
Colquhoun A. 

Source
Department of Cell and Developmental Biology, Biomedical Sciences Institute, University of São Paulo, São Paulo, Brazil.

Abstract

PURPOSE:

Eicosapentaenoic acid has been tested in bladder cancer as a synergistic cytotoxic agent in the form of meglumine-eicosapentaenoic acid, although its mechanism of action is poorly understood in this cancer. The current study analyzed the mechanisms by which eicosapentaenoic acid alters T24/83 human bladder cancer metabolism in vitro.

MATERIALS AND METHODS:

T24/83 human bladder cancer cells were exposed to eicosapentaenoic acid for 6 to 24 hours in vitro and incorporation profiles were determined. Effects on membrane phospholipid incorporation, energy metabolism, mitochondrial activity, cell proliferation and apoptosis were analyzed. Reactive oxygen species and lipid peroxide production were also determined.

RESULTS:

Eicosapentaenoic acid was readily incorporated into membrane phospholipids with a considerable amount present in mitochondrial cardiolipin. Energy metabolism was significantly altered by eicosapentaenoic acid, accompanied by decreased mitochondrial membrane potential, and increased lipid peroxide and reactive oxygen species generation.
species generation. Subsequently caspase-3 activation and apoptosis were detected in eicosapentaenoic acid exposed cells, leading to decreased cell numbers.

CONCLUSIONS:

These findings confirm that eicosapentaenoic acid is a potent cytotoxic agent in bladder cancer cells and provide important insight into the mechanisms by which eicosapentaenoic acid causes these changes. The changes in membrane composition that can occur with eicosapentaenoic acid likely contribute to the enhanced drug cytotoxicity reported previously in meglumine-eicosapentaenoic acid/epirubicin/mitomycin studies. Dietary manipulation of the cardiolipin fatty acid composition may provide an additional method for stimulating cell death in bladder cancer. In vivo studies using intravesical and dietary manipulation of fatty acid metabolism in bladder cancer merit further attention.

PMID:19237174