We have previously reported that activation of K$^+\text{--}\text{Cl}^-\text{--}cotransport (KCC) by N-ethylmaleimide (NEM) induces apoptosis through generation of reactive oxygen species (ROS) in HepG2 human hepatoblastoma cells. In this study we investigated the possible role of phospholipase A$_2$ (PLA$_2$)–arachidonic acid (AA) signals in the mechanism of the NEM actions. In these experiments we used arachidonyl trifluoromethylketone (AACOCF$_3$), bromoenol lactone (BEL) and p-bromophenacyl bromide (PBp) as inhibitors of the calcium-dependent cytosolic PLA$_2$ (cPLA$_2$), the calcium-independent PLA$_2$ (iPLA$_2$) and the secretory PLA$_2$ (sPLA$_2$), respectively. BEL significantly inhibited the NEM–induced KCC activation, ROS production and apoptosis, whereas AACOCF$_3$ and PBp did not.

NEM increased AA liberation in a dose–dependent manner, which was markedly prevented only by BEL. The NEM–induced actions (KCC activation, ROS generation and apoptosis) were not significantly altered by treatment with indomethacin and nordihydroguaiaretic acid (NDGA), selective inhibitors of cyclooxygenase (COX) and lipooxygenase (LOX), respectively. Treatment with AA or 5, 8, 11, 14-eicosatetraynoic acid (ETYA), a non-metabolizable analogue of AA, markedly activated the KCC. produced ROS and induced apoptosis. Collectively, these results suggest that AA liberated through activation of iPLA$_2$ may mediate the NEM–induced ROS generation, KCC activation, and apoptosis induction in HepG2 cells.

Matrix metalloproteinases (MMPs) play an important role in tumor invasion and metastasis by matrix degradation. To analyze the effect of 2-amino-3-ethoxycarbonyl-1-methyl pyrrolo (3,2-b) naphtho-4,9-dione on tumor invasion in human fibrosarcoma cells by downregulating matrix metalloproteinase-2 and 9

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High-Throughput Screening for Novel Inhibitors of Protein-Tyrosine Phosphatase-1B

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Protein–tyrosine phosphatases (PTPs) constitute a family of receptor–like and cytoplasmic enzymes, which catalyze the dephosphorylation of phosphotyrosine residues in a variety of receptors and