs), which degrade the extracellular matrix are implicated in neoplastic invasion and metastasis. A nutrient mixture (NM) containing lysine, proline, arginine, ascorbic acid, and green tea extract has shown significant antitumor effects, including inhibition of MMPs and invasion. Based on this, we investigated the effect of NM on human lung carcinoma cell A-549 cells *in vitro* and *in vivo*.

## **Methods:**

We investigated the effect of NM on the tumor growth of human lung carcinoma cell A-549 xenografts in athymic nude mice. Additionally, we tested the *in vitro* antitumor effect of NM on lung carcinoma A-549 cells by measuring: cell proliferation by MTT assay, MMP-2 and -9 secretion by gelatinase zymography and cell invasion through Matrigel.

## **Results:**

Nutrient supplementation strongly suppressed the growth of tumors without adverse effects in nude mice; tumor weight was reduced by 44% ( $p=0.0001$ ) and tumor burden was reduced by 47% ( $p<0.0001$ ) with supplementation. Zymography demonstrated *in vitro* secretion of MMP-2 by uninduced human lung carcinoma cells and both MMP-2 and -9 by PMA (200 ng/ml)- treated cells. NM inhibited the secretion of both MMPs in a dose-dependent fashion with virtual total inhibition at 500  $\mu\text{g/ml}$  concentration. The invasion of human lung carcinoma cells through Matrigel was significantly reduced at 100  $\mu\text{g/ml}$  (64%) and totally inhibited at 500- $\mu\text{g/ml}$  concentration of NM ( $p=0.01$ ).

## **Conclusion:**

Suppression of lung tumor growth in nude mice and inhibition of MMP secretion and Matrigel invasion suggest NM as a potential non-toxic therapeutic agent for lung cancer.