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Localization of superoxide radical- generating Nox1 in lipid rafts is associated with cellular transformation and apoptosis

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Our study presents Nox1 expression in lipid rafts in untreated epithelial cells with different degree of transformation and elucidates how β-MCD- and Edelfosine (ALP) treatment may alter the expression of Nox1 in the cell lines with increased malignancies (human colon carcinoma cell line HT29, fibroblast-like FIB and epithelium-like EPI human gingival keratinocytes).

Here we give evidence that Nox1 is abundant in lipid rafts of HT29, while Nox1 expression decreases gradually from intermediated transformed FIB cells to non – transformed EPI cells.

β-MCD treatment of the same cell lines cause a distribution of Nox1 out of lipid rafts, which may be associated with ligand independent apoptosis that would correlate with EGFR and Fas displacement out of lipid rafts while β-MCD treatment.

We furthered our investigations by measuring apoptosis level after β-MCD treatment in HT29 to elucidate whether Nox1 distrubition is due to ligand-independent apoptosis or it is because of a functional inhibition of EGF-Nox 1 signalling pathway caused by dysregulated cholesterol metabolism. Also an immunoprecipitation experiment for Nox1 and Fas interaction may provide novel information about cellular function of Nox1 during apoptosis.

In our study we compared β-MCD effect on epithelial cells with Edelfosine (alkyl-lysophospholipids) induced ligand-dependent apoptosis. We demonstrated that Edelfosine

treatment caused an increase of Nox1 in lipid rafts of epithelial cells, and this is correlated with Fas displacement into the lipid rafts (shown by other studies).

Taken together we provide unique information about the antithetic regulation of Nox1 during cell proliferation and apoptosis in epithelial cells. Taken into account the central role of reactive oxygen species generated from NADPH oxidase isoforms for activation of EGFR and involvement of EGFR and related receptors in carcinogenesis, our study may shed new lights on the pathogenesis of tumor growth of cancer cells and may provide further rationale to the use of cholesterol modulating compounds and alkyl-lysophospholipids in cancer therapy.