

**Molecular mechanisms for cigarette smoke tar phase-induced cell death**

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Cigarette smoke is divided in tar phase containing nicotine and gas phase. The gas phase of cigarette smoke is prepared by passing cigarette smoke through Cambridge filter. The tar phase is extracted from Cambridge filter by 2-propanol. We have previously elucidated that the gas phase induce cell death by intracellular  $\text{Ca}^{2+}$ - and protein kinase C (PKC)-dependent manner, and identified acrolein and methyl vinyl ketone as the major cytotoxic compounds in the gas phase (Mai et al., 2012; Noya et al., 2013; Higashi et al., 2014). In this study, we examined molecular mechanism (s) for cigarette smoke tar phase-induced cell death in lung cancer cells. Lung adenocarcinoma, small cell carcinoma, and non-small cell carcinoma cell lines are all sensitive to cigarette smoke tar phase. Tar phase-induced cell death is intracellular  $\text{Ca}^{2+}$ - and PKC-independent, whereas intracellular  $\text{Ca}^{2+}$  chelator and PKC inhibitor effectively suppressed gas phase-induced cell death. These results indicate that the molecular mechanisms for cell death induction by cigarette tar phase is different from that of cigarette smoke gas phase.