A-13 Modulation of breast cancer cell growth by long chain fatty acids

S M D Nalinie Wickramasinghe[1], R W Hardy[2]
([1]*Div. of Biochemistry, Faculty of Medical Sciences, Univ. of Sri Jayewardenepura, Nugegoda,* [2]*Dept. of Pathology, Univ. of Alabama, Birmingham, USA*)

Epidemiological and animal studies have linked excessive dietary fat to the development of breast cancer. However, little is known about the biochemical processes responsible for this effect.

In order to understand how dietary fat modulates the signal transduction mechanisms involved in breast cancer cell growth, the effects of long chain saturated fatty acids (LCSFA) most commonly found in the diet, on epidermal growth factor (EGF)-induced cell growth in the breast cancer cell line Hs578T, were investigated. Cell growth was determined using ^{3}H thymidine incorporation and cell counts. It was found that LCSFA inhibited cell growth in a chain length dependent manner. Treatment (0.15_{m} M, 6h) with stearate (C:18) completely inhibited the EGF-induced cell growth while treatment with palmitate (C:16) inhibited by 68% and myristate had no effect. A pertussis toxin sensitive, 41 kDa, G-protein specifically coimmuno-precipitates with the EGF-Receptor (EGFR) in this cell line, Time course studies indicated that the maximum ADP-ribosylation of the EGFR-associated G-protein occurs at 1 min of stimulation with EGF. Treatment of cells with stearate inhibited the EGF-induced, EGFR-associated, G-protein ADP-ribosylation. In contrast to LCSFA, treatment with oleate increased both basal and EGF-induced cell growth. Also in contrast to stearate, oleate increased the ADP-ribosylation of the EGFR-associated G-protein in both basal and EGF-induced states.

Thus the differential effects of long chain fatty acids on breast cancer cell growth are likely mediated *via* EGFR-associated G-proteins.

Conclusions: (1) Long chain saturated fatty acids inhibit EGF-induced cell growth in a chain length dependent manner. Stearate (C : 18) completely inhibits, while palmitate (C : 16) inhibits by 68% and myristate (C : 14) has no effect. (2) The long chain unsaturated fatty acid oleate (C 18:1) stimulated the EGF-induced cell growth by 125%. (3) EGFR-associated G-Protein ADP-ribosylation is inhibited by stearate and stimulated by oleate. (4) Long chain fatty acids modulate cell growth in Hs578T breast cancer cells possibly *via* a mechanism involving EGFR-associated G-proteins.