Dietary Fat Composition and Intake Affects DMBA Metabolism and DNA Adduct Formation in Breast Organoids.

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Intake of specific lipids such as saturated fats have been shown to have an impact on human health. We have earlier reported a diet rich in a specific lipid rapidly alters the composition of cellular membranes. Many of the metabolic enzymes responsible for the metabolic activation and detoxification of carcinogens are membrane-bound. Since these enzymes (e.g., the CYP superfamily) actually require the lipid membrane for activity, we hypothesized that altering the lipid composition by feeding animals singular sources of lipids might affect carcinogen metabolism and, hence, DNA binding, a critical step in cancer initiation.

Taconic rats were fed high fat diets (n=4) where the fat source was from fish (menhaden) (HFF), safflower (HFS), butter (HFB), Olive oil (HFO) or chow (CHOW). Rats were on the diet for 30 days then sacrificed and their breast organoids were isolated and cultured as described earlier. On Day 3, a set of three dishes per rat dosed were dosed with either DMSO (vehicle), 100 nM BaP or 100 nM DMBA. The next day (24 hrs later), medium was removed and frozen along with controls spiked with DMSO, BaP and DMBA. This fraction was analyzed by HPLC to determine the fraction of DMBA that remained as parent compound. Organoids were collagenased, washed, and frozen dry at -80 C for postlabelling.analysis DNA was isolated from the cell in the cultures and the DMBA DNA adduct levels determined by ^{32}P-postlabelling.

Animals on the HFO diet metabolized significantly more DMBA and animals on the HFO diet metabolized significantly less DMBA than did animals fed chow or HFB. More important than total metabolism is the fraction of metabolism that allows the carcinogen to bind to the critical target: DNA. We found that DMBA-treated breast organoids from animals fed the HFF diet had the lowest level of DMBA DNA than any other treatment, significantly lower in pairwise comparison to the HFS group ($p=0.0346$) which had the highest level of DMBA adducts. These data suggest that specific dietary lipids can affect the metabolism and DNA binding of a model carcinogen