Preclinical breast cancer biology

ARACHIDONIC ACID INDUCES MMP-9 SECRETION IN NON-TUMORIGENIC MCF10A CELLS THROUGH A LIPOXYGENASE AND SRC DEPENDENT PATHWAY

R.A. Martinez-Orozco¹, J.E. Perez-Salazar²
¹Unidad Académica de Ciencias Químicas, Universidad Autonoma de Zacatecas, Zacatecas, MEXICO, ²Biología Celular, CINVESTAV IPN, Mexico DF, MEXICO

Arachidonic acid and its metabolites, collectively known as eicosanoids, are key mediators of a wide variety of physiological and pathophysiological states. The eicosanoids are a large family of bioactive compounds produced by arachidonic acid oxygenation through cyclooxygenase, lipoxygenase and cytochrome P-450 pathways. An increasing number of investigations support their significant role in cancer biology, although the precise molecular mechanisms that link levels of arachidonic acid and its metabolites with cancer progression remains unclear. In a previous study where the non-tumorigenic MCF10A cells were used as models, it has been reported that arachidonic acid could modulate some cancer-related genes, including matrix metalloproteinase-9. We examined in this cell line whether MMP-9 secretion induced by arachidonic acid was metabolite and Src kinase activity dependent. We demonstrate that treatment of MCF10A cells with arachidonic acid induces MMP-9 secretion in a dose-dependent manner. Moreover, treatment with LOX inhibitor NDGA or Src inhibitor PP2 abolishes this secretion. Our findings suggest that arachidonic acid could promote MMP-9 secretion in human breast epithelial cells via metabolites produced by the lipoxygenase pathway and also in a Src kinase dependent fashion.

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