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Preclinical breast cancer biology

63P FATTY ACID COMPOSITION OF TISSUE CULTURED BREAST CARCINOMA: EFFECT OF STEAROYL-COA DESATURASE-1 (SCD-1) INHIBITOR

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Introduction: Stearoyl-CoA desaturase 1 (SCD1) has been introduced as a novel therapeutic target in malignancies, including breast cancer. The present study was designed to investigate the effect of pharmacologic inhibition of SCD1 on fatty acid profile in tissue explant culture of human breast cancer, and also to compare these effects with those in adjacent non-neoplastic breast tissue.

Methods: Paired samples of tumor and adjacent non-cancerous tissue were isolated from twelve patients with infiltrating ductal breast cancer, explant cultured in vitro, exposed to a highly selective SCD1 inhibitor CAY10566, and investigated with respect to fatty acid composition by gas liquid chromatography (GLC). Anti-proliferative and cytotoxic effects were evaluated by quantification of lactate dehydrogenase (LDH) release and by sulforhodamine B (SRB) measurement.

Results: In the breast cancer tissue, levels of monounsaturated fatty acids (MUFA, $P < 0.001$) and arachidonic acid (20:4n-6; $P < 0.001$) were higher, and the level of linoleic acid (18:2n-6; $P = 0.02$) was lower than that in the normal-appearing breast. While exhibiting no evident cytotoxicity, treatment with SCD1 inhibitor (0.1-1 μM) for 48 hours significantly increased linoleic acid (18:2n-6) in both tumor and adjacent normal tissue (≃1.2 fold, $P < 0.05$). However, the levels of MUFA and 20:4n-6, and the ratio of oleic acid (18:1n-9) to stearic acid (18:0) showed larger fold changes in the breast cancer than in normal-appearing breast ($P = 0.02$). SCD1 inhibitor also repressed growth/proliferation (≃50%, $P = 0.001$) and elevated SFA (1.4-fold, $P = 0.001$) level only in the tumor tissue explant.

Conclusion: There were differences in the fatty acid composition and response to SCD1 inhibition between the explant cultures from breast cancer compared to adjacent non-neoplastic tissue. Altered fatty acid composition induced by SCD1 inhibition may modulate other reactions in de novo fatty acid synthesis, lipogenesis and subsequently overall breast cancer survival and progression.

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